IJCD

JDA Indian Journal of Clinical Dermatology

Volume 2 | Issue 2 | October 2019

₹ 800 - Jaipur
Four Monthly

HIGHLIGHTS

- Hypersensitivity Reactions to Metal Implants: Clinical, Diagnostic and Treatment Overview
- The Spectrum of Genodermatoses in Early Neonates of Western Rajasthan
- A Rare Case of Angioma Serpiginosum

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Volume 02 | Issue 01 | August 2019

Printed and Published by Dr. Dinesh Mathur on behalf of Jaipur Dermatology Association and
Printed at Popular Printers, Fateh Tiba Marg, Moti Doongri Road, Jaipur (Raj.)
Published From : Indian Journal of Clinical Dermatology, D-712, Park Avenue Road, Malviya Nagar, Jaipur (Raj.)
Editor : Dr. Dinesh Mathur

*Available online at : **www.e-ijcd.in**

ISSN (Online): 2582-7612
ISSN (Print): 2581-7604

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INDIAN JOURNAL OF CLINICAL DERMATOLOGY
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FROM THE DESK OF EDITOR

Greetings from IJCD!!

It makes me immensely proud to share with you that with the support of our authors and reviewers we have indexed our journal in INDEX COPERNICUS. Since you know that index Copernicus is recognized by MCI and thus now articles published in this journal would also be recognized. This is an important step in our journey and I thank my team, our authors and reviewers. This would give more people a chance to publish their work and get recognized. I hope you like the articles in this issue. Happy reading!!

Dr. Dinesh Mathur
Editor

REVIEW
Year: 2019 • Volume: 2 • Issue: 2 • Page: 29-34

HYPERSENSITIVITY REACTIONS TO METAL IMPLANTS: CLINICAL, DIAGNOSTIC AND TREATMENT OVERVIEW

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Abstract

Metal allergy is common in the general population. Cutaneous reactions are elicitated by daily life articles such as watch bands, jewellery etc. In contrast little is known regarding metal sensitization following insertion of implants. Implants are commonly used in orthopaedic, gynaecological, dental and endovascular surgeries. With increasing life expectancy, the number of these surgeries has drastically increased. Nickel, cobalt and chromium have been most commonly implicated in the causation of hypersensitivity following metal implants. Clinical manifestation include peri implant eczema, effusion, swelling etc. Although diagnostic tests such as patch testing, histology, radiology and lymphocyte transformation are available, the diagnosis still remains a challenge. The review provides a brief overview of the pathophysiology, clinical features, diagnostic tests and management in a scenario of suspected metal allergy.

Key Words - Metal implant allerg, Cutaneous allergic reaction, Peri implant eczema, Hypersensitivity reaction to metals, Implant failure.

Introduction

Metal implants are widely being used in today's medical practice. These find uses in osteosynthesis materials, endoprosthesis, cardiac stents, cardiac replacements, nose, ear, gynaecological surgeries, dentistry etc. As the ageing population is increasing, so is the incidence of these implant surgeries. Contact allergy to nickel, cobalt and chromium is frequent in the general population . Its incidence has been reported to be as high as 14% in case of nickel and 1-2% with cobalt and chromium . The exposure to these metals occurs by the cutaneous route (exposure to daily life article such as wrist band, jewellery, leather articles etc). The implanted metal devices also form an important cause of metal allergy in today's world. On one hand ample amount of literature is present pertaining to cutaneous contact sensitization to metals, little is known regarding the contact sensitization that follows metal implant insertion. The metal alloys employed in these implants also include these metals as their constituents. The first report of metal sensitivity in an orthopaedic implant was reported in 1966 by Foussereau and Laugier . These metals not only constitute a major part of orthopaedic implants, but are also used in endovascular devices, pacemakers, dental surgery, ear, nose, throat devices and gynaecology practice. Wide variety of manifestation occur due to implant allergy, including eczematous reactions, delayed fracture healing, implant loosening, persistent pain effusion, endovascular restenosis etc. Thus it is important that other differential diagnosis should be ruled out before arriving at the diagnosis of implant allergy. In a report by Australian arthoplasty registry in 2012, "metal sensitivity" was reported to be the cause of implant failure in 0.9% cases following shoulder endoprosthesis and 5.7% cases following hip arthoplasty . Metal hypersensitivity is difficult to diagnose and its prevalence is thus underreported.

Materials

Usually cobalt-chromium- molybdenum (CoCrMo) and titanium alloys are used in endoprosthesis devices. Stainless steel and titanium alloys are used in osteosynthesis devices. Oxidized Zirconium is a newer metal used primarily in knee prosthesis. The bone cements used are acrylate based. Dental implants are primarily composed of mercury amalgam, gold alloys, chromium based alloy, stainless steel, palladium, titanium and cobalt alloys . Metals alloys used in endovascular surgery in the form of endovascular stents, patent foramen ovale occluders, aortic aneurysm endografts etc use metal alloys such as stainless steel and nitinol. Titanium is commonly implicated in pacemaker induced dermatitis as it is an constituent of pacemaker .

CoCrMo alloys

These alloys are commonly used in shoulder, hip and knee arthoplasty. The composition includes 64% cobalt, 28% chromium, 6% molybdenum and 0.5% nickel .

Stainless steel

This is commonly used in multifilamentary wires, Kirschner wire, intramedullary nails, osteosynthetic plates and screws. It consists of mainly iron along with 18% chromium, 15% nickel and 3% molybdenum

Titanium alloys

Titanium is mainly used in dental and spine surgeries. It consists mainly of titanium along with traces of aluminium, vanadium

and niobium. Table 1 enumerates the metal alloys used in various implants.

First generation metal on metal hip bearings used in 1960s and 1970s were associated with high rate of metal sensitization(28-46%) . Use of these prosthesis was associated with increased levels of cobalt, nickel and chromium in the body fluids . These were followed by metal on plastic implants in the 1970s and 1990s. These prosthesis were less likely to induce allergic sensitization as the large polyethylene wear particles did not form the allergenic polymer protein complexes . Later on second generation metal on metal bearings came to be used. These prosthesis had high fracture toughness, lower wear rate, and better postoperative stability .

Table 1: Enumerates the metal alloys used in various implants

	Metal Alloy	Uses
1.	Stainless Steel SAE 316 L	Cardiac devices, orthopaedic prosthesis, pins, plates, nails, screws, fixators, surgical clips
2.	Cobalt–chromium–molybdenum steel	Dental implants, orthopaedic prosthesis, pins, plates, nails, screws, fixators, surgical clips
3.	Vitallium	Orthopaedic prosthesis, plates, nails, screws, fixators
4.	Titanium alloy	Orthopaedic prosthesis, pacemakers, surgical clips
5.	Titanium–tantalum –niobium	Orthopaedic devices
6.	Nitinol	Intravascular devices, septal defect devices and implants, contraceptive device, urological implant
7.	Oxinium	Orthopaedic joint prosthesis

Bone cement

It consists of two reacting components, liquid component constituted by methyl methacrylate and powder component constituted by polymethylmethacrylate. Other additives present includes dibenzoyl peroxide, N, N dimethyl –p- touludine and 2-(4-(dimethylamino-phenyl) ethanol. Other constituents are X ray contrast agents, colorants, and antibiotics (gentamycin).

Mechanism of hypersensitivity

Following implant surgery metal ions increase in the circulation. Hypersensitivity response is mounted against these released particles in the circulation. This increase is attributed to corrosion, wear and tear. Osteoclastic activity over the implant also cause release of metal ions into the circulation and subsequent implant loosening. The released metal ions elicit a local inflammatory process. Increased metal levels have also been demonstrated in periprosthetic tissue as well as liver, spleen, lymph nodes, serum and urine. The released metal particles (haptens) complex with proteins to form complexes which in turn stimulate the circulating lymphocytes. The haptens induce a type I, II, III type of immune response following exposure, but most importantly they induce a type IV hypersensitivity response following stimulation of CD4+ Th 1 lymphocytes. Stimulation of Th 1 lymphocytes, causes release of pro inflammatory cytokines such as IL-1, IL2, TNF alpha, TNF gamma. These cytokines in turn recruit macrophages to the site of implant. A study by Vermes et al concluded that that metal hypersensitivity was related to the duration of metal exposure, with number increasing from 12 to 18% from 6 to 36 months after surgery .

Another proposed mechanism for implant loosening involves haptogenic stimulation of toll like receptors in periprosthetic tissue. Studies have shown nickel to stimulate TLR 4 in the periprostetic tissue .

Clinical manifestation

The clinical manifestation of implant allergy varies from skin lesions to impaired wound healing. Recurrent pain, loosening and reduced range of motion have been documented following knee arthoplasty . Other causes of implant failure such as infection etc must be excluded before making a diagnosis of implant allergy. In a study comparing 200 symptomatic patients who had undergone arthoplasty to 100 symptom free patients, it was found that the group with complications had a higher rate of metal sensitization. The common complications included reduced range of motion, recurrent effusion and aseptic loosening . In a study by Krecisz et al 14 patients were followed up with symptoms of suspected implant allergy such as skin lesions and sterile fistula formation. Eight of these 14 patients had reported cutaneous lesions within a year of surgery, among these three were found to be symptom free following revision surgery.

Most common skin manifestation is eczema seen following osteosynthetic implants, containing nickel, cobalt and chromium . These present as itchy, eczematous lesions in the vicinity of the implant. Other clinical manifestations include erysipelas like erythema, urticaria , swelling and vasculitis like lesion. Metal sensitivity has also been shown to cause symptoms of chronic fatigue syndrome, fibromyalgia,etc . Fistulas, eczema and local redness has been reported following bone cement allergy . Allergic reaction to bone cement have been reported in 24.8% in a series of 239 patients . Bircher et al reported complications in five patients following knee and shoulder replacement, who where eventually found to be allergic to benzyl peroxide. Complaints noted among these patients were pain, swelling, pruritus. Metal particles remaining following use of saw/drilling instruments have been shown to cause local allergy related complications. Figure 1 (a and b)demonstrates eczematous lesions over lower limb, buttocks and back in a patient 6 months following total hip replacement surgery. Diagnostic criteria proposed for metal induced allergic dermatitis are listed in Table 2.

Table 2: Proposed diagnostic criteria for metal allergy

1.	Chronic eczema beginning weeks or month after implant
2.	Eczema severe around the implant site
3.	Absence of other contact allergen or systemic cause
4.	Patch test positive or strongly positive for one of the metals in the alloy
5.	Complete recovery after total removal of foreign metal implant

A broken drill tip causing dermatitis, redness and swelling in the overlying skin in close proximity to the tibia have been reported in a nickel allergic patient . In a report by Maldonado-Naranjo et al patient developed erythema, itching, macroglossia and pain

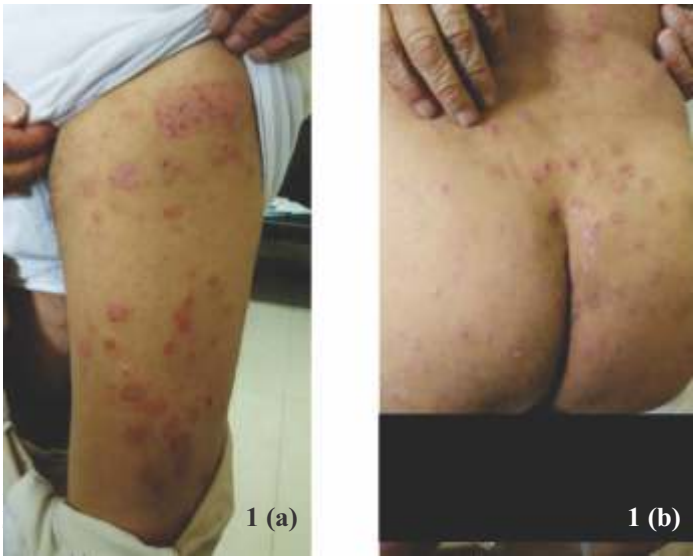

Figure 1: Itchy eczematous lesions over lower limb, buttocks and back in patient undergone total hip replacement (6 months post surgery)

due to polyetheretherketone following spinal surgery.

Diagnostic workup

The clinician can be faced with two scenarios . A patient with known metal allergy may approach prior to an planned implant surgery or a patient can present post surgery with suspected implant allergy. The clinician should first exclude other causes for the skin eruption before making a diagnosis of metal allergy. In a review by Schalock and Thyssen , they stated that pre surgery testing should only be considered in patients with definitive metal allergy. The role of patch test as a prophetic testing has not been encouraged . The proposed reason for the same could be " de novo" sensitization from the metal following continuous corrosion. Prophetic testing in these cases would lead to negative results. Carlsson and Moller followed 18 patients with confirmed pre surgery metal allergy for a mean of 6.3 years. None of these patients developed systemic or cutaneous reactions. The role of allergy testing in patients with failed implants is limited.

Patch test

Patch test is the gold standard test for delayed hypersensivity reactions, however its role in cases of suspected implant allergy is not clear. Many studies have concluded that patch test does not establish a causal role cutaneous allergic reaction and implant failure . Patch test with 2+/3+ readings are considered more consistent with complications compared to the milder reactions. The unreliability of the patch testing method is further highlighted by the observation that patients with previous metal hypersensitivity become desensitized following implant surgery. Rooker and Wilkinson demonstrated that among six patients who tested positive for metal hypersensitivity via patch testing, five were found to be negative post operatively at 3-19 months . Metal hypersensitivity in patients with failed implants is six times more common compared to general population, and about three times commoner in those with known metal allergy . The diagnosis is arrived by ruling out other causes, positive patch test findings, presence of the metal as a constituent of the implant, disappearance of the lesions on implant removal.

For a suspected case of metal allergy, patch testing with single/ handful of allergens is not recommended, a more comprehensive testing should be performed. Extended series such as extended North American standard series, international comprehensive baseline series are indicated. The patch test battery should include the metals currently being used in orthopaedic implants and should be continuously updated. Prosthesis series have been suggested by many authors .

Radiology

Radiological findings of patients with implant failure include periprosthetic osteolysis and aseptic loosening due to the inflammatory response mounted against the metal particles. Imaging studies also show pseudotumor formation around the prosthesis due to collection of inflammatory cells . None of these findings are however specific for metal hypersensitivity.

Histology

Histology of the peri implant tissue has a adjuvant role in the diagnosis of implant allergy. Four reaction patterns have been described in the histological evaluation of periprosthetic membrane in case of endoprostehetic loosening. Type 1 is foreign body like, type 2 granulocyte dominated infectious type, type 3 is a combination type and type 4 is fibrotic type. Neutrophils number exceeding 23/10 high power field is indicative of infection . The criteria for implant allergy reaction pattern is not yet established. Although histology is included in the diagnostic workup of suspected implant allergy patient, its efficacy is unproven. Lymphocytic infiltrate is seen predominantly in cases of suspected allergy . Histological appearance in cases of suspected metal allergy includes localized areas of necrosis, bleeding and fibrin exudation along with perivascular lymphocytic and plasma cell collection. The evaluation of local cytokine pattern may also add on to the diagnosis of metal allergy. Rarely aseptic lymphocyte dominated vasculitis associated lesions (ALVAL), which represents a delayed hypersensitivity reaction mediated by T lymphocytes have been described . Locally destructive pesudotumors have also been reported specially in females with hip surgeries .

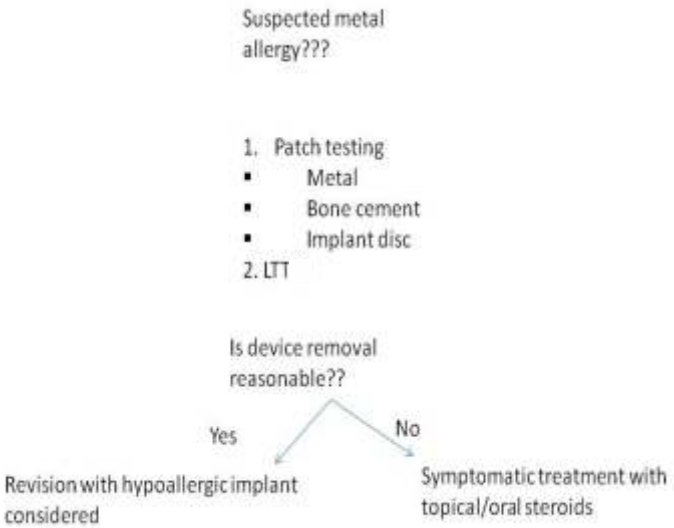

Figure 2: Algoritham for a case of suspected metal allergy

Lymphocyte transformation test

It is an in vitro test that measure the proliferation of lymphocytes from patients blood in presence and absence of antigens. The result is expressed as an stimulation index of proliferation in relation to an antigen vs baseline proliferation. Stimulation index >3 is kept the limit for sensitization in most settings . It is mostly used as a complementary test, when results of the patch test are equivocal. The quality assessment of this test are very rare even for nickel allergy. The specificity and sensitivity of this test are yet to be established by studies in the future. Issues faced by this test include limited availability, pricing and inability to test for certain metals. Currently it is impractical to be used routinely.

Figure 2 outlines the diagnostic algoritham for suspected cases of implant allergy.

Treatment

If a case of implant failure is suspected due to metal allergy (all causes excluded) further contact with the allergen warrants termination. Alternative materials in implant allergic patients includes titanium, oxinium and ceramide based/coated materials. In instances of bone cement allergy, the suspected allergen is omitted when considering revision of the implant. Amini et al stated in a review that currently there are no FDA cleared "hypoallergic implant" .

Dental implants

Metals are extensively used in dentistry in artificial teeth, implants, restorative materials etc. These are exposed to variations in temperature, pH inside the oral cavity. Cases of allergic contact dermatitis following dental prosthesis placement have been reported in the literature. A case of generalised allergic dermatitis in the setting of Nickel Chromium denture was reported in 1966 by Foussereau and Langier. The patient was found to be allergic to Nickel and Chromium on patch testing and the skin lesions settled completely following denture removal .

Most common manifestation of allergic contact dermatitis in the oral cavity is lichen planus like lesions. These are commonly placed near to the dental implant and include reticular, plaque like, atrophic and erosive variants. Lichenoid eruption have been reported most commonly in association with dental amalgam and gold. Other clinical manifestations of metal allergy in the oral cavity include loss of taste, oral swelling and dryness. Other manifestation of oral allergy include erythema of oral mucosa, purpuric patches on palate, labial edema, perioral eczematous eruption, lichenoid eruption and angular chelitis. Swelling of the oral and pharyngeal cavity are some of the manifestations of type 1 hypersensitivity in the oral cavity .

Mercury amalgam are commonly used in dental practice as restorative material. Metal ions release cause allergic reactions in the oral cavity. The use of mercury amalgam has been abandoned largely in the recent years. Mercury amalgam are also implicated in the formation of amalgam tattoos. Amalgam tattoos are the result of small metal particles being implanted in the oral soft tissue. Gold allergy is also a common cause of contact dermatitis in patients undergoing dental restoration procedure. One series have reported its incidence to be as high as 33.8%. Patients having confirmed patch test positivity to gold, have been shown to tolerate gold containing dental restoration. Lower rates of allergic dermatitis have been reported with nickel containing restorative materials .

Cardiac implants

Allergic contact dermatitis have been reported following intravascular placement of implants. Two common types of intravascular stents used are bare metal and drug eluting stents. The metal alloys in the bare metal stents cause expression of intercellular adhesion molecule on the surface of endothelial cells. This stimulates neointimal hyperplasia due to recruitment of inflammatory cells, which leads to intravascular restenosis. Drug eluting intravascular stents are coated with polymer impregnated with drug, which inhibits the intimal hyperplasia and thus have a lower rate of allergic reaction . Nickel, chromate, manganese are among the metals which are frequently implicated in inducing an allergic contact dermatitis.

