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ACNE VULGARIS TREATMENT : THE CURRENT SCENARIO

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Introduction

Acne vulgaris is one of the commonest skin disorders which dermatologists have to treat, mainly affect adolescents, though it may present at any age. Acne by definition is multifactorial chronic inflammatory disease of pilosebaceous units.[1] Various clinical presentations include seborrhoea, comedones, erythematous papules and pustules, less frequently nodules, deep pustules or pseudocysts, and ultimate scarring in few of them. Acne has four main pathogenetic mechanism—increased sebum productions, follicular hyperkeratinization, *Propionibacterium acne (P. acne)* colonization, and the products of inflammation.[2–5]

In recent years, due to better understanding of the pathogenesis of acne, new therapeutic modalities are designed.[3] Availability of new treatment options to compliment the existing armamentarium should help to achieve the successful therapy of greater numbers of acne patients, ensure improved tolerability and fulfil patient expectations. Successful management of acne needs careful selection of anti-acne agents according to clinical presentation and individual patient needs.

The purpose of this article is to review the treatment options available with us in the present scenario.

Topical therapy

Topical therapy is useful in mild and moderate acne, as monotherapy, in combination and also as maintenance therapy.

A. Benzoyl peroxide

It is an effective topical agent since many years and is available in different formulations (washes, lotions, creams, and gels) and concentrations (2.5–10%).[4,6]

The stability is very dependent on its vehicle. Gels are generally more stable and active and water-based gel being less irritant is more preferred over creams and lotions.[7,8] Benzoyl peroxide is a broad spectrum bactericidal agent which is effective due to its oxidizing activity.[7]

The drug has an anti-inflammatory, keratolytic, and comedolytic activities, and is indicated in mild-to-moderate acne vulgaris. Clinicians must make a balance among desired concentration, the vehicle base, and the risk of adverse effects, as higher concentration is not always better and more efficacious.[9]

The main limitation of benzoyl peroxide is concentration dependent cutaneous irritation or dryness and bleaching of clothes, hair, and bed linen.[10] It can induce irritant dermatitis with symptoms of burning, erythema, peeling, and dryness.[11] This occurs within few days of therapy and mostly subsides with continued use.

B. Topical retinoids

Retinoids have been in use for more than 30 years. Topical retinoids target the microcomedo–precursor lesion of acne. There is now consensus that topical retinoid should be used as the first-line therapy, alone or in combination, for mild-to-moderate inflammatory acne and is also a preferred agent for maintenance therapy.

Its effectiveness is well documented, as it targets the abnormal follicular epithelial hyperproliferation, reduces follicular plugging and reduces microcomedones and both noninflammatory and inflammatory acne lesions.[12–14] Their biological effects are mediated through nuclear hormone receptors (retinoic acid receptor RAR and retinoids X receptor RXR with three subtypes α, β, and γ) and cytosolic binding proteins.[15] Retinoic acid metabolism blocking agents (RAMBAs) such as liarozole have been developed recently to overcome the emergence of all-*trans*-retinoic acid resistance.[16]

Tretinoin, adapalene, tazarotene, isotretinoin, metretinide, retinaldehyde, and β-retinoyl glucuronide are currently available topical retinoids.[17] The most studied topical retinoids for acne treatment worldwide are tretinoin and adapalene.[18] There is no consensus about relative efficacy of currently available topical retinoids (tretinoin, adapalene, tazarotene, and isotretinoin). The concentration and/or vehicle of any particular retinoid may impact tolerability.[19] Adapalene was generally better tolerated than all other retinoid with which it was compared.[20,21] Tretinoin has recently become available in formulations with novel delivery systems which improves tolerability. One

such product Retin-A Micro (0.1% gel) contains tretinoin trapped within porous copolymer microspheres. Avita, the tretinoin is incorporated within a polyoylprepolymer (PP-2). Each of the theses formulations releases tretinoin slowly within the follicle and onto the skin surface, which in turn reduces irritancy with the same efficacy.[22]

The main adverse effects with topical retinoid is primary irritant dermatitis, which can present as erythema, scaling, burning sensation and can vary depending on skin type, sensitivity, and formulations.

C. Topical antibiotics

Many topical antibiotics formulations are available, either alone or in combination. They inhibit the growth of*P. acne* and reduce inflammation. Topical antibiotics such as erythromycin and clindamycin are the most popular in the management of acne and available in a variety of vehicles and packaging.[23] Clindamycin and erythromycin were both effective against inflammatory acne in topical form in combination of 1–4% with or without the addition of zinc.[24–26] An addition of topical 2% zinc sulfate and nicotinamide was no different than placebo for the treatment of acne.[27–29] Topical clarithromycin, azithromycin, and nadifloxacin are available in India, but trials for their efficacy and safety are lacking.

Side effects though minor includes erythema, peeling, itching, dryness, and burning, pseudomembranous colitis which is rare, but has been reported with clindamycin.[30] A most important side effect of topical antibiotics is the development of bacterial resistance and cross resistance; therefore, it should not be used as monotherapy.