Initially gold plated stents were used because of higher stability and lesser allergic reactions. However studies have shown a higher risk of contact dermatitis following insertion of gold plated intravascular stents. Three cases of allergic contact dermatitis have been reported following patent foramen ovale occluders. All three patients were patch test positive and improved on device removal. Titanium is the most common metal implicated in allergic reactions following implantable pacemakers. The first case was reported in 1970. The use of polytetrafluroethylene wraps in pacemakers have shown to decrease the incidence of allergic dermatitis .

Gynaecological implants

Metals are used in contraceptive devices in gynaecological practice. Three cases of allergic contact dermatitis have been reported in literature following insertion of copper containing IUCD, which resolved on removal . Copper containing IUCD are contraindicated in patients with copper allergy, while nitinol (alloy of Ni and Ti) is contraindicated in Ni allergic subjects.

Conclusion:

With the recent advancement in medical science and healthcare, the number of implant surgeries has been on a rise. However little is known about the metal allergies that these implants may cause and the possible clinical manifestations. The scenario of implant allergy still remains a challenge to diagnose as well as treat. This review aims at highlighting few important aspects pertaining to metal hypersensivity. A systematic approach is provided for workup of patients with suspected implant allergy. Carefully interpretation of the medical history, clinical examination, patch testing and lymphocyte transformation test(LTT) help to establish the diagnosis of metal sensitization. A collaborative effort by the dermatologist, allergists and the surgeon is necessary for the patient care.

References

How to cite this article:

Ghunawat S, Relhan V, Garg VK. Hypersensitivity reactions to metal implants: clinical, diagnostic and treatment overview. JDA Indian Journal of Clinical Dermatology. 2019;2:29-34.

1. Schafer T, Bohler E, Ruhdorfer S, Weigl L, Wessner D, Filipiak B, et al. Epidemiology of contact allergy in adults. Allergy. 2001;56(12):1192-6.
2. Thyssen JP, Linneberg A, Menne T, Johansen JD. The epidemiology of contact allergy in the general population--prevalence and main findings. Contact dermatitis. 2007;57(5):287-99.
3. Foussereau J, Laugier P. Allergic eczemas from metallic foreign bodies. Transactions of the St John's Hospital Dermatological Society. 1966;52(2):220-5.

4. Graves SE, Rothwell A, Tucker K, Jacobs JJ, Sedrakyan A. A multinational assessment of metal-on-metal bearings in hip replacement. The Journal of bone and joint surgery American volume. 2011;93 Suppl 3:43-7.
5. Hubler WR, Jr., Hubler WR, Sr. Dermatitis from a chromium dental plate. Contact dermatitis. 1983;9(5):377-83.
6. Gawkrodger DJ. Metal sensitivities and orthopaedic implants revisited: the potential for metal allergy with the new metal-on-metal joint prostheses. The British journal of dermatology. 2003;148(6):1089-93.
7. Merritt K, Brown SA. Distribution of cobalt chromium wear and corrosion products and biologic reactions. Clinical orthopaedics and related research. 1996(329 Suppl):S233-43.
8. Tilsley DA, Rotstein H. Sensitivity caused by internal exposure to nickel, chrome and cobalt. Contact dermatitis. 1980;6(3):175-8.
9. Elves MW, Wilson JN, Scales JT, Kemp HB. Incidence of metal sensitivity in patients with total joint replacements. British medical journal. 1975;4(5993):376-8.
10. Benson MK, Goodwin PG, Brostoff J. Metal sensitivity in patients with joint replacement arthroplasties. British medical journal. 1975;4(5993):374-5.
11. Carlsson AS, Magnusson B, Moller H. Metal sensitivity in patients with metal-to-plastic total hip arthroplasties. Acta orthopaedica Scandinavica. 1980;51(1):57-62.
12. Jacobs JJ, Urban RM, Hallab NJ, Skipor AK, Fischer A, Wimmer MA. Metal-on-metal bearing surfaces. The Journal of the American Academy of Orthopaedic Surgeons. 2009;17(2):69-76.
13. Schalock PC, Menne T, Johansen JD, Taylor JS, Maibach HI, Liden C, et al. Hypersensitivity reactions to metallic implants - diagnostic algorithm and suggested patch test series for clinical use. Contact dermatitis. 2012;66(1):4-19.
14. Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. The Journal of bone and joint surgery American volume. 2001;83-a(3):428-36.
15. Vermes C, Kuzsner J, Bardos T, Than P. Prospective analysis of human leukocyte functional tests reveals metal sensitivity in patients with hip implant. Journal of orthopaedic surgery and research. 2013;8:12.
16. Aquino M, Mucci T. Systemic contact dermatitis and allergy to biomedical devices. Current allergy and asthma reports. 2013;13(5):518-27.
17. Thomas P, Thomas M, Summer B, Dietrich K, Zauzig M, Steinhauser E, et al. Impaired wound-healing, local eczema, and chronic inflammation following titanium osteosynthesis in a nickel and cobalt-allergic patient: a case report and review of the literature. The Journal of bone and joint surgery American volume. 2011;93(11):e61.
18. Thomas P, Stauner K, Schraml A, Mahler V, Banke IJ, Gollwitzer H, et al. [Characteristics of 200 patients with suspected implant allergy compared to 100 symptom-free arthroplasty patients]. Der Orthopade. 2013;42(8):607-13.
19. Krecisz B, Kiec-Swierczynska M, Bakowicz-Mitura K. Allergy to metals as a cause of orthopedic implant failure. International journal of occupational medicine and environmental health. 2006;19(3):178-80.
20. Kanerva L, Forstrom L. Allergic nickel and chromate hand dermatitis induced by orthopaedic metal implant. Contact dermatitis. 2001;44(2):103-4.
21. Stejskal V. Metals as a common trigger of inflammation resulting in non-specific symptoms: diagnosis and treatment. The Israel Medical Association journal : IMAJ. 2014;16(12):753-8.
22. Thomas P, Schuh A, Eben R, Thomsen M. [Allergy to bone cement components]. Der Orthopade. 2008;37(2):117-20.
23. Bircher A, Friederich NF, Seelig W, Scherer K. Allergic complications from orthopaedic joint implants: the role of delayed hypersensitivity to benzoyl peroxide in bone cement. Contact dermatitis. 2012;66(1):20-6.
24. Thomas P, Gollwitzer H, Maier S, Rueff F. Osteosynthesis associated contact dermatitis with unusual perpetuation of hyperreactivity in a nickel allergic patient. Contact dermatitis. 2006;54(4):222-5.
25. Maldonado-Naranjo AL, Healy AT, Kalfas IH. Polyetheretherketone (PEEK) intervertebral cage as a cause of chronic systemic allergy: a case report. The spine journal : official journal of the North American Spine Society. 2015;15(7):e1-3.
26. Schnuch A, Aberer W, Agathos M, Becker D, Brasch J, Elsner P, et al. [Performing patch testing with contact allergens]. Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology : JDDG. 2008;6(9):770-5.
27. Carlsson A, Moller H. Implantation of orthopaedic devices in patients with metal allergy. Acta dermato-venereologica. 1989;69(1):62-6.
28. Granchi D, Cenni E, Giunti A, Baldini N. Metal hypersensitivity testing in patients undergoing joint replacement: a systematic review. The Journal of bone and joint surgery British volume. 2012;94(8):1126-34.
29. Rooker GD, Wilkinson JD. Metal sensitivity in patients undergoing hip replacement. A prospective study. The Journal of bone and joint surgery British volume. 1980;62-b(4):502-5.
30. Honari G, Ellis SG, Wilkoff BL, Aronica MA, Svensson LG, Taylor JS. Hypersensitivity reactions associated with endovascular devices. Contact dermatitis. 2008;59(1):7-22.
31. Reed KB, Davis MD, Nakamura K, Hanson L, Richardson DM. Retrospective evaluation of patch testing before or after metal device implantation. Archives of dermatology. 2008;144(8):999-1007.
32. Pandit H, Vlychou M, Whitwell D, Crook D, Luqmani R, Ostlere S, et al. Necrotic granulomatous pseudotumours in bilateral resurfacing hip arthoplasties: evidence for a type IV immune response. Virchows Archiv : an international journal of pathology. 2008;453(5):529-34.
33. Krenn V, Otto M, Morawietz L, Hopf T, Jakobs M, Klauser W, et al. [Histopathologic diagnostics in endoprosthetics: periprosthetic neosynovialitis, hypersensitivity reaction, and arthrofibrosis]. Der Orthopade. 2009;38(6):520-30.
34. Willert HG, Buchhorn GH, Fayyazi A, Flury R, Windler M, Koster G, et al. Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints. A clinical and histomorphological study. The Journal of bone and joint surgery American volume. 2005;87(1):28-36.
35. Galbraith JG, Butler JS, Browne TJ, Mulcahy D, Harty JA. Infection or metal hypersensitivity? The diagnostic challenge of failure in metal-on-metal bearings. Acta orthopaedica Belgica. 2011;77(2):145-51.
36. Thomas P, von der Helm C, Schopf C, Mazoochian F, Frommelt L, Gollwitzer H, et al. Patients with intolerance reactions to total knee replacement: combined assessment of allergy diagnostics, periprosthetic histology, and peri-implant cytokine expression pattern. 2015;2015:910156.
37. Summer B, Paul C, Mazoochian F, Rau C, Thomsen M, Banke I, et al. Nickel (Ni) allergic patients with complications to Ni containing joint replacement show preferential IL-17 type reactivity to Ni. Contact dermatitis. 2010;63(1):15-22.
38. Van Opstal N, Verheyden F. Revision of a tibial baseplate using a customized oxinium component in a case of suspected metal allergy. A case report. Acta orthopaedica Belgica. 2011;77(5):691-5.
39. Haddad FS, Cobb AG, Bentley G, Levell NJ, Dowd PM. Hypersensitivity in aseptic loosening of total hip replacements. The role of constituents of bone cement. The Journal of bone and joint surgery British volume. 1996;78(4):546-9.
40. Amini M, Mayes WH, Tzeng A, Tzeng TH, Saleh KJ, Mihalko WM. Evaluation and management of metal hypersensitivity in total joint arthroplasty: a systematic review. Journal of long-term effects of medical implants. 2014;24(1):25-36.
41. Segura-Egea JJ, Bullon-Fernandez P. Lichenoid reaction associated to amalgam restoration. Medicina oral, patologia oral y cirugia bucal. 2004;9(5):423-4; 1-3.
42. Lygre GB, Gjerdet NR, Gronningsaeter AG, Bjorkman L. Reporting on adverse reactions to dental materials--intraoral observations at a clinical follow-up. Community dentistry and oral epidemiology. 2003;31(3):200-6.
43. Vamnes JS, Lygre GB, Gronningsaeter AG, Gjerdet NR. Four years of clinical experience with an adverse reaction unit for dental biomaterials. Community dentistry and oral epidemiology. 2004;32(2):150-7.
44. Gawkrodger DJ. Investigation of reactions to dental materials. The

British journal of dermatology. 2005;153(3):479-85.

45. Martin JM, Nagore E, Cremades A, Botella-Estrada R, Sanmartin O, Sevila A, et al. An amalgam tattoo on the oral mucosa related to a dental prosthesis. Journal of the European Academy of Dermatology and Venereology : JEADV. 2005;19(1):90-2.

46. Koch P, Bahmer FA. Oral lichenoid lesions, mercury hypersensitivity and combined hypersensitivity to mercury and other metals: histologically-proven reproduction of the reaction by patch testing with metal salts. Contact dermatitis. 1995;33(5):323-8.

47. Vilaplana J, Romaguera C. Contact dermatitis and adverse oral mucous membrane reactions related to the use of dental prostheses. Contact dermatitis. 2000;43(3):183-5.

48. Svedman C, Tillman C, Gustavsson CG, Moller H, Frennby B, Bruze M. Contact allergy to gold in patients with gold-plated intracoronary stents. Contact dermatitis. 2005;52(4):192-6.

49. Ekqvist S, Svedman C, Moller H, Kehler M, Pripp CM, Bjork J, et al. High frequency of contact allergy to gold in patients with endovascular coronary stents. The British journal of dermatology. 2007;157(4):730-8.

50. Fukahara K, Minami K, Reiss N, Fassbender D, Koerfer R. Systemic allergic reaction to the percutaneous patent foramen ovale occluder. The Journal of thoracic and cardiovascular surgery. 2003;125(1):213-4.

51. Dasika UK, Kanter KR, Vincent R. Nickel allergy to the percutaneous patent foramen ovale occluder and subsequent systemic nickel allergy. The Journal of thoracic and cardiovascular surgery. 2003;126(6):2112.

52. Singh HR, Turner DR, Forbes TJ. Nickel allergy and the amplatzer septal occluder. The Journal of invasive cardiology. 2004;16(11):681-2.

53. Raque C, Goldschmidt H. Dermatitis associated with an implanted cardiac pacemaker. Archives of dermatology. 1970;102(6):646-9.

54. Abdallah HI, Balsara RK, O'Riordan AC. Pacemaker contact sensitivity: clinical recognition and management. The Annals of thoracic surgery. 1994;57(4):1017-8.

55. Basko-Plluska JL, Thyssen JP, Schalock PC. Cutaneous and systemic hypersensitivity reactions to metallic implants. Dermatitis : contact, atopic, occupational, drug. 2011;22(2):65-79.

ORIGINAL ARTICLE
Year: 2019 • Volume: 2 • Issue: 2 • Page: 35-38

A CLINICAL STUDY OF THERAPEUTIC EFFICACY AND SAFETY OF ORAL TRANEXAMIC ACID IN MELASMA

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Abstract

Introduction: Melasma is a localized, chronic pigmentary disorder marked by irregular hyperpigmented macules or patches and most commonly occurs in women. It is chronic often-relapsing condition despite several treatments available and that causes negative psychosocial effect in those affected. Current treatments such as hydroquinone, kojic acid and retinoids, among others, demonstrate variable efficacy and side-effect profile. Melasma can often be refractory to treatment. Also, recurrences are common.

Methodology: A prospective open-label study was carried out between September 2018 to August 2019.Trenaxamic acid was given in dosage of 250 mg BD for 3 months. Patients were evaluated at 15 days and thereafter at 1, 2, 3- and 6-months post treatment. Response was assessed at each visit.

Results: 41 patients (31 females, 10 male) of melasma were included. Complete resolution occurred in 29 (70.73%) patients and partial response was seen in 12(29.27%). No adverse events were seen in any patient.

Conclusion: Oral tranexamic acid is a promising modality in the treatment of melasma. It can not only reduce the development of melasma, but also reduce the possibility of recurrence. TXA can be used as stand- alone therapy or as adjuvant to other treatment modalities.

Key Words- Melasma, tranexamic acid.

Introduction

Melasma is a chronic, acquired symmetrical pigmentary disorder characterized by gray brown macule and patches affecting photo-distributed part of the face such as the bridge of the nose, cheek, upper lip, forehead, and mandible. This condition is more common in woman accounting for 90% of cases. Men have been reported to represents only 10% of cases[1]. Melasma is more common in individuals with Fitzpatrick skin types 4-5 than those with fairer skin[2]. The exact pathogenesis of melasma is likely multifactorial. Histopathology studies of melasma showed hyperactive epidermal melanocytes, enlarged, with prominent dendrites and increased synthesis of eumelanin. There is an increased synthesis of melanosomes in melanocytes and increased transfer of melanosomes to keratinocytes. Melasma may be actually the consequence of genetically predisposed hyperactive melanocytes, which can be stimulated by UV light. Various modalities of treatments include sun protection and topical depigment creams containing Azelaic acid, Glycolic acid, Hydroquinone, Hydrocortisone, Mometasone, Kojic acid, Fluocinolone, Tretinoin, Licorice extract, Nicotinamide, and Arbutin, chemical peels, dermabrasion and laser therapies have been utilized in different studies with varying, not so satisfactory outcomes[3,4,5].

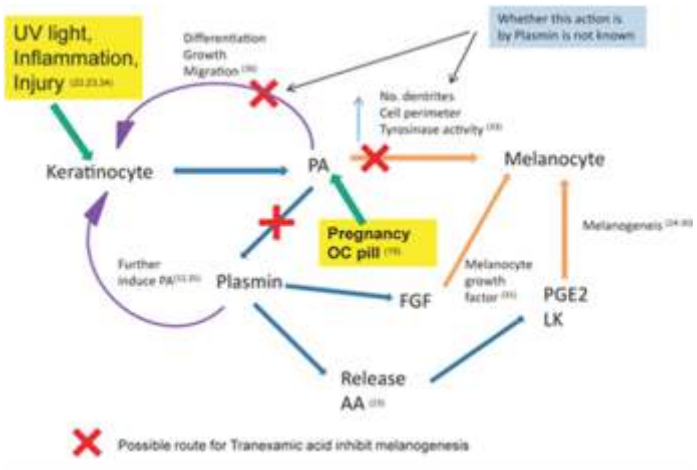
Recently Tranexamic acid (TA) (trans-4-aminomethyl cyclohexane carboxylic acid) has been introduced for the treatment of melasma as a novel concept[5].

Sun exposure of the skin leads to synthesis of plasmin activator, which thereby increases plasmin activity in keratinocytes. This plasmin leads to release of arachidonic acid (AA) via phospholipase A2[6]. Repeated UV damage leads to increased production of mast cell tryptase which weakens and damages the basement membrane, a condition seen in melasma. Contraceptive pills and pregnancy have also shown to increase serum plasminogen activator that can activate the melanogenesis process[7]. TA prevents UV-induced pigmentation by interfering with the plasminogen binding to the keratinocyte[6]. This reduces free AA and thereby reduces prostaglandins in the melanocytes. It also prevents

angiogenesis by blocking the action of plasmin. It also reduces VEGF and endothelin 1 (ET)1; both may be responsible for increased vascularity in melasma[8].

Methodology

A Prospective open-label study was conducted on 41 clinically diagnosed melasma patients. Patients were selected from among those coming to our department during 1 year between September 2018 to August 2019. This study included adult men and women with melasma between age group of 20 and 50 years. Patient with a history of bleeding disorders, use of oral anticoagulant drugs or any other photosensitizing drugs such as nonsteroidal anti-inflammatory drugs, tetracycline,



spironolactone, phenytoin, carbamazepine and other concomitant medical history and use of other depigmenting oral or topical agents in past 1 month were exclusion criteria. Additionally, females with a history of pregnancy/lactation or use of OCP/HRT at the time or during the past 12 months were excluded from the study. Tranexamic acid was given in dosage of 250 mg BD for 3 months. Patients were evaluated at 15 days and thereafter at 1, 2, 3- and 6-months.

Assessment

To assess response, clinical photographs were taken at each visit; Melasma area and severity index (MASI) scores were calculated at the beginning and end of therapy. Subjective response to treatment, according to patient, was graded at the end of the study as follows: no response, no improvement; mild response, <25% improvement; moderate response, 25%-50% improvement; good response, 50%-75% improvement and excellent response, >75% improvement9. Any complications and side effects were also noted during these follow-ups. For another 3 months after treatment, the patients were examined at monthly intervals to look for any relapse and complication.

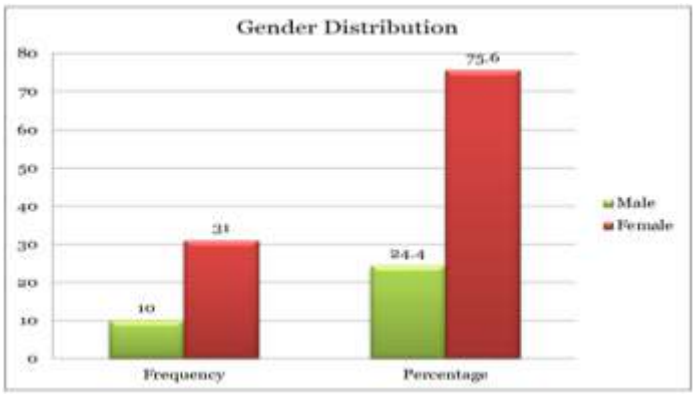
Histopathology was not carried due to apprehension of patients as it involved the face.

Results

Out of 41 patients the number of women was more (31) compared to men (10) as shown in Table- 1 and graph-1.

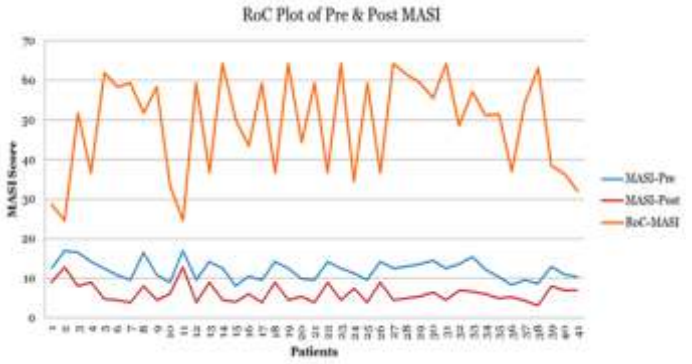
Table 1: Gender Distribution of Patients

Gender	Frequency	Percentage
Male	10	24.4
Female	31	75.6
p-value	**0.000**	



Graph 1: Gender Distribution of Patients

The depicted graph is showing the trend line of the difference of baseline Pre MASI score and Post MASI score at 3 months follow. The difference of baseline Pre MASI score and Post MASI score are showing proportionately equal zig-zag trend. The rate of change is showing sharp upward and downward movements. The possible reason behind the same is the application and outcome of drug is taking place very effectively graph-2.

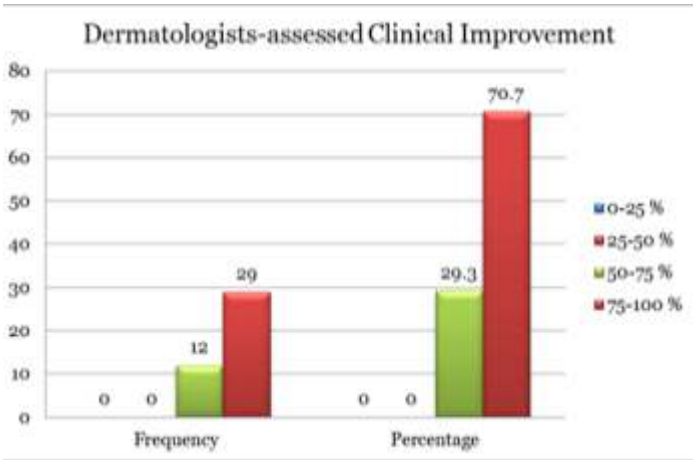


Graph 2: Changes in Pre and Post MASI Scores

A five-point Likert type grading scale was used by another fellow dermatologist to assess the serial photographs. There were29.30% patients who reported 50-75% improvement and 70.7% were reported 75-100% improvement respectively with p value less than 0.05 (P=0.022) which was statistically significant table-2 and graph-3

Table 2: Dermatologists-assessed Clinical Improvement

Response	Frequency	Percentage
0-25 %	0	0
25-50 %	0	0
50-75 %	12	29.3
75-100 %	29	70.7
p-value	**0.022**	



Graph 3: Dermatologists-assessed Clinical Improvement

Among the 41 patients 12.2% patients were very satisfied with the treatment and 87.8% were strongly satisfied. The difference was significant with p value less than 0.05 (P=0.000) table-3 and graph-4.

Table 3: Patients satisfaction

Patients satisfaction	Frequency	Percentage
Strongly Dissatisfied	0	0
Dissatisfied	0	0
Satisfied	0	0
Very Satisfied	5	12.2
Strongly Satisfied	36	87.8
P-value	**0.000**	

Graph 4: Patients satisfaction

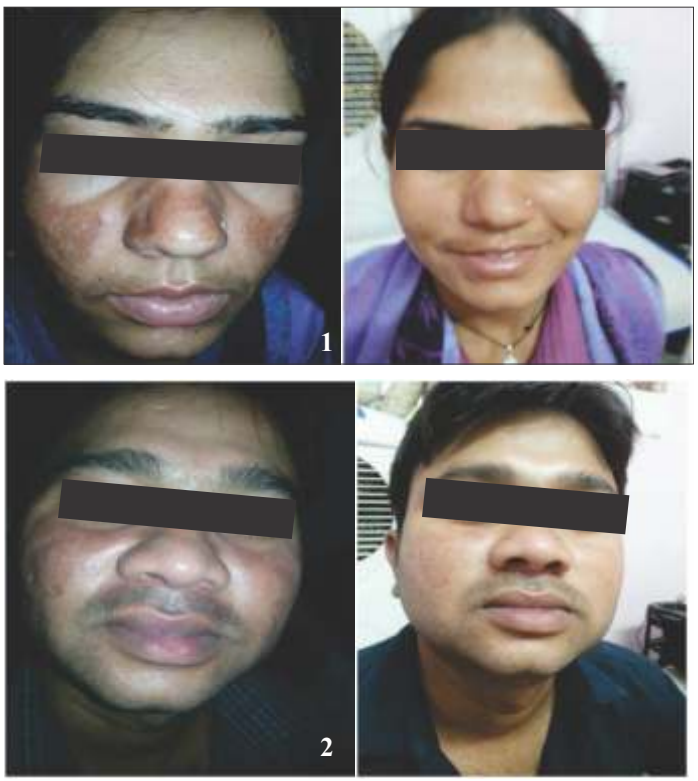


Figure-1 & 2: shows example of clinical improvement in some of patients. (Pre and after 3 month of treatment)

Discussion

Tranexamic acid (trans 4 amino methyl cyclohexane carboxylic acid) is a plasmin inhibitor used to prevent abnormal fibrinolysis to reduce blood loss[10]. Ultraviolet irradiation induces plasminogen activator synthesis and plasmin activity in cultured keratinocytes. Plasmin-activated precursors of secretory phospholipase A2 which participates in the production of arachidonic acid from membrane phospholipids is a precursor to prostaglandins E2 and leukotrienes which can lead to melanogenesis[11]. Plasmin also leads to release of basic fibroblast growth factor which is a potent melanocyte growth factor. Hence, tranexamic acid prevents binding of plasminogen to keratinocyte which results in less arachidonic acid and diminished ability to produce prostaglandins and subsequently reduces melanogenesis in melanocyte[12].

In 1979, Nijor was the first to study and report on the action of tranexamic acid in melasma[13]. In 1985, Hajime et al. showed the forty patients aged 20-60 years had their melasma reduced in severity with 1-1.5 g daily oral tranexamic acid in 10 weeks' time[14]. We noticed similar results with lower doses.

In 2013 Cho et al. performed the first controlled trial by administering 500mg/day TXA as an adjuvant to patients treated with intense pulse light or neodymium-doped yttrium aluminum garnet laser. Six-month treatment led to significant improvement[15]. Comparably we got significant improvement only with TXA.

In 2018, Khurana et al[16]. performed a similar study in India to compare the oral administration of TA and microinjection of TA. The intralesional group received localized microinjections of TA at a dose of 4mg/ml on a monthly basis where the oral group received oral TXA at a dose of 250 mg twice daily. Among 32 patients in oral group 24 patients showed 50-75% improvement and 8 showed >75% improvement. In the intralesional group, out of 32 patients only 14 patients showed 50-75% improvement and 3 showed >75% improvement. They achieved good results with oral TXA as we got in our study.

Conclusion

Oral Tranexamic acid is a promising modality in the treatment of melasma. TXA is possibly the only treatment for melasma that can prevent the activation of melanocyte by sunlight, hormonal influence, and injured keratinocyte (after UV exposure, chemical peeling, laser) through the inhibition of the PA activation system. It can not only reduce the development of melasma, but also reduce the possibility of recurrence. TXA can be used as stand- alone therapy or as adjuvant to other treatment modalities. Due to Sparsity of oral tranexamic acid study in literature, further studies are required.

How to cite this article:

Garg JK, Kothiwala R, Meherda A, Chawla L, Mehra A, Bohra D, Gupta P, Meena P, Anju. A Clinical Study Of Therapeutic Efficacy And Safety Of Oral Tranexamic Acid In Melasma. JDA Indian Journal of Clinical Dermatology. 2019;2:35-38.

References

1. Achar A, Rathi SK. Melasma: A clinico-epidemiological study of 312 cases. Indian J Dermatol 2011; 56:380-2.
2. Sheth VM, Pandya AG. Melasma: A comprehensive update: part 1. J Am Acad Dermatol 2011; 65:689-97.
3. Lee JH, Park JG, Lim SH, Kim JY, Ahn KY, Kim MY, et al. Localized intradermal microinjection of tranexamic acid for treatment of melasma in Asian patients: A preliminary clinical trial. Dermatol Surg 2006; 32:626-31
4. Rendon M, Berneburg M, Arellano I, Picardo M. Treatment of melasma. J Am Acad Dermatol 2006; 54 5 suppl 2:S272-81.

5. Gupta AK, Gover MD, Nouri K, Taylor S. The treatment of melasma: a review of clinical trials. J Am Acad Dermatol 2006; 55:1048-1065.
6. Maeda K, Naganuma M. Topical trans-4-aminomethylcyclohexane carboxylic acid prevents ultraviolet radiation-induced pigmentation. J Photochem Photobiol B 1998; 47;136-41.
7. Hernandez-Barrera R, Torres-Alvarez B, Castanedo-Cazares JP, Oros-Ovalle C, Moncada B. Solar elastosis and presence of mast cells as key feature in the pathogenesis of melasma. Clin Exp Dermatol 2008; 33:305-8.
8. Kim SJ, Park JY, Shibata T, Fujiwara R, Kang HY. Efficacy and possible mechanisms of topical tranexamic acid in melasma. Clin Exp Dermatol 2016; 41:480-5.
9. Lee DB, Suh HS, Choi YS. A comparative study of low-fluence 1064-nm Q-switched Nd:YAG laser with or without chemical peeling using Jessner's solution in melasma patients. J Dermatol Treat 2014; 25:523-528.
10. Shimizu M, Naito T, Okano A, Aoyagi T. Trans-4-aminomethylcyclohexane carboxylic acid as a potent antiplasmin agent. Chem Pharm Bull (Tokyo) 1965; 13:1012-4.
11. Akashima A, Yasuda S, Mizuno N, Determination of the action spectrum for UV-induced plasminogen activator synthesis in mouse keratinocytes in vitro. J Dermatol Sci 1992; 4:11-7.
12. Tse TW, Hui E. Tranexamic acid: An important adjuvant in the treatment of melasma. J Cosmet Dermatol 2013; 12:57-65.
13. Nijor T. Treatment of melasma with tranexamic acid. Chin Res 1979; 13:3129-31.
14. Hajime M, Mineo T, Yoshio T. Oral administration therapy with tranexamic acid for melasma. Nishinihon J Dermatol 1985; 47:1101-4.
15. Cho HH, Choi M, Cho S Lee JH. Role of oral tranexamic acid in melasma patients treated with IPL and low fluence QS Nd:YAG laser. J Dermatol Treat 2013; 24:292-6.
16. Vinod K, Rachita R, Swati A, Akhilesh V. Comparative study of oral tranexamic acid and tranexamic acid microinjections in melasma. IJDVL 2019; 85:39-43.

ORIGINAL ARTICLE
Year: 2019 • Volume: 2 • Issue: 2 • Page: 39-41

THE SPECTRUM OF GENODERMATOSES IN EARLY NEONATES OF WESTERN RAJASTHAN

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Abstract

Background & Aims - Genodermatoses are inherited skin disorders, presenting with multisystem involvement leading to increased morbidity and mortatlity. Many of these disorders are rare. This study is aimed to document the prevalence and diverse clinical presentations of various genetic skin disorders among early neonates from Western Rajasthan, India.

Methods – Five thousand early neonates delivered at tertiary care teaching hospital during March 2016 to Feb 2017 were included and detailed cutaneous and demographic features were studied.

Results – Total 54 neonates presented with genetic skin disorders out of 5000 under study. Prevalence of genodermatoses was found to be 1.08. The most common disorder was collodion baby in 47 neonates followed by harlequin baby in 5 neonates. History of consanguinity was positive in 26 (72.22%) cases, majority of them being from the Muslim community.

Limitation - Lack of genetic testing is the major pitfall of this study.

Conclusion – This is the first of its kind from this part of country, showing prevalence and pattern of genodermatoses in early neonates. Pre-marital genetic counseling can be beneficial in such cases. Prenatal diagnosis would be the first step for early detection of these genodermatoses.

Keywords – Genodermatoses, Collodion baby, Harlequin baby, Goltz syndrome, Incontinentia pigmenti

Introduction

Neonatal skin disorders are quite stressing, physiologically for the newborn and psychologically for the parents. The newborn skin can present with a vast range of conditions, from benign diseases to life-threatening ones. Genodermatoses are group of inherited disorders with cutaneous and systemic involvement causing increased morbidity and mortality.[1] Although, rarely seen, they are quite distressing for the paediatricians who may not be so familiar with skin changes.

The exact prevalence and burden of these diseases is still undefined in India. Only few case reports and series are reported in literature.

Hence, this prompted us to undertake a study to know the incidence and diverse clinical presentations of genodermatoses in early neonates in our area. To the best of our knowledge, this is a study, first of its kind in Western Rajasthan.

Material and method

A hospital-based prospective study of 5000 early neonates was conducted in the period of March 2016 to February 2017. All neonates delivered in tertiary care teaching hospital irrespective of gestational age, sex and mode of delivery were included in the study. Babies born outside the hospital and mothers unwilling to give consent for examination for their words were excluded.

After taking an informed consent from the guardians of the neonate, neonatal cutaneous findings were assessed within 7 days of birth. Detailed demographic data including parental consanguinity, family history and pedigree were recorded. Diagnosis was made on clinical grounds and when needed, relevant investigations were done. The observations pertaining to cutaneous parameters were expressed in percentage. The relationship between skin lesions and various maternal-neonatal aspects was calculated using Z-test, with $p \leq 0.05$ considered statistically significant.

Results

In our study 5000 early neonates were examined, out of them, 54 neonates (1.08%) had genodermatoses. There were more males (33/54) than females (21/54) presenting with genodermatoses. Out of 54 neonates, 32 (59.25%) were full term birth and 22 (40.74%) were preterm newborns. Thirty six (66.67%) mothers were Muslim and remaining 18 (33.34%) were Hindu. Twenty nine (53.70%) were of primiparous mothers whereas the remaining were of multiparous. The most common mode of delivery was normal vaginal delivery in 38 (70.37%) women, followed by Caesarean delivery in 16 (29.62%).

Most common genodermatoses was collodion baby in 47 (0.94%) neonates followed by harlequin baby in 5 (0.1%), Goltz syndrome in 1 (0.02%) and incontinentia pigmenti (IP) in 1 (0.02%) neonate. Out of 47 collodion baby 65.96% (31/47) were male. Amongst 5 harlequin baby 60% (3/5) were female neonates whereas single cases of Goltz syndrome and IP were females. (Figure 1-6)

In genodermatoses all changes were more common in low birth weight neonates except IP which was in normal weight neonate. Collodion baby, harlequin baby and Goltz syndrome were seen more in preterm neonates whereas IP nenonate was a full term baby. All genodermatoses were noted more common in multipara mothers, except harlequin baby which was noted in primipara mothers (80%).

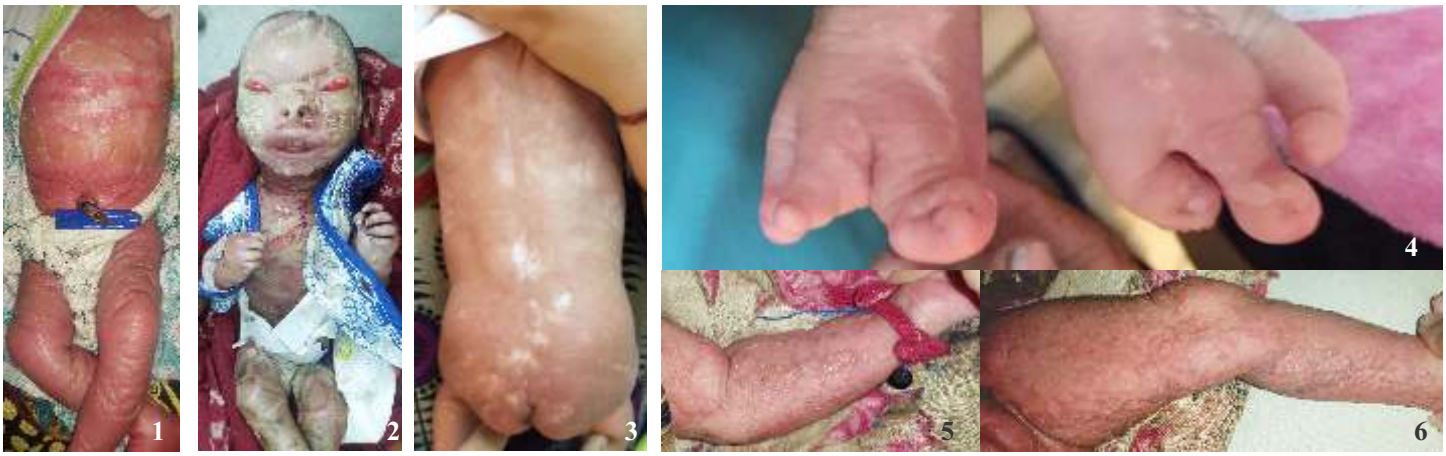

Figure 1: Collodion baby, **Figure 2:** Newborn showing extensive areas of diamond-like skin plates and fissuring characteristic of harlequin baby, **Figure 3:** Case of Goltz syndrome showing asymmetrical linear streaks of hypopigmented atrophic plaques which follows Blaschko's line. **Figure 4:** Case of Goltz syndrome showing ectrodactyly and syndactyly of fingers, **Figure 5 & 6:** Showing multiple linear eruptions of blisters on upper and lower limb along the Blaschko's lines in a newborn, typical of incontinentia pigmenti.

A positive history of the same disorder in the family was observed in 10/54 (18.51%) cases. Out of 36 Muslim neonates, parental consanguinity was noted in 26 (72.22%) neonates of genetic skin disorders. In collodion baby and harlequin baby consanguinous marriage history was statistically significant ($p<0.05$).

Table 1: Prevalence of genodermatoses in neonates

Pathological skin changes	Number of neonates
Collodion baby	47 (0.94%)
Harlequin baby	5 (0.1%)
Goltz syndrome	1 (0.02%)
Incontinentia pigmenti	1 (0.02%)

Discussion

The neonatal life is a phase of rapid adaptation in which the skin plays an important role. The neonatal integument may present with physiological skin changes, transient skin conditions; pathological changes like developmental malformation, genodermatoses, dermatitis, infections and iatrogenic disorders.

Genetic disorders may be grouped into three categories- Chromosomal (numerical-trisomy/monosomy or structural-translocations, deletions, and duplications), Mendelian (autosomal dominant, autosomal recessive or X-linked recessive genes) and Multifactorial.[2]

In our study, 5000 early neonates (the first 7 days of life) were thoroughly examined for genodermatoses related cutaneous changes with analysis of any association between neonatal and maternal factors.

Total 54 neonates with genetic skin disorders were seen among 5000 examined early neonates giving the prevalence of about 1.08 in our population. The exact incidence of these disorders has not been reported in the literature but it is thought that at least 1% of all live births had disorders inherited in a simple Mendelian fashion.[3] The study conducted by Kumar[4] et al showed genodermatoses with a prevalence of 0.62%. The commonest group of disorders was of ichthyosis vulgaris in Kumar[4] et al study whereas collodion baby in 47 neonates followed by harlequin baby in 5 neonates were the most prevalent in our study. Family history was positive (18.51%) in our study similar to other studies.[1,5] The high prevalence of inherited dermatoses amongst family members may be due to traditions that encourage the marriage of relatives. In our study, 72.22% of Muslim parents were married to the first or second-degree relatives which was also noted by Sameem[1] et al study. In this study, there was a male preponderance amongst genodermatoses sufferers similar to other studies.[5,6] Single case of Goltz syndrome and IP each, were noted in our study, both being X-linked dominant; lethal in male. IP neonate was term normal weight baby by a normal vaginal delivery similar to other case reports.[7,8]

All cases were diagnosed clinically and confirmation was done by histopathological examination if required. Therefore, obtaining the family history, consanguinity between the parents, and the presence of other skin disorders in offspring would be very helpful for early diagnosis of the genetic skin diseases. Mutation screening and genetic counseling of family members would be important, especially in families with a consanguinity.

Lack of genetic testing is the major pitfall of this study due to unavailability and prohibited cost in our Institutional setup.

Conclusion

The exact magnitude of genetic skin disorders are unknown because these are rare with increased morbidity and mortality. In this study, prevalence of genodermatoses was about 1.08 in our population. Ichthyosis group of disorders were most common among early neonates. Consanguineous marriage history was positive in 72.22% Muslim mothers. Prenatal diagnosis and genetic counseling are important tool for preventing these disorders.

How to cite this article:

Choudhary P, Mehta RD, Ghiya BC, Sharma D. The Spectrum of Genodermatoses in Early Neonates of Western Rajasthan. JDA Indian Journal of Clinical Dermatology. 2019;2:39-41.

References

1. Sameem F, Jeelani S, Lanker AM, Sultan J. The Spectrum of

Genodermatosis in Muslim Majority Population of North India. DNA.;14:11.

2. Al-Hamami HR, Noaimi AA, Al-Waiz MM, Al-Kabraty AS. Frequency of genodermatoses among Iraqi patients. Iraqi Academic Scientific Journal. 2010;9(1):62-7.
3. Pembrey ME. Genetic factors in disease. In: Weather Hall DJ, Leelingham JGG, Warell DA, eds. Oxford textbook of medicine. London: Oxford University Press, 1987:4.1-4.40.
4. Kumar S, Sharma R C. Genodermatoses in paediatric age group. Indian J Dermatol Venereol Leprol 1996;62:235-6.
5. Baruah MC, Oeducoumar P, Garg BR, Kumar V. Clinico-epidemiological profile of ichthyosis in south Indian patients. J Dermatol 1995; 22: 485–491.
6. Al-Zayir AA1, Al-Amro Alakloby OM.Primary hereditary ichthyoses in the Eastern Province of Saudi Arabia. Int J Dermatol. 2004;43:415-9.
7. Gianfaldoni S, Tchernev G, Wollina U, Lotti T. Incontinentia Pigmenti: A Case Report of a Complex Systemic Disease. Open access Macedonian journal of medical sciences. 2017 Jul 25;5(4):501.
8. Rafatjoo R, Kashani AT. Incontinentia pigmenti; a rare multisystem disorder: case report of a 10-year-old girl. Journal of Dentistry. 2016 Sep;17(3):233.

ORIGINAL ARTICLE
Year: 2019 • Volume: 2 • Issue: 2 • Page: 42-46

COMPARATIVE STUDY OF CLINICAL EFFICACY AND SIDE EFFECTS OF ORAL ISOTRETINOIN AS DAILY CONVENTIONAL DOSE AND FIXED LOW DOSE REGIMEN IN MODERATE TO SEVERE ACNE

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Abstract

Background : Retinoids are a key component of anti-acne therapy. Oral isotretinoin reduces sebum, influences comedogenesis, lowers Propionibacterium acnes and is anti-inflammatory. It is given in a dose of 0.5 to 1.0 mg/kg/day, but this leads to various dose-dependent mucocutaneous and systemic side effects. To overcome this limitation, lower dose regimens of isotretinoin are being tried. **Aim** : To compare clinical efficacy and side effects of oral isotretinoin as daily conventional dose and fixed low-dose therapy in moderate to severe acne. **Materials and methods**: By grading into mild, moderate and severe acne, 100 patients with moderate to severe acne were randomized into 2 groups of 50 patients each: Group A was prescribed oral isotretinoin 0.5 mg/kg/day and group B was given fixed dose of 5mg/day. Follow up was done in every 4 weeks till 16 weeks. Total acne load, side effects and laboratory investigations were recorded on each visit. **Results** : At the end of treatment, mean percentage decrease in total acne load was 99.16% in group A and 90.91% in group B. Statistically significant difference was observed according to decrease in total acne load, grade of acne improvement and response according to reduction in number of lesions, in both the groups. Early response was seen in group A. Most common side effect was cheilitis and overall frequency of side effects was higher in group A. **Limitations :** Limitations of this study were small sample size, shorter duration of treatment and absence of follow up period to look for relapses. **Conclusion :** Fixed low-dose oral isotretinoin is almost equal in efficacy to daily conventional dose regimen at the end of therapy with advantages of lesser side effects, increased patient compliance and cost effectiveness, but it needs to be given for a longer period of time in severe acne and carries a risk of relapse.

Keywords: isotretinoin, acne vulgaris, nodulocystic acne, low dose.

Introduction

Acne is estimated to affect 9.4% of the global population; making it the eighth most prevalent disease worldwide.[1] It commonly affects adolescence, which is a time of physical, emotional, and social development. Although some consider acne to be merely a cosmetic problem, it may have significant and enduring emotional and psychological effects. This necessitates timely treatment to reduce further complications.

There are various treatment modalities for acne according to its grade, which can be in the form of topical and systemic therapy. The introduction of isotretinoin in 1982, a first generation synthetic retinoid, for the treatment of patients with moderate to severe acne vulgaris is regarded as a major therapeutic advancement in dermatology.[2] Cumulative effects of multiple actions make this compound the single most effective treatment of severe recalcitrant nodulocystic acne.

Isotretinoin is given in a dose of 0.5 to 1.0 mg/kg/day after meals in severe acne and the treatment is continued till a cumulative dose of 120-150 mg/kg has been achieved. But this causes many dose-dependent mucocutaneous and systemic side effects. Hence it is important to target the treatment in such a way that good efficacy is obtained but with minimal side effects.

To overcome this limitation lower doses of isotretinoin are being tried. Lower doses of isotretinoin may be effective in terms of side effects and cost; therefore, other regimens may be used instead of daily conventional dose. To compare the efficacy and tolerability of two regimens of oral isotretinoin in acne vulgaris (0.5 mg/kg/day conventional dose and 5 mg/day fixed low dose), the present prospective study was undertaken.

Methods

This prospective randomized comparative study included 100 patients with moderate to severe acne vulgaris attending the outpatient clinic in the dermatology department. Patients in the age group of 18-30 years including both males and females, with pre-existing or recently developed moderate to severe acne were included in the study. Pregnant females, females desiring to get pregnant or using temporary methods of contraception and patients having family and/or personal history of hyperlipidemia or diabetes were excluded. Written and informed consent was obtained from all patients. Baseline investigations comprised of complete blood counts (CBC), fasting lipid profile (FLP) and liver function test (LFT).

The lesions of acne were examined under good illumination and were graded into mild, moderate and severe on the basis of

severity described by Pochi et al[3].

Mild disease: Few to several papules/pustules with no nodule

Moderate disease: Several to many papules/pustules with few to several nodules

Severe disease: Numerous and/or extensive papules/pustules with many nodules. (Few: <5, Many: 5-15 and Several: >15 lesions)

100 patients with moderate to severe acne were randomized into two different treatment regimen groups according to a computer generated random number table by software WinPepi. Each group consisted of of 50 patients: Group A was prescribed oral isotretinoin 0.5 mg/kg/day and group B was prescribed oral isotretinoin fixed low dose of 5 mg/day.

For analysis of treatment response following methods were used:

A. Total acne load (TAL) on the basis of Definition Severity Index[4] (Table 1)
B. Grade of acne (mild, moderate and severe).
C. According to the reduction in the number of lesions: No response=0; Poor response= + 1 (<30% reduction in the number of lesions); Fair response=+2 (30-60% reduction in the number of lesions); Good response = +3 (60-90 % reduction in the number of lesions); Excellent response = +4 (>90% reduction in the number of lesions)

Table 1: Definition severity index.

S. No.	Type of acne lesions	Severity index
1	Non-inflamed comedones, open and closed (no erythema)	0.5
2	Comedones/papules with surrounding erythema Superficial pustules < 2 mm with no or little erythema	1
3	Pustules with a diameter > 2 mm Pustules with a significant erythema	2
4	Deep infiltrates with or without pustules, nodules & cysts	3

Table 2: Comparison of Total Acne Load (TAL) score at 0wk, 4wks, 8wks, 12wks, 16wks in group A and group B.

TAL	Group A (n=50)		Group B (n=50)	
	Mean	SD	Mean	SD
At 0wk	101.88	41.161	96.76	44.392
At 4wks	52.72	29.694	65.56	36.432
At 8wks	18.72	13.909	41.08	24.908
At 12wks	5.64	7.626	20.80	15.743
At 16wks	0.92	1.913	10.36	9.669
F Value *	34.93		34.41	
P Value	<0.0001		<0.0001	

Along with oral isotretinoin, patients were advised to apply topical clindamycin phosphate cream (1.0%) once daily and topical adapalene gel (0.1%) in night all along the duration of treatment. Due to a common side effect of cheilitis, all patients were advised to apply white petroleum jelly on lips as and when needed. Sunscreen protection was advised to each patient.

Follow up was done after every 4 weeks till 16 weeks. Lesion type and number along with side effects were recorded on each subsequent visit. Patients were evaluated for complete blood cell counts, liver function tests and serum lipid profile at baseline, at 4 weeks, 12 weeks and 16 weeks.

Categorical data were assessed in the form of absolute numbers and percentages. Quantitative data was assessed by calculating range and measures of central tendency such as mean and standard deviation. All the findings were analyzed by Chi square, student T Test, one way ANOVA (Analysis of variance), repeated ANOVA, post hoc Turkey's test and Wilcoxon statistical test, wherever applicable.

Results

Total 100 patients were included in the study. Out of which 57% were below the age of 20 years, 39% belonged to age group of 21-25 years and 4% were above 25 years of age. Mean age was 21.12 years. 83% patients were males and 17% were females. Majority of the patients (78%) belonged to urban areas and 22% belonged to rural areas. Oily skin was observed in 89% of the patients. Season was the most common factor associated (overall 60%), followed by stress (44%), seborrhoea (41%), sweating, solar radiation (38%), diet (31%) and drug induced acne or premenstrual flare in few. Three female patients were diagnosed cases of polycystic ovarian syndrome. No statistically significant difference was observed in age, gender, and disease characteristics between the two groups.

Table 3: Comparison of percentage change in Total Acne Load (TAL) at 4wks, 8wks, 12wks, 16wks in group A and group B

TAL	Group A (n=50)		Group D (n=50)	
	Mean (%)	SD	Mean (%)	SD
At 4wks	49.68	15.43	34.20	12.51
At 8wks	82.04	10.36	59.76	11.56
At 12wks	94.86	6.22	80.64	10.49
At 16wks	99.16	1.57	90.91	7.17
F Value *	117.22		163.53	
P Value	<0.0001		<0.0001	

Initial mean total acne load score in group A and group B was 101.88 and 96.76 respectively. Mean total acne load scores at 0, 4, 8, 12, and 16 weeks in group A and group B are shown in table 2. Line diagram depicting the comparison of decreasing total acne load in both the groups is shown in figure 1. By repeated measures of ANOVA and post hoc Tukey's test, at 8, 12, and 16 weeks, statistically significant difference ($p<0.0001$) in total acne load scores were observed between group A and group B. By applying wilcoxon paired two tailed probability test it was observed that there was significant decrease ($p<0.0001$) in mean total acne load score during each follow up from the initial mean total acne load.

Mean percentage decrease in total acne load was higher in group A than in group B, as shown in table 3. Response curve depicting the comparison of mean percentage decrease in acne load in both the groups is shown in figure 2. By ANOVA test and post hoc

Table 4: Grade of acne wise distribution of cases in group A and group B

Grade of acne		Group A (n=50)	Group D (n=50)	Chi-square P Value
At 0 wk	Mild	0	0	0.32 0.96
	Moderate	26(52)	24(48)	
	Severe	24(48)	26(52)	
At 4 wk	Mild	6(12)	4(8)	4.63 0.59
	Moderate	28(56)	34(68)	
	Severe	16(32)	12(24)	
At 8 wk	Mild	30(60)	18(36)	7.75 0.26
	Moderate	14(28)	28(56)	
	Severe	6(12)	4(8)	
At 12 wk	Normal	12(24)	2(4)	12.59 0.05
	Mild	26(52)	26(52)	
	Moderate	12(24)	22(44)	
	Severe	0	0	
At 16 wk	Normal	36(72)	8(16)	32.48, <0.0001
	Mild	14(28)	26(52)	
	Moderate	0	16(32)	
	Severe	0	0	

Table 5: Reduction in number of lesions wise distribution of cases in group A and group B

No of lesion		Group A (n=50)	Group D (n=50)	Chi-square P Value
At 4 wk	1+	6(12)	26(52)	34.10, <0.0001
	2+	26(52)	22(44)	
	3+	18(36)	2(4)	
	4+	0	0	
At 8 wk	1+	0	2(4)	49.16, <0.0001
	2+	2(4)	34(68)	
	3+	34(68)	14(28)	
	4+	14(28)	0	
At 12 wk	1+	0	0	45.74, <0.0001
	2+	0	10(20)	
	3+	10(20)	32(64)	
	4+	40(80)	8(16)	
At 16 wk	1+	0	0	18.95, <0.0001
	2+	0	0	
	3+	2(4)	24(48)	
	4+	48(96)	26(52)	

Tukey's test there was statistical significant differences in mean percentage decrease between group A vs group B ($p<0.0001$).

At the beginning, group A patients consisted of 52% moderate and 48% severe acne cases, group B had 48% moderate and 52% severe acne. On evaluation of response according to grade of acne (i.e. mild, moderate, severe) at the end of therapy, in group A, 72% were acne free, 28% patients improved to mild acne, none of the patients had moderate or severe grade acne, while in group B 16% were acne free, 52% patients had mild acne, 32% had moderate acne and no patients had severe grade acne (Table 4). At 12 and 16 weeks, statistically significant difference was observed according to grade of acne improvement in both the groups ($p<0.0001$).

On evaluation of response according to reduction in number of lesions, a statistically significant difference was seen between both the groups during whole study period ($p<0.0001$). At the end of 4 weeks, none of the patients in all the groups had developed excellent response. At the end of 8 weeks, group A was the earliest to present with excellent response in 28% of the patients. Distribution of cases according to reduction in number of lesions is shown in table 5.

Most common side effect was cheilitis (92% in Group A and 52% in group B) followed by dry skin (20% in group A). Dry eyes were noted in 16%, pruritus in 8% and alopecia in 4% of group A patients. One patient each of dry mouth, dry nose, facial erythema, headache, oral aphthous ulcers, arthralgia and myalgia was noted in group A. Liver function tests were two fold increased in one patient of group A. Moderately increased triglycerides were noted in 12% patients of group A. CBC was in normal range in all the groups. There was statistical significant difference in cheilitis, dry skin and dry eyes among both the treatment groups ($p<0.05$). All the side effects were successfully managed and no patient required stopping of therapy.

Discussion

Acne severity is directly related to degree of anxiety and extent of impaired self-image.[5] More than a cosmetic problem, acne affects every aspect of patient's life: social, vocational, and academic. Patients with severe acne have higher unemployment rates and worse academic functioning compared to those without acne.[5] Acne can negatively impact mood, self-esteem, and interpersonal relationships and may lead to depression and

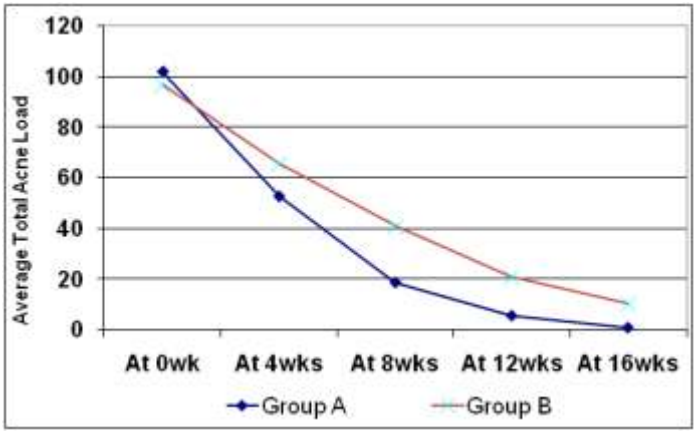

Figure 1: Line diagram showing comparison of Total Acne Load (TAL) at 0wk, 4wks, 8wks, 12wks, 16wks in group A and group B

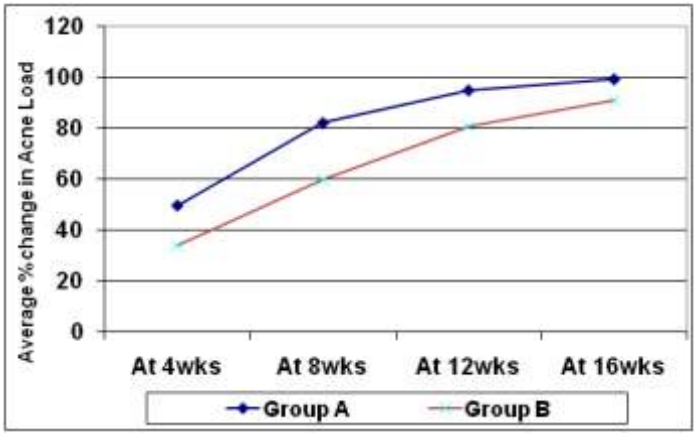

Figure 2: Line diagram showing comparison of percentage change in Total Acne Load (TAL) at 4wks, 8wks, 12wks, 16wks in group A and group B.

appreciable among young adults due to social and occupational functioning.[6]

Since the introduction of isotretinoin, the management of acne has been revolutionized and, over two decades later, isotretinoin remains the most clinically effective anti-acne therapy, producing long-term remission or significant improvement in many patients; the reason being multimodal action in controlling the factors which induce acne. It acts by multiple mechanisms, including the suppression of sebaceous gland activity, normalization of pattern of keratinization in the sebaceous gland follicle, reduction of growth of Propionibacterium acnes, inhibition of inflammation and normalization of expression of matrix tissue metalloproteinases.[7,8]

Various studies have highlighted that the duration of remission achieved by an initial course of isotretinoin is variable and depends on multiple contributory factors, for example, age of the patient, male gender, hyperandrogenemia or polycystic ovarian syndrome, cumulative dose administered, patient compliance and presence of severe symptoms or complicated acne.[9] Although isotretinoin was FDA approved for treatment of severe recalcitrant nodular acne, it can also be used in patients with moderate-to-severe acne or mild-to-moderate acne carrying a risk of scarring or psychological distress and in patients who are unresponsive or resistant to other therapies.[10]

After many studies it was postulated that an isotretinoin dose in the range of 0.5–1.0 mg/kg daily until a total cumulative dose of 120–150 mg/kg is reached, is a reasonable therapeutic plan. This is the conventional dose followed till date. Van der Meeren (1983) used 0.5mg/kg and 1.0 mg/kg doses in 58 patients for 6 months and noticed 90% reduction in acne but with dose related side effects.[11] Layton et al (1993), Cunliffe et al (1997) and Bellosta et al (1987) prescribed conventional doses of 0.5-1.0mg/kg/day isotretinoin and concluded that higher doses seemed to achieve a better clinical response.[12,13,14] Strauss et al (1984) assessed results of isotretinoin as 0.1mg/kg, 0.5mg/kg and 1.0mg/kg doses in a study group of 150 patients for a duration of 4 months. It was observed that although all doses were effective, with lower dose of 0.1mg/kg/day, 90% reduction in acne lesions was observed but a 42% relapse was seen.[15] Goulden et al (1997) studied 80 patients and prescribed isotretinoin 0.5mg/kg/day intermittent dose (1 week / month). This regimen was given for a period of 24 weeks and they observed 88% reduction in total acne load but 39% relapse rate.[16]

It has been suggested that isotretinoin should be initiated early in the management of acne; even lower-dose isotretinoin (0.25–0.5 mg/kg/day for 24 weeks) offers a good balance between efficacy and dose-related adverse effects.[17,18.]

To decrease the incidence of adverse effects and to increase adherence of patients to therapy, the different low-dose isotretinoin regimens for different duration have been tried: Hermes et al (1998) assessed results of isotretinoin as 0.43mg/kg dose in a study group of 94 patients for a duration of 35 weeks and observed 99.3% reduction in total acne load but a 33% relapse rate. Mandekov – Lefaki et al (2003) assesed low doses of isotretinoin (0.15-0.4mg/kg/day) and compared with conventional doses (0.5-1.0mg/kg/day) in 32 patients for 24 weeks. They observed 69% resolution of lesions in low dose regimen.[19] Plewig et al (2004) prescribed low doses of 0.14,0.27,0.29mg/kg/day isotretinoin in 28 patients for 20 weeks and reported 91.8% resolution.[20] Amichai et al (2006) prescribed low doses of 0.3-0.4mg/kg/day isotretinoin in a large study group of 638 patients for 24 weeks and reported 93.7% resolution and 5% cases of relapse. Agarwal et al (2011) compared the efficacy and tolerability of oral isotretinoin as daily(A), alternate(B), pulse(C) and low-dose regimens(D) in 120 patients with acne.[21] Frequency and severity of side-effects were significantly higher in Group A as compared to Group B, C and D. It was concluded that in severe acne, either conventional high doses of isotretinoin should be used or conventional high dose for initial eight weeks followed by maintenance on low doses can be used. Rademaker et al (2013) 5 mg/day of isotretinoin was prescribed in low-grade adult acne for 16 weeks and concluded that 5 mg/day isotretinoin is effective in reducing acne lesions as well as in improving patients' dermatologic quality of life with minimal adverse effects.[22]

In our study, at the end of therapy mean percentage decrease in acne load was 99.16% in group A and 90.91% in group B. Both the groups performed well as far as the end result is concerned. But if percentage decrease is observed in each follow up visit, significant difference in mean percentage decrease appeared between group A and B at 4 weeks. Group A performed better with almost three fourth proportion of the patients cured, rest one fourth moved to mild grade and none of the patients left with moderate or severe acne at the end of therapy. In group B less than a quarter were cured. But overall result at the end of therapy was appreciable in both the groups as none of them had any patient with severe acne by the end of 12 weeks. Group A had advantage of early response; excellent response noted as early as in 8 weeks. Group B performed satisfactory in efficacy but carried the disadvantage of late response.

Most common side effects observed in our study were cheilitis, dry skin, dry eyes, hair fall and pruritus. Less frequent side effects were urticaria, dry mouth, dry nose, headache, facial erythema, myalgia, arthralgia, oral aphthous and moderately deranged triglycerides level and abnormal liver function test. Although the frequency of side effects was not significantly high but whichever existed, were present in higher proportion in group A. Similar incidence of side effects was reported by Agarwal et al (2011). But a higher incidence of hyperlipidemia (35%) and elevated liver enzymes (10%) were reported by Sardana K (2003) and Altman RS (2002)[23,24]

Limitations

Limitations of this study were small sample size, shorter duration of treatment and absence of follow up period to look for relapses.

Conclusion

Overall efficacy of oral isotretinoin at the end of therapy is satisfactory and almost comparable in both the dosage forms. Daily conventional dose has slightly higher efficacy and marked

early response but it is associated with higher incidence of side effects. Low fixed dose of 5 mg oral isotretinoin has slightly lower efficacy, has slow response but minimal side effects. It needs to be given for a longer period of time in severe acne and carries a risk of relapse. We conclude that moderate cases of acne can be treated with fixed low dose regimen of oral isotretinoin because of good efficacy, minimal side effects and cost effectiveness; but we suggest severe cases to be treated with daily conventional dose during initial few weeks for a rapid response, followed by a fixed low dosage regimen for rest of the duration of treatment.

References

How to cite this article:

Mathur R, Talanikar HV, Deora MS, Kharat R. Comparative study of clinical efficacy and side effects of oral isotretinoin as daily conventional dose and fixed low dose regimen in moderate to severe acne. JDA Indian Journal of Clinical Dermatology. 2019;2:42-46.

1. Bhate K, Williams HC. Epidemiology of acne vulgaris. Br J Dermatol 2013;168:474-85.
2. Shahidullah M, Tham SN, Goh CL. Isotretinoin therapy in acne vulgaris: A 10 year retrospective study in Singapore. Int J Dermatol. 1994;33:60–3.
3. Pochi PE, Shalita AR, Strauss JS et al. Report of the consensus conference on acne classification. J Am Acad Dermatol 1991; 24 : 495–500.
4. F Liden S, Goransson K, Odsell L. Clinical evaluation in acne. Acta Dermatovener (Stockholm) 1980; 89 : 47–52.
5. Uhlenhake E, Yentzer BA, Feldman SR. Acne vulgaris and depression: A retrospective examination. J Cosmet Dermatol 2010;9:59-63.
6. Durai PC, Nair DG. Acne vulgaris and quality of life among young adults in South India. Indian J Dermatol 2015;60:33-40.
7. King K, Jones DH et at. A double- blind study of the effects of 13-cisretinoic acid on acne, sebum excretion rate and microbial population. Br. J. Dermatol 1982; 107: 583-90.
8. Dalziel K, Barton S, et at. The effects of isotretinoin on follicular and sebaceous gland differentiation. Br. J. Dermatol. 1987; 117: 317-23.
9. Stainforth JM, Layton AM, Taylor JP, Cunliffe WJ. Isotretinoin for the treatment of acne vulgaris: Which factors may predict the need for more than one course? Br J Dermatol 1993;129:297-301.
10. Sheth R, Poonevala V. Isotretinoin: An Indian experience. Indian J Dermatol Venereol Leprol 2001;67:180-2.
11. Van der Meeren HL, van der Schroeff JG, Stijnen T, van Duren JA, van der Dries HA, van Voorst Vader PC. Dose-response relationship in isotretinoin therapy for conglobate acne. Dermatologica 1983;167:299-303.
12. Layton AM, Knaggs H, Taylor J, Cunliffe WJ. Isotretinoin for acne vulgaris 10 years later: A safe and successful treatment. Br J Dermatol 1993;129:292-6.
13. Cunliffe WJ, van de Kerkhof PC, Caputo R, Cavicchini S, Cooper A, Fyrand OL, et al. Roaccutane treatment guidelines; Results of an international survey. Dermatology 1997;194:351-7.
14. Bellosta M, Vignini M, Miori L, Rabbiosi G. Low-dose isotretinoin in severe acne. Int J Tissue React 1987;9:443-6.
15. Strauss JS, Rapini RP, Shalita AR, Konecky E, Pochi PE, Comite H, et al. Isotretinoin therapy for acne: Results of a multicenter dose-response study. J Am Acad Dermatol 1984;10:490-6.
16. Goulden V, Clark SM, McGeown C, Cunliffe WJ. Treatment of acne with intermittent isotretinoin. Br J Dermatol 1997;137:106-8.
17. Lee JW, Yoo KH, Park KY, Han TY, Li K, Seo SJ, et al. Effectiveness of conventional, low-dose and intermittent oral isotretinoin in the treatment of acne: A randomized, controlled comparative study. Br J Dermatol 2011;164:1369-75.
18. Sardana K, Garg VK. Efficacy of low-dose isotretinoin in acne vulgaris. Indian J Dermatol Venereol Leprol 2010;76:7-13.
19. Mandekou-Lefaki I, Delli F, Teknetzis A, Euthimiadou R, Karakatsanis G. Low-dose schema of isotretinoin in acne vulgaris. Int J Clin Pharmacol Res 2003;23:41-6.
20. Plewig G, Dressel H, Pfleger M, Michelsen S, Kligman AM. Low dose isotretinoin combined with tretinoin is effective to correct abnormalities of acne. J Dtsch Dermatol Ges 2004;2:31-45.
21. Agarwal US, Besarwal RK, Bhola K. Oral isotretinoin in different dose regimens for acne vulgaris: A randomized comparative trial. Indian J Dermatol Venereol Leprol 2011;77:688-94.
22. Rademaker, M. (2018), Very low-dose isotretinoin in mild to moderate papulopustular rosacea; a retrospective review of 52 patients. Australas J Dermatol, 59: 26-30.
23. Sardana K, Sehgal VN. Retinoids: fascinating up-and-coming scenario. J Dermatol 2003; 30: 355–380.
24. Altman RS, Altman LJ, Altman JS. A proposed set of new guidelines for routine blood tests during isotretinoin therapy for acne vulgaris. Dermatology 2002; 204: 232 235.

ORIGINAL ARTICLE
Year: 2019 • Volume: 2 • Issue: 2 • Page: 47-50

EVALUATION OF SERUM ZINC, IRON PROFILE AND VITAMIN D IN FEMALES OF REPRODUCTIVE AGE GROUP WITH DIFFUSE HAIR LOSS: A CASE CONTROL STUDY

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Abstract

Context: Female pattern hair loss (FPHL) and chronic telogen effluvium (CTE) are two common causes of diffuse hair loss in females. Although nutritional deficiencies have been implicated in the etiopathogenesis of diffuse alopecia, the results from various studies have been conflicting. **Aims:** To compare the serum levels of iron, ferritin, vitamin D and zinc in patients of diffuse alopecia with a control population. **Settings and Design:** Case control study conducted at a tertiary care centre. **Methods and Material:** 102 female patients with diffuse hair loss, in form of 58 FPHL, 44 CTE cases and 49 healthy age-matched female controls were included in the study. Serum levels of iron, ferritin, vitamin D and zinc were estimated in both the groups. **Statistical analysis used:** Chi square test was applied for the qualitative variables and independent t test was used for comparing means of quantitative data. Non parametric tests were applied for analysis of qualitative and quantitative data as appropriate. **Results:** Only CTE cases had significantly lower levels of serum zinc when compared to controls (p=0.029). Ferritin deficiency was associated with cases of diffuse alopecia versus the control population (p=0.047) and in cases of FPHL vs controls (p=0.016). There were no significant differences of serum Iron and serum vitamin D levels, between cases and controls. **Conclusions:** Diffuse alopecia in females needs laboratory evaluation. Chronic telogen effluvium is associated with low levels of serum zinc. Ferritin deficiency is significantly associated with female pattern hair loss.

Key Words : Female pattern hair loss, iron, vitamin D, Zinc, Telogen effluvium, diffuse hair loss.

Key Messages: Micronutrient deficiencies like zinc and protein like ferritin status should be assessed in all cases of diffuse hair loss.

Introduction

Telogen effluvium and female pattern hair loss are the two most commonly seen causes of non-scarring hair loss in females.[1] Various nutritional deficiencies such as that of iron, vitamin D and zinc have been found to be associated with hair loss.[2,3,4,5] There can be regional differences in socio cultural habits like dietary and environmental exposures reflected in the nutritional status of patients. So, this study was undertaken to evaluate the association of serum iron, ferritin, vitamin D and zinc levels in females with diffuse alopecia compared to control in a subset of population from eastern India.

Subjects and Methods

A case control study was conducted in the Dermatology outpatient clinic of a tertiary care centre in eastern India from December 2016 to May 2018. Institutional Ethical Committee approval was obtained prior to study. Considering the prevalence of diffuse hair loss in our outpatient department the sample size of the study for a confidence interval of 95% and 5 % margin of error was calculated to be 105 using Raosoft software.[6] Half the number of healthy age matched females were chosen as controls.

Inclusion criteria:

All female patients with complaints of diffuse hair loss of duration more than 6 months visiting our OPD were screened. Patients of 18 to 45 years of age with a clinico-dermoscopic diagnosis of chronic telogen effluvium (CTE), Female pattern hair loss (FPHL) were included.

Exclusion criteria

Patients with known systemic illness and other scalp and hair cycle disorders causing hair loss were excluded. Patients on medications that could cause alopecia and patients receiving supplements containing vitamin D, iron, and zinc were also excluded.

Methodology

A thorough history about onset, duration, concurrent and past medical illness and drugs was obtained from the patients. Clinical examination including a hair pull test was conducted. A trichogram examination was done and anagen to telogen ratio was calculated. All the patients were evaluated by a Dermlite DL4 3 Gen® dermoscope. Hair diameter diversity more than 20% was diagnostic of FPHL [Figure 1]. In CTE, empty follicles and short regrowing hairs were considered diagnostic after excluding all other non cicatricial causes of hair loss [Figure 2]. FPHL was graded according to the Ludwig scale.

Serum levels of iron, ferritin, vitamin D levels and zinc were measured in all cases as well as controls.

Statistical Analysis:

Data were analysed using (Statistical Package for Social

Scientists) SPSS Version 20.0, IBM, USA. Chi square test was applied to compare categorical data. Independent sample t test was used to analyse continuous variables between two groups. Mann Whitney test was applied to compare means of nonparametric data. A 'p' value of ≤0.05 was considered significant.

Figure 1: Dermoscopy of FPHL Ludwig grade III showing hair diversity more than 20 %. (DermLite DL4; 3Gen; polarized mode, 10x)

Figure 2: Empty hair follicles and short regrowing hair in CTE. (DermLite DL4; 3Gen; polarized mode, 10x)

Results

A total of 102 females with diffuse hair loss met the inclusion criteria and were analysed [Figure 3].49 healthy age matched females were taken as controls in the study. The mean age of the patients and controls were 28.9 ± 8.0 and 28.8 ± 7.2 years respectively (Table 1). Fifty eight patients were diagnosed with FPHL [Figure 4]. The cause of alopecia was found to be CTE in 44 (43.13 %) cases [Figure 5]. Among patients of FPHL, maximum number of patients (70 % cases) had LUDWIG grade 1 disease. Age and grade wise distribution of FPHL is

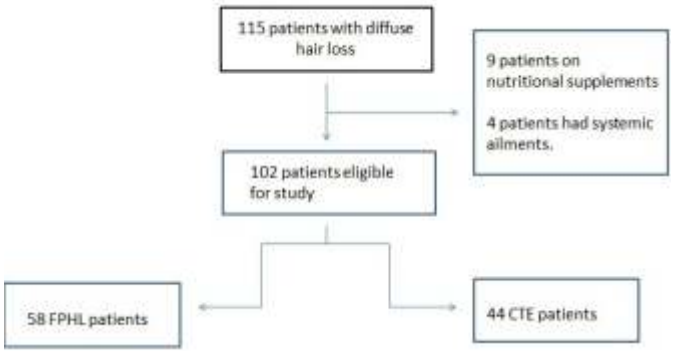

Figure 3: Flow chart of cases in the study

summarized in (Table 2). Biochemical parameters of cases and controls are presented in (Table 3).

The mean serum zinc level in cases was 85.76 ± 47.32 and 137.26 ± 203.97 µmol/L in controls. Though the cases had a lower value than controls, this difference was not statistically significant (p=0.087).Only CTE cases had significantly lower levels of serum zinc when compared to controls (p=0.029). The study did not reveal any association between grades of FPHL and serum zinc levels. (p=0.862).

The study did not show statistically significant difference in the serum vitamin D levels in patients of CTE and controls (p=0.455), FPHL and controls (p=0.455).Across LUDWIG grades of FPHL, there was no significant difference in serum levels of vitamin D (p = 0.255).On analysis of vitamin D deficiency status, we did not find significant difference between cases and controls (p=1.00).

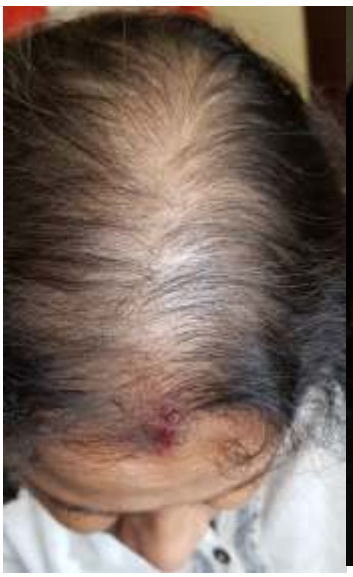

Figure 4: FPHL Ludwig grade III.

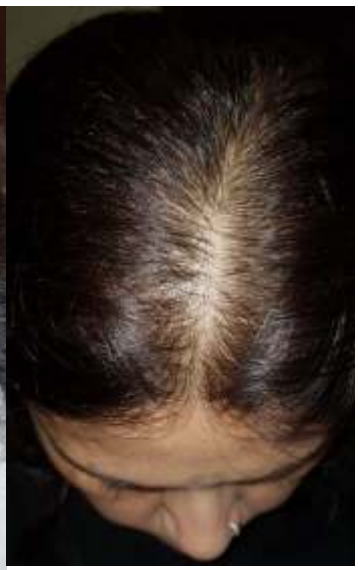

Figure 5: Chronic Telogen Effluvum.

Mean serum iron level did not vary significantly across CTE and controls (p=0.90).Mean serum iron level in CTE cases was 79.39 ± 50.66 and that of controls was 70.48 ± 29.08 micro gm/dl. According to severity of condition, mean serum iron level was not significantly associated with change in LUDWIG score (p =

Table 1: Age-wise distribution of cases and controls.

Age groups	CONTROL	CTE	FPHL
18 -30	32(65.3 %)	24(61.5 %)	41(70%)
31 -45	17(34.6%)	20(38.5%)	17(29.3%)
Total	49(32.5%)	44(38.2%)	58(56.8%)

Table 2: Distribution of severity of FPHL (n = 58)

AGE GROUP	LUDWIG 1	LUDWIG 2	LUDWIG 3	TOTAL NO. OF CASES(%)
18-30 YEARS	37	4	0	41(70.6)
31-45 YEARS	4	8	5	17(29.4)

0.267). There was no significant difference in serum iron deficiency status among cases and controls (p=0.75).

Serum ferritin levels did not vary significantly across CTE and FPHL. No significant difference was seen between cases and that of controls. (p=0.37) There was no significant difference in serum ferritin levels observed in cases of FPHL and controls (p = 0.073), CTE and controls (p =0.617).However, serum ferritin deficiency was significantly associated with cases when compared to controls as seen in our study (p=0.047).Table 4.

Discussion

The mean age of presentation of patients in our study was 28.9 ± 8.0 years [7].In the present study, FPHL was seen mostly among women of age 18 to 30 years. The possible cause could be the increased cosmetic concern among the younger women and early consultation compared to women in higher age groups. CTE is common in females in their forties, and presents with sudden hair loss in large number. Two third of CTE patients were in the 18-30 age group in our study similar to a observation made by Fatani et al.[8]

Serum Zinc acts as co-enzyme in the synthesis of protein and nucleic acids, and consequently plays an important role in cellular functions.[9] In FPHL, zinc acts as a strong inhibitor of hair follicle involution, thus helps in recovery of hair follicle. Kil et al noticed significantly lower zinc in FPHL in comparison to alopecia areata and telogen effluvium.[9] Abdel studied zinc levels in cases of chronic telogen effluvium and control population and didn't find any significant difference in the levels between them.[21]We found significantly lower levels of serum zinc in cases of chronic telogen effluvium as compared to controls.

Table 3: Biochemical parameters in women with FPHL, CTE and controls

	CTE cases	Controls	P value	FPHL cases	Controls	P value
Zinc (µmol/dl)	73.0±39.5	137±203	0.029	95.39±50.71	137±203	0.876
Iron (µgm/dl)	79.39± 50.66	70.48±29.08	0.908	72.50±43.61	70.48±29.08	0.985
Ferritin (ng/ml)	58.41±80	47.9±46.4	0.617	56.03±37.91	47.9±46.4	0.073
VitaminD (ng/ml)	17.41±11.3	17.63±8.57	0.455	17.86±11.4	17.63±8.57	0.455

In animal models, Vitamin D was shown to play a vital role in the hair follicle cycle, specifically anagen initiation.[11] Recent studies reveal that vitamin D2 receptor regulates the expression of hair cycle genes which includes the hedgehog pathway.[12] Nayak et al and Rashid et al have found Vitamin D levels in females with CTE and FPHL to be significantly lower as compared to the controls.[18,19] However, different studies have variable results of vitamin D levels in cases of telogen effluvium. Karadag et al found higher levels of vitamin D among patients of telogen effluvium compared to controls.[20] We did not observe any significant difference in serum vitamin D levels among patients and controls. Complex biochemical pathways governing vitamin D levels in body and variable sun exposure could possibly be the explanation for different results obtained in our study.

Table 4: Deficiency status in cases vs controls.

Deficiency	Cases(102)	Controls(49)	P value
zinc	36	14	0.463
Iron	9	3	0.752
Ferritin	56	37	0.047
Vitamin D	45	92	1.000

Role of a low serum ferritin in diffuse alopecia has been debatable.[13] Deloche et al demonstrated an association between low serum ferritin and diffuse alopecia.[14] Bregy and Trueb found no significant difference in rate of telogen hair loss among groups of women with low and high serum ferritin.[15] Kantor found that the mean ferritin level in patients with androgenetic alopecia and alopecia areata were statistically significantly lower than in healthy controls without hair loss in their study.[5] Different authors have considered varying levels of serum ferritin as low to study hair loss association. Elise studied ferritin levels in patients of FPHL and CTE across pre and postmenopausal groups of women and observed no statistically significant increase in the incidence of iron deficiency in these cases versus control subjects. [17] We considered serum values of ferritin lower than 50 ng/ml to be the cut off value for deficiency. It was significantly associated with cases of diffuse alopecia than that of controls. Ferritin being a sensitive and specific indicator of iron deficiency warrants iron supplementation in patients of diffuse alopecia.

Iron is postulated to upregulate certain genes like NDRG1, ALAD, RRM 2 present in bulge region of the hair follicle which promote hair regrowth.[16] Iron depletion retards the optimum functioning of the enzymes where it acts as a cofactor leading to inhibition of proliferation of hair follicle. State of iron deficiency may not be reflected as low serum iron in the initial stages when serum ferritin serves as a sensitive index for the same. Our study did not show significant difference in serum iron between subjects with alopecia and controls.

Serum iron, zinc and vitamin D level were not significantly associated across different Ludwig grades of FPHL. Banihashemi did not find any significant difference in vitamin D levels across Ludwig grades of FPHL.[22]

Limitations

Active screening of systemic diseases causing diffuse alopecia was not done in the cases. Higher age groups of patients including post-menopausal women were not included.

Conclusion

Early age for consultation for diffuse alopecia is possibly due to

increased cosmetic awareness. In our study population, FPHL outnumbered other types of diffuse non scarring alopecia; Ludwig type 1 being most common. CTE cases had significantly lower levels of serum zinc when compared to controls. Serum ferritin deficiency was significantly associated with all cases of diffuse alopecia and FPHL. Micronutrients like zinc and serum proteins like ferritin as a representative of iron should be screened in patients presenting with diffuse alopecia.

How to cite this article:

Malakar S, BSTP Singh, Jena K A, Kar RB. Evaluation of serum zinc, iron profile and vitamin D in females of reproductive age group with diffuse hair loss: A case control study. JDA Indian Journal of Clinical Dermatology. 2019;2:47-50.

Reference

1. Torres F, Tosti A. Female pattern alopecia and telogen effluvium: figuring out diffuse alopecia. Semin Cutan Med Surg 2015;34:67-71
2. Poonia K, Thami GP, Bhalla M, Jaiswal S, Sandhu J. NonScarring Diffuse Hair Loss in Women: a Clinico-Etiological Study from tertiary care center in North-West India. J Cosmet Dermatol. 2019;18:401-7
3. Moeinvaziri M, Mansoori P, Holakooee K, SafaeeNaraghi Z, Abbasi A: Iron status in diffuse telogen hair loss among women. Acta Dermatovenerol Croat 2009;17:279-84.
4. Deloche C, Bastien P, Chadoutaud S, Galan P, Bertrais S, Hercberg S, de Lacharrière O. Low iron stores: a risk factor for excessive hair loss in non-menopausal women. Eur J Dermatol 2007;17:507-12.
5. Kantor J, Kessler LJ, Brooks DG, Cotsarelis G. Decreased serum ferritin is associated with alopecia in women. J Invest Dermatol 2003;121:985-88.
6. http://www.raosoft.com/samplesize.html
7. Malkud S. A Hospital-based Study to Determine Causes of Diffuse Hair Loss in Women. J Clin Diagn Res. 2015;9:WC01-4.
8. Fatani MI, Bin Mahfoz AM, Mahdi AH, Alafif KA, Hussain WA, Khan AS et al. Prevalence and factors associated with telogen effluvium in adult females at Makkah region, Saudi Arabia: a retrospective study. J Dermatol Dermatol Surg 2015;19:27–30.
9. Min SeongKil, Chul Woo Kim, Sang Seok Kim. Analysis of Serum Zinc and Copper Concentrations in Hair Loss. Ann Dermatol 2013;25:405-9.
10. Abdel Aziz AM, Sh Hamed S, Gaballah MA. Possible Relationship between Chronic Telogen Effluvium and Changes in Lead, Cadmium, Zinc, and Iron Total Blood Levels in Females: A Case-Control Study. Int J Trichology. 2015 ;7:100-6.
11. Hamad WA, Said AF, Hamid A. Role of some trace elements in the pathogenesis of telogen effluvium in Egyptian females. J Egypt Women Dermatol 2010;7:44-8.
12. Demay MB. The hair cycle and Vitamin D receptor. Arch Biochem Biophys 2012;523:19-21.
13. Teichert A, Elalieh H, Bikle D. Disruption of the hedgehog signaling pathway contributes to the hair follicle cycling deficiency in Vdr knockout mice. J Cell Physiol. 2010;225:482–89.
14. Nayak K, Garg A, Mithra P, Manjrekar P. Serum vitamin D3 levels and diffuse hair fall among the student population in South India: A case–control study. Int J Trichol 2016;8:160-4.
15. Rasheed H, Mahgoub D, Hegazy R, El Komy M, Abdel Hay R, Hamid MA, et al. Serum ferritin and Vitamin D in female hair loss: Do they play a role? Skin Pharmacol Physiol 2013;26:101-7.
16. Karadag AS, Ertugrul DT, Tutal E, Akin KO. The role of anemia and Vitamin D levels in acute and chronic telogen effluvium. Turk J Med Sci2011;41:827-33.
17. Rushton DH. Decreased serum ferritin and alopecia in women. J Invest Dermatol 2003;121:xvii-iii.
18. Deloche C, Bastien P, Chadoutaud S, Galan P, Bertrais S, Hercberg S, et al. Low iron stores: a risk factor for excessive hair loss in non-menopausal women. Eur J Dermatol 2007;17:507-12.
19. Bregy A, Trueb RM. No association between serum ferritin levels >10 microg/l and hair loss activity in women. Dermatology 2008;217:1–6.
20. Olsen EA, Reed KB, Cacchio PB, Caudill L. Iron deficiency in female pattern hair loss, chronic telogen effluvium, and control groups. J Am Acad Dermatol.2010 ;63:991-99.
21. St Pierre SA, Vercellotti GM, Donovan JC, Hordinsky MK. Iron deficiency and diffuse nonscarring scalp alopecia in women: more pieces to the puzzle. J Am Acad Dermatol 2010;63:1070–6.
22. Banihashemi M, Nahidi Y, Meibodi NT, Jarahi L, Dolatkhah M. Serum vitamin D3 level in patients with female pattern hair loss. Int J Trichol 2016;8:116-20

LETTER TO EDITOR
Year: 2019 • Volume: 2 • Issue: 2 • Page: 51-52

SIGNIFICANCE OF A SIMPLE BEDSIDE TEST IN THE EARLY DIAGNOSIS OF A RARE CASE OF KAPOSI'S VARICELLIFORM ERUPTION

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Sir,

Kaposi's varicelliform eruption (KVE) is a disseminated Herpes simplex virus (HSV) infection which is superimposed on a pre-existing dermatosis. Hailey-Hailey disease (HHD) is a rare genetic dermatosis which is characterized by chronic, recurrent vesicles, erosions and fissures in flexural areas. It is an autosomal dominant condition due to mutations in ATP2C1 gene, leading to defects in keratinocyte adhesion and intraepidermal acantholysis.[1,2] The occurrence of KVE along with HHD is very uncommon. We hereby report a case of Hailey-Hailey disease who developed KVE and an early diagnosis was arrived at with a simple bedside test, i.e. Tzanck smear.

A 49-year-old male, a known case of HHD, with seasonal recurrences and remissions since 9 years was referred to our hospital with an acute exacerbation of lesions in the form of macerated lesions with oozing and crusting involving neck, both armpits and groins and multiple red raised lesions over the chest and back of one month duration. On examination, he had macerated and crusted plaques on the neck, both axilla and genitocrural folds and multiple erythematous macules and papules over the chest and back. (Figure 1, Figure 2). 10% potassium hydroxide (KOH) mount of skin scraping from axilla was positive for Candida. In view of the widespread involvement, he was started on oral corticosteroids and antihistamines along with oral and topical antifungal agents for the axilla and groins. However, while on therapy, after about a month, he developed fever and sudden eruption of multiple red raised and fluid filled lesions on the body. On examination, he was febrile and had multiple, discrete vesicles over on an erythematous base with central umbilication and multiple pustules distributed primarily on the chest, abdomen and back (Figure 3) along with increase in oozing and crusting of pre-existing lesions over the flexures (Figure 4). Tzanck smear showed multinucleated giant cells (Figure 5). His total leukocyte count was raised along with increase in the neutrophils but other hematological and biochemical parameters were within normal limits. Serology for IgM and IgG antibodies to HSV was positive. Polymerase chain reaction (PCR) for HSV was also positive. Skin biopsy from one of the lesions showed intraepidermal acantholytic keratinocyte separation with perivascular lymphocytic infiltrate in the dermis. (Figure 6). Based on the clinical features and Tzanck smear he was diagnosed as a case of KVE which was confirmed later with serology and PCR for HSV infection. He was managed with intravenous Acyclovir initially for four days followed by oral Acyclovir along with Injection Amoxycillin with Clavulanic acid and nursing care. Systemic corticosteroids were continued and gradually tapered and stopped. After ten days of treatment, there was complete resolution of the herpetic lesions and other lesions also started improving.

KVE is a serious life-threatening HSV infection that arises in pre-existing skin disorders. In some cases, it may progress to a life-threatening condition in the form of disseminated infection with visceral involvement and death. The most common predisposing factor is the breach in the stratum corneum secondary to skin disease.

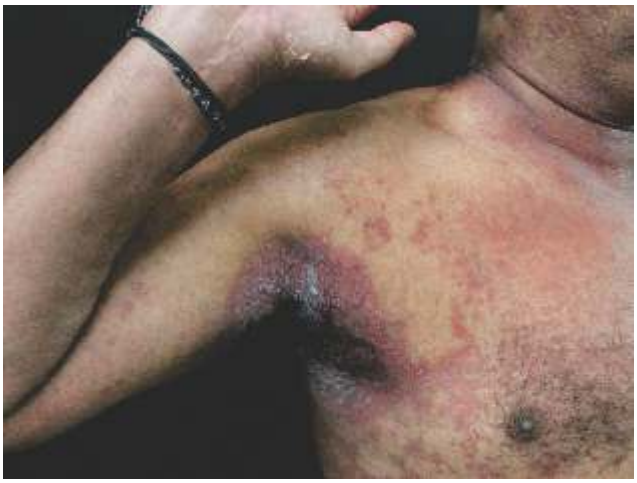

Figure 1: Macerated and crusted plaques involving axilla

Figure 2: Macerated and crusted plaques involving genitocrural folds

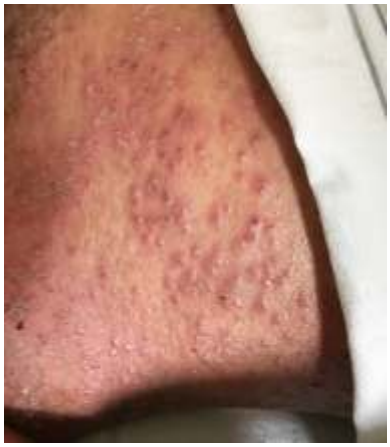

Figure 3: Discrete vesicles over on an erythematous base with central umbilication and multiple pustules

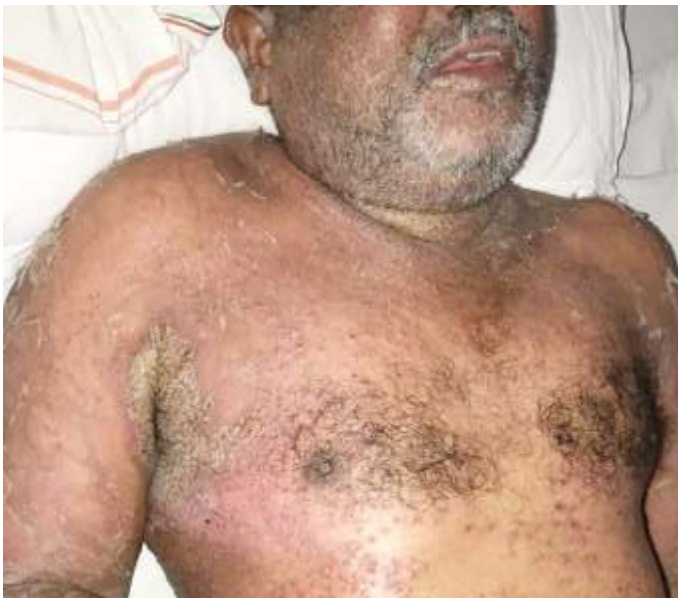

Figure 4: Discrete vesicles over on an erythematous base with central umbilication and multiple pustules

It has been reported to occur in various pre-existing dermatoses namely, Darier's disease, mycosis fungoides, Sézary syndrome, atopic dermatitis, seborrheic dermatitis, pemphigus foliaceus, ichthyosis vulgaris, and Hailey-Hailey disease.[1] It begins as clusters of umbilicated vesicles and pustules in the areas where the skin has been affected by a pre-existing dermatosis. Tzanck smear from scraping of vesicle base showing multinucleated giant cells supports the diagnosis. Importance to this bed side test cannot be stressed enough as in our case it helped us for an immediate bed side diagnosis when he was examined for this eruption. Diagnosis can be confirmed by polymerase chain reaction for viral DNA, electron microscopic detection of herpes virus from blister fluid or immunofluorescence tests for cells affected by HSV.[3]

Treatment with intravenous acyclovir should be started without delay in case of high suspicion of KVE or a positive Tzanck smear as was done in our case. The other antiviral drugs which can be used are valacyclovir and famciclovir.

The occurrence of KVE with HHD has rarely been reported. We came across a few such cases in literature.[4] Our case emphasizes the fact that a simple bedside test like Tzanck smear can be

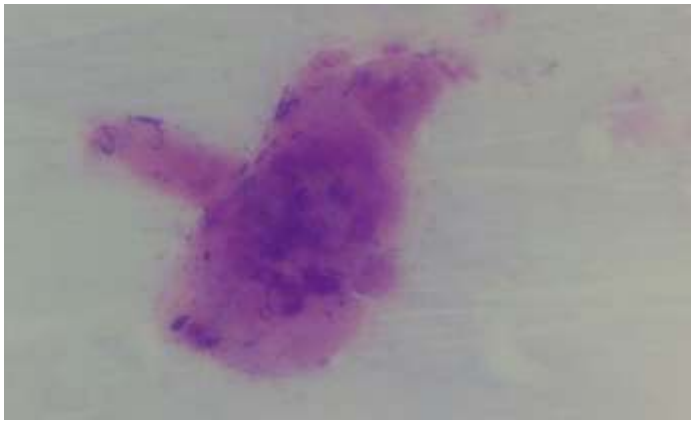

Figure 5: Tzanck smear (1000 X) showing multinucleated giant cell

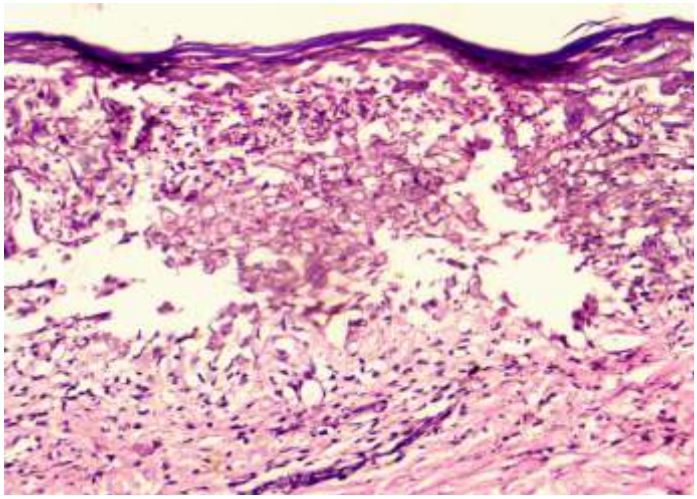

Figure 6: Histopathology (H & E 100X) showing intraepidermal acantholytic keratinocyte separation with perivascular lymphocytic infiltrate in dermis.

crucial in early diagnosis and also, if there is a high index of suspicion of HSV infection, systemic antiviral treatment should be started without delay in order to prevent serious complications and achieve clinical cure.

How to cite this article:

Dabas R, Ranjan E, Arora S, Donaparthi N, Rout A. Significance of a simple bedside test in the early diagnosis of a rare case of Kaposi's varicelliform eruption. JDA Indian Journal of Clinical Dermatology. 2019;2: 51-52.

Reference

1. Lee GH, Kim YM, Lee SY, Lee JS, Park YL, Whang KU. A case of eczema herpeticum with hailey-hailey disease. Ann Dermatol. 2009;21:311–4.
2. Burge SM. Hailey-Hailey disease: the clinical features, response to treatment and prognosis. Br J Dermatol. 1992;126:275–82.
3. Wollenberg A, Zoch C, Wetzel S, Plewig G, Przybilla B. Predisposing factors and clinical features of eczema herpeticum: a retrospective analysis of 100 cases. J Am Acad Dermatol. 2003;49:198–205.
4. Zamperetti M, Pichler M, Perino F, Eisendle K. A case of Hailey-Hailey herpeticum. J Dtsch Dermatol Ges J Ger Soc Dermatol JDDG. 2016;14:1036–9.

LETTER TO EDITOR
Year: 2019 • Volume: 2 • Issue: 2 • Page: 53-54

COMPARISON OF TWO EUTECTIC MIXTURE OF LOCAL ANAESTHETICS FOR REDUCING PAIN DURING MICRO-NEEDLING: A HEMIFACE, CROSS-OVER ANALYSIS OF A FEW CASES

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Sir,

The use of micro-needling in minimally invasive dermatologic and aesthetic procedures are widespread. Although the procedure is very superficial, it is associated with pain and discomfort to the patients. Local anesthetics are commonly used in many cosmetic procedures, and they have been used in the dermatological procedure too. They act through voltage-gated sodium channel and block the conductance of the pain impulse to the higher center through the nerve. Topical anesthesia is one of such anesthetic technique used in dermatology and aesthetic surgeries. A few numbers of local anesthetics are available in clinical practice. However, the choice of the local anesthetic depends on multiple factors, i.e., effectiveness, cost, easy availability, etc. [(1).] A eutectic mixture of local anesthetic is capable of melting at the below room temperature into an oil base, which helps in penetrating the skin and mucosa [(2)]. This retrospective evaluation of prospectively collected database was aimed to analyze the efficacy in terms of controlling pain and safety in terms of complications of two eutectic mixture of local anesthetics for micro-needling of the face.

Data were collected from young adult patients of both sexes, who attended our outpatient department for the micro-needling procedure only for acne scar. Patients received a eutectic mixture of local anesthetics (EMLA) is non-random, hemiface, and cross-over manner. The EMLA used were Asthesia (Unichem Laboratories Ltd., Mumbai, India) a combination of Lignocaine 2.5% and Prilocaine 2.5%, and Viveta (Ajanta Pharma Ltd., Mumbai, India), a combination of Lignocaine 7% and Tetracaine 7% w/w. All patients were subjected to topical application skin test for both the EMLA applied over the post-auricular region and inspected for a reaction after 30 minutes, and suspected/reactive patients were excluded. The procedure was part of the treatment, and no separate consent for this was taken but, informed consent for the data collection and possible publication/presentation were taken. All the patients were introduced to the numerical rating scale from 0 to 10 with a visual depiction, where, 0 indicated no pain at all and 10 indicated the worst possible pain imaginable. The face was cleaned using an alcohol-based antiseptic and allowed to dry spontaneously. Subsequently, Asthesia was applied in one half of the face, and Viveta was applied on the other half, and the patient was asked to wait for 45 minutes. The patient was asked about any adverse symptoms and also face was inspected for any adverse effects, and the findings were noted. After 45 minutes, micro-needling (1.5 mm) was started. A total of 4 reading for each side of the face was taken; one at the beginning, one at the end and two readings in between. The patient was asked to attend for the second session when the patient wants, preferably within three months. In the second session, again hemiface application of the drugs was made, but the site was switched. The pain data were collected in the same manner again. Data were entered in the Microsoft Excel, and complications were expressed in number and percentage scale. The reported pain score was categorized as the highest, lowest, and the average (of four readings) pain scores. The pain data were then analyzed using INSTAT software (Graphpad Prism Software Inc., La Jolla, CA, United States). The pain scores of Asthesia and Viveta were compared using the unpaired t-test, and the pain scores of first and second sessions in the respective drug group were analyzed using the paired t-test. Pain data are presented as median, mean, and standard deviation (SD) and a $P < 0.05$ was considered significant.

A total of 12 patients; 8 (66.67%) male and 4 (33.33%) female, underwent a total of 20 sittings (8 patients underwent twice) of micro-needling. Entire patients were cases of acne scar. All were adults with age ranged between18 – 40 years; mean + SD 24.4 + 4.3 years.

The highest self-reported pain in the NRS scale experienced by the cohort after Asthesia application ranged from 2 – 8 while in the Viveta group it ranged from 2 – 7. The median, mean, and standard deviation of the highest pain, lowest pain score and average pain scores were statistically indifferent; lowest P 0.09 (Table 1). However, a statistically significant lower pain was reported during second sitting by the patient after application of Asthesia, but, although the highest, lowest, and the average pain reported during second sitting by the patient after application of Viveta was lower than first sitting, it was not statistically significant (Table 2).

Erythema was the most common complications in both the group and both during the first and second sitting. Although the Asthesia group has relatively lower erythema as compared to Viveta group (40% versus 55%), the difference was not statistically significant; P 0.52. Similarly, no difference in the wheel formation was noted between the groups (Table 3).

Results of this analysis indicate that both the eutectic mixtures

i.e., Asthesia (Lignocaine 2.5% plus Prilocaine 2.5%) and Viveta (Lignocaine 37% plus Tetracaine 7%) are well tolerated. A meta-analysis of pooled data of trials in terms of safety and adequacy of cutaneous anesthesia indicated that the lidocaine/tetracaine medicated patch or peel is an effective, safe, and well-accepted method for minor dermatologic procedures [3]. Despite having erythema in nearly half of the patients in our cohort, none of the patients were intolerant to the adverse effects and the adverse symptoms and signs subsided by itself without needing any further medication or intervention. However, the pain scores in both the group were very much variable, and a good number of patients reported the highest pain > 4. This indicates that pain control was not adequate.

Table 1: Comparison of pain scores reported during all sittings analyzed using the unpaired t-test.

Pain Category	Asthesia		Viveta		Two-tailed P-value
	Median	Mean±SD	Median	Mean ± SD	
Highest Pain	5	5±1.85	5	4.47±1.64	0.410
Lowest Pain	2	2.53±1.68	2	1.8±1.21	0.181
Average Pain	3.5	3.87±1.66	2.78	3.34±1.47	0.355

The variation of the pain intensity in our cohort may be explained by the interpersonal variation of pain thresholds. Moreover, although the micro-needling was done after a minimum of 45 minutes of application of the local anesthetic mixtures, the time

Table 2: Comparison of pain scores reported during first and second sittings for each drug analyzed using the paired t-test

Drug and pain category	Fist sitting		Second sitting		Two-tailed P-value
	Median	Mean±SD	Median	Mean±SD	
Asthesia					
Highest Pain	6	6±0.71	3	3.6±1.34	0.051
Lowest Pain	3	3.2±1.30	2	1.6±0.55	0.099
Average Pain	5.25	4.7±0.89	2.75	2.8±0.94	0.069
Viveta					
Highest Pain	5	5±1.58	3	3.4±1.52	0.294
Lowest Pain	2	1.6±0.55	1	1.4±1.14	0.778
Average Pain	3.5	3.7±1.17	2.75	2.8±0.94	0.345

to start actually varied between 45 minutes to 60 minutes. Study indicates that topical lignocaine typically takes 60 minutes to anesthetize the skin surface [4]. Pre-treatment with fractional micro-needling has been found to effective in the shortening of the onset time. A study found automated fractional skin micro-needling of 0.5 mm depth followed by topical anesthetic cream application was more effective in reducing pain as compared to topical anesthesia alone for full-face fractional micro-needling treatment of 2.5 mm depth [5]. Furthermore, according to the results of the reported study, triple anesthesia involving of a combination of a painkiller drug, EMLA cream, and infraorbital nerve block was proved as the most effective method of

Table 3: Comparison of complications noted during all sittings analyzed using Fisher's exact test.

Complications	Yes / No	Yes / No	Two-tailed P-value
	Asthesia	Viveta	
Erythema	8 (40%) / 12 (60%)	11 (55%) / 9 (45%)	0.527
Wheal	0 / 20 (100%)	02 (10%) / 18 (90%)	0.487
	Asthesia 1st	Asthesia 2nd	
Erythema	3 (37.5%) / 5 (62.5%)	4 (50%) / 4 (50%)	1.000
Wheal	0 / 8 (100%)	0 / 8 (100%)	1.000
	Viveta 1st	Viveta 2nd	
Erythema	5 (62.5%) / 3 (37.5%)	5 (62.5%) / 3 (37.5%)	1.000
Wheal	1 (12.5%) / 7 (87.5%)	1 (12.5%) / 7 (87.5%)	1.000

anesthesia [6]. Infraorbital nerve block, although, is relatively more straightforward, is probably not widely practiced by the dermatologists and aesthetic surgeons.

Both the eutectic mixtures are well available and relative less costly. Our experience with hemiface and switch-over method showed that both the mixtures are equally effective, but for better results and pain control, multi-modal approach, at least by adding an oral or injectable painkiller might be better.

Our results and observations are, however, limited by the fact that we have observed only a few cases and the allocation was non-randomized. Future studies with larger samples and employing both single and multi-modal approach will give better evidence.

Conclusion

Both Asthesia and Viveta are well-tolerated, but the anesthetic efficacy in terms of analgesic effect for facial micro-needling surgery is not adequate.

How to cite this article:

Ahmed G, Mishra DK. Comparison of two eutectic mixture of local anaesthetics for reducing pain during micro-needling: A hemiface, cross-over analysis of a few cases. JDA Indian Journal of Clinical Dermatology. 2019;2: 53-54.

References

1. Sobanko JF, Miller CJ, Alster TS. Topical anaesthetics for dermatologic procedures: A review. Dermatol Surg 2012;38:709-21.
2. Buckley MM1, Benfield P.Eutectic lidocaine/prilocaine cream. A review of the topical anaesthetic/analgesic efficacy of a eutectic mixture of local anaesthetics (EMLA).Drugs. 1993;46:126-51.
3. Kim WO, Song BM, Kil HK. Efficacy and safety of a lidocaine/tetracaine medicated patch or peel for dermatologic procedures: a meta-analysis. Korean J Anesthesiol 2012; 62: 435-440.
4. Ito Y, Ohta J, Imada K, et al. Dissolvingmicroneedles to obtain rapid local anesthetic effect of lidocaine at skin tissue. J Drug Target. 2013;21(8):770-775.
5. El-Fakahany H, Medhat W, Abdallah F, Abdel-Raouf H, Abdelhakeem M. Fractional Microneedling: A Novel Method for Enhancement of Topical Anesthesia Before Skin Aesthetic Procedures.Dermatol Surg. 2016;42(1):50-5.
6. Zdybski J, Trznadel-Grodzka E. Topical anesthesia in cosmetic dermatological procedures. Our Dermatol Online. 2018;9(3):265-268.

LETTER TO EDITOR
Year: 2019 • Volume: 2 • Issue: 2 • Page: 55

CUTANEOUS ULCERS DUE TO PENTAZOCINE ABUSE

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Dr. Sucheta Pathania

Sir,

A 30 year- old male presented with painful ulcers over the limbs for last one month. The ulcers were preceded by blisters. Examination revealed multiple round to oval ulcers of variable sizes ranging from 2-3cm*1-2cm with well defined margins, sloping edges and floor consisting of pale granulation tissue at some places with peripheral hyperpigmentation over dorsal aspect of both hands and feet. Patchy gangrenous changes with areas of normal skin in between were present on dorsal and ventral aspect of ring and little finger of left hand,[Figure1] There was history of repeated pentazocine injection (for backache) abuse for last 6 months at the sites of ulcers. Histopathological examination revealed partly ulcerated orthokeratotic epidermis with adherent neutrophillic exudates. Superficial dermis showed perivascular and periadnexal mixed inflammatory infiltrate comprising of neutrophils, eosinophils and few lymphocytes,[Figure2].

Pentazocine is one of the commonly used drug for the management of chronic pain. Its abuse can lead to varied presentations on the skin, which may include irregular ulcers with surrounding hyperpigmentation, induration, nodules, fibrous papules or scars along the blood vessels,[1] One of the characteristic of these lesions is that they are mostly present on accessible sites like arms. forearms, abdomen and thighs.

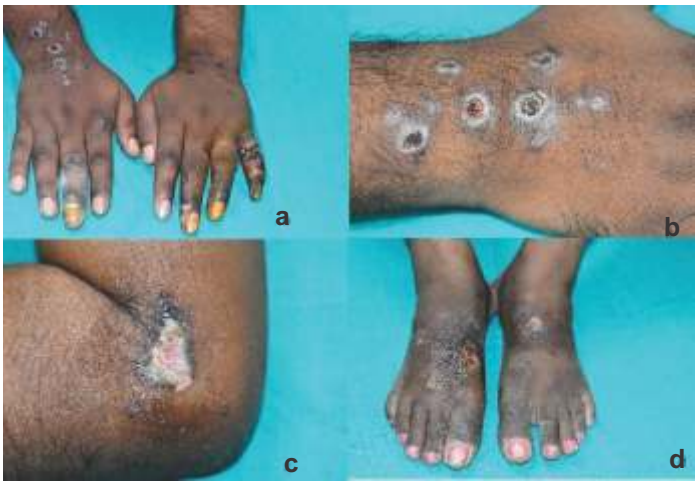

Figure 1 (a,b,c,d): **a**. multiple round to oval ulcers of variable sizes ranging from 2-3cm*1-2cm with well defined margins, sloping edges, overlying crusting and surrounded by peripheral hyperpigmentation present over dorsal aspect of both hands. Patchy gangrenous changes with areas of normal skin in between present on dorsal aspect of ring and little finger of left hand. **b**. close up view of variable sized multiple round to oval ulcers arranged in linear pattern on dorsal aspect of right hand. **c.** single triangular ulcer with sloping edges, floor covered by pale granulation tissue and surrounded by peripheral hyperpigmentation present on extensor aspect of left elbow. **d**. well defined variable sized ulcers surrounded by peripheral hyperpigmentation present on dorsal aspect of feet.

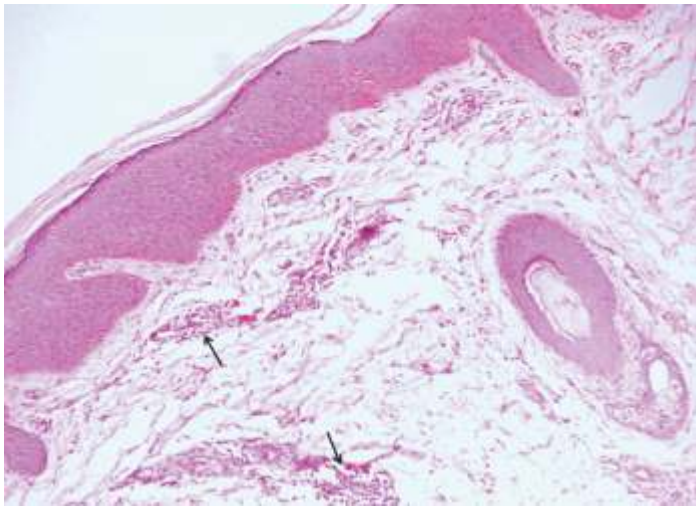

Figure 2: section shows mixed inflammatory infiltrate around superficial dermal vessels (arrows; Hematoxylin and Eosin,100x)

Exact pathogenesis is unknown however it is believed that pentazocine gets precipitated in extracellular fluid thus leading to chronic inflammatory response. Also the vasoconstrictive and vaso-occlusive effects of pentazocine leads to an ischaemic response.[2]

Histopathology shows mixed inflammatory infiltrate. Neutrophilic septal panniculitis can be seen if subcutaneous fat is involved. Pentazocine induced ulcers rarely respond to conservative treatment. Surgical excision followed by skin grafting is the treatment of choice.[2,3]

How to cite this article:
Suvirya S, Pathania S, Malhotra KP, Verma P, Kumar A. Cutaneous ulcers due to Pentazocine abuse. JDA Indian Journal of Clinical Dermatology. 2019;2:55

References

1. De D, Dogra s, Kanwar AJ. Pentazocine-induced leg ulcers and fibrous papules. Indian J Dermatol Venereol Leprol 2007;73:112-3
2. Sarraf S, Singh S, Pandey SS. Cutaneous complications of parenteral pentazocine abuse. Ind J Dermatol, Venereol, and Leprol 1996;3:191.
3. Prasad HR, Khaitan BK, Ramam M, Sharma VK, Pandhi RK, Agarwal S et al. Diagnostic clinical features of pentazocine-induced ulcers. Int J Dermatol 2005;44:910-5.

CASE REPORT
Year: 2019 • Volume: 2 • Issue: 2 • Page: 56-57

CUTANEOUS LARVA MIGRANS - A CASE REPORT

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Abstract

Cutaneous larva migrans or creeping eruption is one of the most common acquired tropical dermatosis caused by the filariform larvae of hookworm. We report a case of 55 years old female patient, farmer by occupation with cutaneous larva migrans over anterior abdominal wall which is an unusual site and was treated successfully with oral albendazole. We present this case for its occurrence on an unusual site.

Key words: Creeping eruption, Cutaneous larva migrans.

Introduction

Cutaneous larva migrans (syn, creeping eruption, sand worm eruption, plumbers itch, duck hunters itch) is common tropically acquired dermatosis caused by the accidental penetration of skin by third-stage larvae of animal hookworm; Ancylostoma brasiliense, A. caninum, A. ceylonicum, Uncineria stenocephala, and Bubostomum phlebotomum. [1] A. brasiliense (dog hookworm) is the commonest cause of these creeping eruptions in humans who act as dead-end hosts. The adult worms inhabit the small intestine of human, mainly jejunum and attach themselves to the mucous membrane by means of buccal armature and causes anemia. Cutaneous parasitic infestations are major source of morbidity affecting millions of people worldwide and tropical climate; overcrowding, poor hygiene and sanitary problems play very important role in their causation.[2] Humans acquire the infection while walking barefoot on sandpits, seashore or areas with loose and wet soil.Most frequent sites of infection are distal extremities, back , and buttocks.[3]

Case Report

A 55-year old female presented with the complaint of intensely itchy serpiginous lesion on the anterior abdominal wall of eight weeks duration. The eruption progressed daily, despite the application of some lotion to the eruption. She gave no history of trauma or bathing in ponds. She had no associated cough, wheezing, urticaria or fever. On examination, there was an erythematous, raised, curvilinear tract of approx. 25 cms long on the anterior abdominal wall, healing at one end and progressing at the other. [Figure 1a & 1b] The clinical picture was typical of cutneous larva migrans.[Figure 2a & 2b] Systemic examination and routine laboratory investigations were within normal limits.

She was treated with albendazole 400mg once a day for 3 consecutive days, pruritis diminished within 48 hours and the lesion showed signs of healing with hyperpigmentation 1 week after the initiation of treatment.

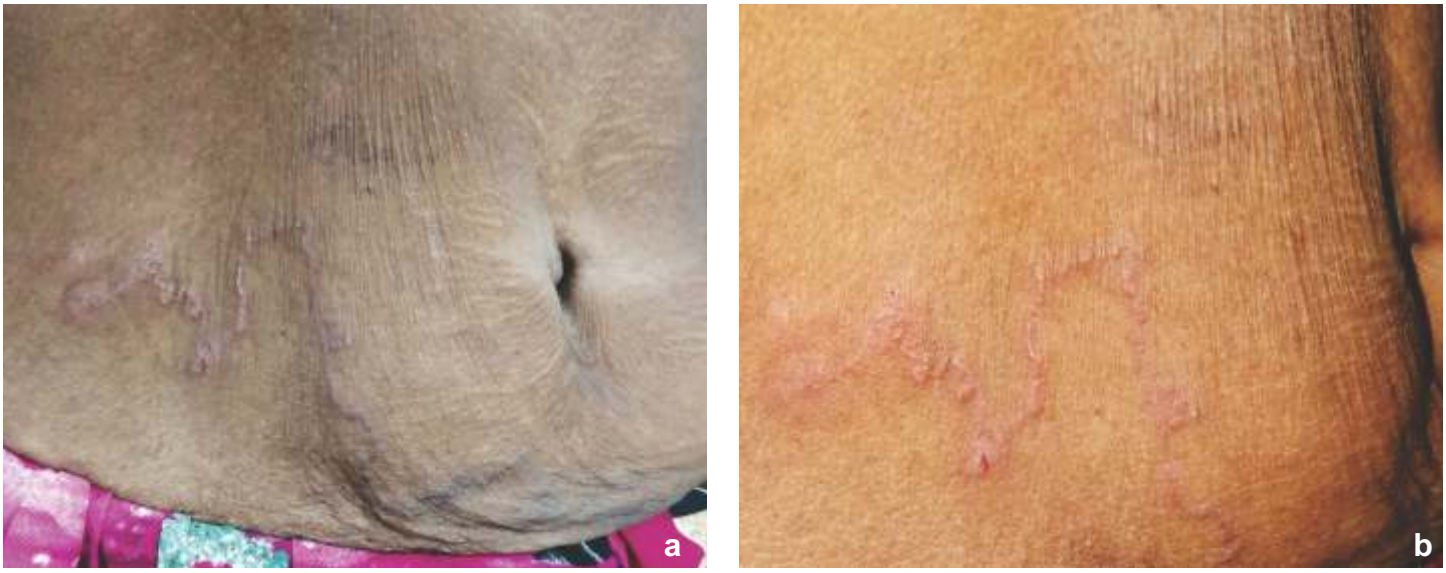

FIGURE 1 (a,b) : Characteristic curvilinear serpiginous erythematous lesions on the anterior abdominal wall

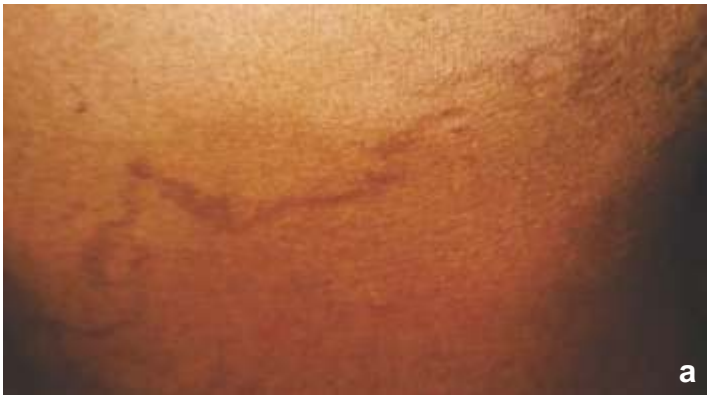

FIGURE 2 (a,b) : A curvilinear tract, about 25 cms long on the anterior abdominal wall, healing at one end and progressing at the other

Discussion

Creeping eruption is a parasitic dermatosis caused by the penetration of larvae of hookworm into the epidermis of human.[4] It is most commonly found in tropical and sub-tropical geographic areas and the southwestern United States with an overall prevalence of 8.2% . It has become an endemic in the Central America, South America, Southeast Asia, and Africa. It is characterized by an erythematous, serpiginous, pruritic, cutaneous eruption caused by percutaneous penetration and subsequent migration of the larvae of various nematode parasite.[5] The most frequent location is the distal lower extremities or buttocks. The most common cause is Ancylostoma braziliense and less common species are Ancylostoma caninum, Uncinaria stenocephala and Bunostomum phlebotomum.[3] The incubation period ranges from 1-6 days.Every larvae produces a single tract and migrates at a speed of 1-3cm/day in epidermis because of lack of enzymes necessary to penetrate and survive in the deeper dermis. In our patient, diagnosis was based on clinical features as there was no history of fever, pulmonary or intestinal symptoms. Biopsy is not much useful as the larvae may advance upto 2cm ahead of the visible burrow. Extensive lesions can be associated with wheezing, dry cough and urticaria. Creeping eruption is a self-limiting dermatosis which usually resolves in 2-8 weeks but rarely may persist for 2 years and the prognosis is excellent. Secondary infection and eczematization are common complications. Now a days, treatment of choice is 10% to 15% topical thiabendazole suspension, made by crushing a 500mg tablet of thiabendazole in 5g of a water-soluble cream, applied four times a day, for atleast 2 days after the last sign of burrow activity. This regimen is of great efficacy and least toxicity. Oral thiabendazole suspension of 500mg/5ml can be used twice per day for 2 days. Other useful drugs are albendazole 400mg/day for 3 consecutive days and oral ivermectin 150-200 ug/kg as a single dose.[6] Albendazole is a powerful antihelminthic against infections caused by intestinal nematodes and was first used to treat creeping eruption in 1982.[7] Liquid nitrogen cryotherapy can be used for a progressive end of larvae burrow. Avoidance of direct skin contact with contaminated soil by covering the ground with impenetrable material, wearing footwears, avoiding bare feet walking, and de-worming the pets are preventive measures. Literature review showed that only very few case with lesions on anterior abdominal wall have been reported till date so we present this case for its rarity. We conclude that sporadic cases of creeping eruption should be kept in mind in differential diagnosis of any creeping lesion even in non-endemic areas.

How to cite this article:
Goel B, Singh K, Agrawal S, Jain S, Agrawal S. Cutaneous Larva Migrans - A Case Report. JDA Indian Journal of Clinical Dermatology. 2019;2:56-57.

References

1. Davies HD, Sakuls P Keystone JS. Creeping eruption. A review of clinical presentation and management of 60 cases presenting to a tropical disease unit. Arch Dermatol 1993; 129:528-529.
2. Meffert JI. Parasitic infestations. In: Dermatology secrets 1st Ed. Fitzpatrick, Aeling J, editors. New Delhi, India: Jaypee Brothers; 1977. p.217.
3. Karthikeyan K, Thappa DM. Cutaneous larva migrans. Indian J. Dermatol Venerol Leprol 2001;68:252-8.
4. Heukelbach J, Feldmeier H. Epidemiological and clinical characteristics of hookworm-related cutaneous larva migrans. Lancet Infect Dis 2008;8:302-9.
5. Brenner MA, Patel MB. Cutaneous larva migrans: The creeping eruption. Cutis 2003;72:111-5.
6. Coumas E, Datry A, Paris L, et al. Efficacy of Ivermectin in the treatment of cutaneous larva migrans. Arch Dermatol 1992;128:994-5.
7. Coulaud JP, Binet D, Voyer C, Samson C, Moreau G, Rossignol JF. Treatment of the cutaneous larva migrans syndrome “Larbish” with albendazole. Apropos of 18 cases. Bull Soc Pathol Exot Filiales 1982;75:534-7.

CASE REPORT
Year: 2019 • Volume: 2 • Issue: 2 • Page: 58

A RARE CASE OF ANGIOMA SERPIGINOSUM

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Abstract

Angioma serpiginosum, a rare vascular nevoid disorder due to ectatic dilation of capillaries in the papillary dermis, is found almost exclusively in females. Affected individuals tend to have grouped erythematous punctate lesions on the lower limbs or buttocks.

Key words: Angioma serpiginosum, vascular nevoid disorder

Introduction

Angioma serpiginosum, a rare vascular nevoid disorder due to ectatic dilation of capillaries in the papillary dermis, is found almost exclusively in females. It was first described by Hutchinson in 1889.[1] Affected individuals tend to have grouped erythematous punctate lesions on the lower limbs or buttocks.

Case Report

A 26 year-old man presented to our dermatology department, with complaint of asymptomatic red, non raised skin lesions over left half of the neck, left upper part of abdomen and penis for 11 years. The patient's and family medical history were unremarkable. On examination there were well areas of multiple, small, asymptomatic, non-palpable, red punctate macules organized in small sheets over left side of neck, left upper part of abdomen and penis (figure no.1 & 2). Laboratory investigations like complete blood count, liver function test, renal function test, bleeding time and clotting time were within normal limit. Histopathologic examination of skin biopsy from abdomen, revealed multiple areas of congested dilated capillaries in the papillary dermis (figure no.3).

Discussion

Angioma serpiginosum is a rare, benign, acquired, vascular nevoid condition. It has female preponderance and mainly affects lower extremities and buttocks. The condition is an asymptomatic. It usually starts in early childhood and stabilizes in adults. It is rarely undergo complete spontaneous involution. Clinically, lesions are copper to bright red, punctate, non-blanchable or partially blanchable, grouped macules that may develop into papules with a background of erythema. Lesions enlarge by developing new lesions at the periphery with clearing of lesions in the center and this leads to a serpiginous or gyrate ring like morphology.[2]

It has no known etiology. Estrogen was considered to be an important hormone in the development of angioma serpiginosum supporting the role of hormones for the cause of increased incidence of angioma serpiginosum in women.[3] However, recently, the role of hormones in its pathogenesis was disproved due to the absence of estrogen and progesterone receptors on the involved blood vessels.[4]

Another proposed etiology is an abnormal vascular response to cold that manifests as formation and aggregation of newly formed capillaries that leads to large ectatic vessels in the papillary dermis.[1] Though rare it may also occur in men, as in our case.[5] There are rarely any reports in literature of angioma serpiginosum that involves genitalia and neck. We are reporting this case because of its rarity and atypical presentation.

How to cite this article:
Singh SK, Singh N, Rai T, Bohara A. A rare case of Angioma serpiginosum. JDA Indian Journal of Clinical Dermatology. 2019;2:58.

Reference

1. Chen JH, Wang KH, Hu CH, Chiu JS. Atypical angioma serpiginosum. Yonsei Med J2008;49:509-13.
2. Namazi MR, Handjani F. Angioma serpiginosum. Dermatol Online J2003;9:19
3. Xiao X, Hong L, Sheng M. Promoting effect of estrogen on the proliferation of hemangioma vascular endothelial cells in vitro. J Pediatr Surg1999;34:1603-5.
4. Bayramgurler D, Filinte D, Kiran R. Angioma serpiginosum with sole involvement. Eur J Dermatol2008;18:708-9.
5. Ilknur T, Fetil E, Akarsu S, Altiner DD, Ulukus C, Günes AT. Angioma serpiginosum: Dermoscopy for diagnosis, pulsed dye laser for treatment. J Dermatol 2006;33:252-5.

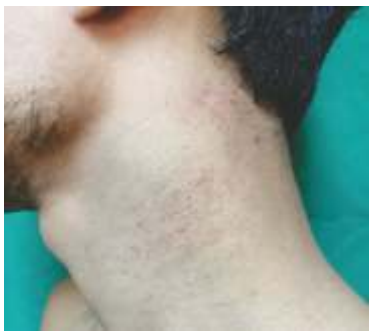

Figure 1: Sheet of red macule over left side of neck.

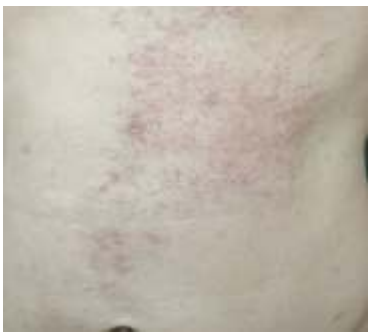

Figure 2: Sheet of red macule over left upper aspect of abdomen.

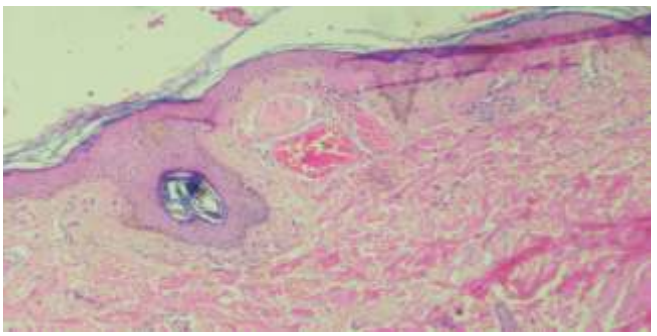

Figure 3: Congested dilated capillaries in papillary dermis. (HPE 100×)

CONCISE COMMUNICATIONS
Year: 2019 • Volume: 2 • Issue: 2 • Page: 59-60

COMPARATIVE STUDY OF TWO DIFFERENT CONCENTRATIONS OF KOH FOR ISOLATION OF DERMATOPHYTES ON DIRECT MICROSCOPSY

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Sir,

Mycotic infections, which depend on specific geographical and climatic areas, lifestyle, patient age, occupation, migration, sport activities, and drug therapy, are very common infections of skin, hair, and nails in many countries.[1,2] They are the fourth most common cause of health care problems affecting millions of people worldwide-especially in the pediatric group.[2] Superficial fungal infections have become a major cause of morbidity and mortality in clinically debilitated or immune compromised patients .[3]

Major etiological agents of dermatomycoses include dermatophytes and yeasts (Candida spp. and Malassezia spp.).[4] Diagnosis of superficial mycosis is often clinically established; however, laboratory confirmation is required for more difficult and atypical lesions and for type determination of causative fungi. Laboratory diagnostic procedures in dermatological mycology are based on direct microscopy and culture.

Potassium hydroxide (KOH) wet mount preparation used for direct microscopy is generally considered as conventional rapid test.[5]

Potassium hydroxide is a keratin digestion reagent that will dissolve proteins, lipids, and lyse epithelium. The fungus element will withstand the KOH solution (10%–30%), because it contains chitin and glycoproteins in the cell wall. KOH determines fungal elements between keratin cells quickly and irreversibly without staining particular specimens. This clearing agent provides a significant difference in brightness between fungal cells and the sample background and helps to improve quality of results.

A total 300 Samples were collected from clinically suspected cases of ringworm infection between January 2019 to June 2019, attending the outpatient department of Skin and V.D. at JNU medical college and hospital ,Jaipur.

Suspected lesions were cleaned with 70% alcohol to remove the dirt and contaminating bacteria. Samples were collected in sterile paper, folded, labeled and brought to the laboratory for further processing.

For direct microscopy the sample collected was screened for the presence of fungal elements by two methods:

(1) 10% Potassium hydroxide mount (KOH) and,

(2) 15% Potassium hydroxide mount(KOH) .

KOH Mount: A drop of 10% KOH and 15% KOH was kept on a clean, grease free glass slides separately. The sample from skin scrapings only (nail and hair samples were not included in this study) was placed in the KOH drop and slide passed through a

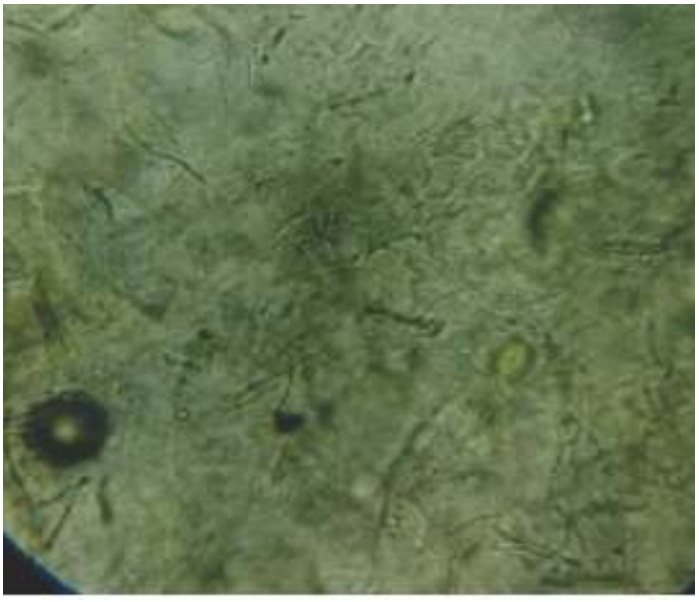

Figure 1: No fungal hyphae seen on 10 % KOH after 5 min.

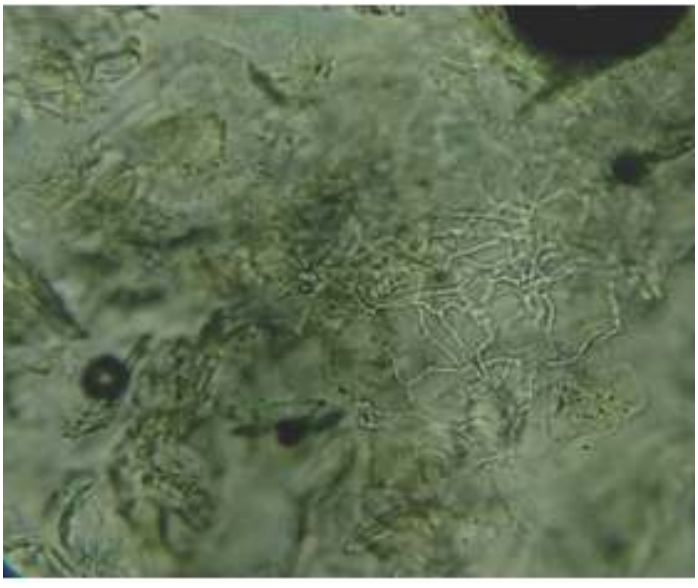

Figure 2: Fungal hyphae are visualised on 15 % KOH after 15 min.

burner flame to hasten keratolysis. When keratolysis softened the sample, a clean glass cover slip was kept on the sample and pressed, preventing formation of air bubbles.

The sample was kept in KOH for a variable duration ranging from 5 minutes to 15 minutes, depending upon the thickness of the scales and examined every 5 minutes. Each slide was thoroughly examined for the presence of filamentous, septate, branched hyphae with or without arthrospores crossing the margins of the squamous epithelial cells of the skin.

In total 300 clinically suspected cases, 240 cases were positivity for fungal hyphae. While comparative direct microscopic examination, it was observed that 15% KOH preparation produced rapid clearing of keratin and faster visualization of fungal hyphae as compared to 10 % KOH preparation (Figure 1,2). In 15% KOH fungal hyphae could be visualized in 5 minutes, while 10% KOH took 10 to 15 minutes for complete clearing of keratin (Table 1).

Time duration	No. of positive cases on 10% KOH	No. of positive cases on 15 % KOH
After 5 min.	---	150
After 15 min.	240	90
Total positive cases	240	240

How to cite this article:
Sharma K, Mathur D. Comparative study of two different concentrations of KOH for isolation of dermatophytes on direct microscopsy. JDA Indian Journal of Clinical Dermatology. 2019;2:59-60.

References

1. Faure-Cognet O, Fricker-Hidalgo H, Pelloux H, Leccia MT. Superficial fungal infections in a French teaching hospital in Grenoble area: retrospective study on 5470 samples from 2001 to 2011. Mycopathologia 2016;181:59–66.
2. Prakash R, Prashanth HV, Ragunatha S, Kapoor M, Anitha T, Krishnamurthy V. Comparative study of efficacy, rapidity of detection, and cost-effectiveness of potassium hydroxide, calcofluor white, and Chicago sky blue stains in the diagnosis of dermatophytoses. Int J Dermatol 2016;55:e172–175.
3. Kumar RS, Ganvir S, Hazarey V. Candida and calcofluor white: Study in precancer and cancer. J Oral Maxillofac Pathol 2009;13:2–8.
4. Babayani M, Salari S, Hashemi S, Almani PGN, Fattahi A. Onychomycosis due to dermatophytes species in Iran: Prevalence rates, causative agents, predisposing factors and diagnosis based on microscopic morphometric findings. J Mycol Med 2018;28:45–50.
5. Afshar P, Khodavaisy S, Kalhori S, Ghasemi M, Razavyoon T. Onychomycosis in north-East of iran. Iran J Microbiol 2014;6:98–103.

A Publication of Jaipur Dermatology Association