D. Other topical/new agents

Combination therapy: Benzoyl peroxide has the advantage to prevent and eliminate the development of *P. acne* resistance. Therefore it is being more preferred as combination therapy. Its efficacy and tolerability are enhanced when combined with topical erythromycin or clindamycin, confirmed on various trials.[6,31–34] Benzoyl peroxide can be combined with tretinoin and found to be superior to monotherapy. Both the molecules should not be applied simultaneously as benzoyl peroxide may oxidize tretinoin.[35] A combination of topical retinoid and topical antimicrobial is more effective in reducing both inflammatory and noninflammatory acne lesions than either agent used alone.[36] Topical clindamycin and benzoyl peroxide applied once daily and fixed clindamycin phosphate 1.2% and tretinoin 0.025% in aqueous-based gel formulation used once daily are both found to be effective treatment for acne. Addition of zinc acetate to clindamycin and erythromycin gel showed equivalent efficacy but probably reduces the development of microbial resistance.[37]

Salicylic acid: It has been used for many years in acne as a comedolytic agent, but is less potent than topical retinoid.[38]

Azelaic acid: It is available as 10–20% topical cream which has been shown to be effective in inflammatory and comedonal acne.[39,40]

Lactic acid/Lactate lotion: It is found to be helpful in preventing and reduction of acne lesion counts.[41]

Tea tree oil 5%: Initial clinical response with this preparation is inevitably slower compared to other treatment modalities.[42]

Picolinic acid gel 10%: It is an intermediate metabolite of the amino acid, tryptophan. It has antiviral, antibacterial, and immunomodulatory properties. When applied twice daily for 12 weeks found to be effective in both type of acne lesions, but further trials are needed to confirm its safety and efficacy.[43]

Dapsone gel 5%: It is a sulfone with anti-inflammatory and antimicrobial properties. The trials have confirmed that topical dapsone gel 5% is effective and safe as monotherapy and in combination with other topical agents in mild-to-moderate acne vulgaris.[44]

Systemic Therapy

Systemic antibiotics

0Oral antibiotics are indicated in mainly moderate-to-severe inflammatory acne.[5] Tetracyclines and derivatives still remain the first choice. Macrolides, co-trimoxazole, and trimethoprim are other alternatives for acne.[45] The following agents should not be used in acne due to lack of efficacy and safety consideration such as cephalosporins, sulphonamide, and gyrase inhibitors.[4]

Tetracycline (500 mg–1 g/day), doxycycline (50–200 mg/day), minocycline (50–200 mg/day), lymecycline (150–300 mg/day), erythromycin (500 mg–1 g/day), co-trimoxazole, trimethoprim, and recently azithromycin (500 mg thrice weekly) are being used successfully in acne.[46–50] Minocycline and doxycycline are more effective than tetracycline and erythromycin.[46,47] Recently, doxycycline in subantimicrobial dose (20 mg twice daily) and an extended-release minocycline tablet (1 mg/kg/day) were used and found to be effective, but further controlled trials are needed.[37,51]

Gastrointestinal upset and vaginal candidiasis are most common side effects. Doxycycline can be associated with photosensitivity. Minocycline may produce pigment deposition in the skin, mucous membrane, and teeth. Autoimmune hepatitis, systemic

lupus erythematosus-like syndrome, and serum sickness-like reactions occur rarely with minocycline.

Long-term therapy with oral antibiotic not only threat to resistant of *P. acne*, but also to coagulase negative staphylococci on the skin, *Staphylococcus aureus* in the nares, and streptococci in the oral cavity.[52,53] There is a significant association between antibiotic used in acne and the incidence of upper respiratory tract infection.[54]

Optimizing antibiotic therapy: Research has demonstrated that problem of antibiotic-resistant *P. acne* is increasing, and it is most common with erythromycin. Therefore there is need to consider for antibiotic prescribing policies and to advocate the use of nonantibiotic preparations wherever possible.

- Antibiotic monotherapy is to be avoided and it can be combined with topical retinoid or benzoyl peroxide as per need.
- Wherever possible the duration of therapy should be limited. The usual minimum duration of therapy is 6–8 weeks but can be given up to 12–18 weeks and more.
- It is advisable to use the same antibiotic if retreatment is necessary and use benzoyl peroxide for a minimum of 5–7 days between antibiotic courses to reduce resistant organism.
- Concomitant use of oral and topical therapy with chemically dissimilar antibiotics is to be avoided.

Hormonal therapy

It may be needed in female patients with severe seborrhoea, clinically apparent androgenetic alopecia, seborrhoea/acne/hirsuitism/alopecia (SAHA) syndrome, late-onset acne (acne tarda), and with proven ovarian or adrenal hyperandrogenism.

The main approach of hormonal therapy in acne is to prevent the effects of androgens on the sebaceous gland and probably follicular keratinocytes as well. It is wiser to take consultation with gynecologist before starting therapy.

a) Oral contraceptives

Estrogen is commonly combined with progestin to avoid the risk of endometrial cancer. Anti-acne effect of oral contraceptive governed by decreasing level of circulatory androgens through inhibition of luteinizing hormones (LH) and follicle stimulating hormone (FSH).[55,56] The currently FDA approved agents include norgestimate with ethinyl estradiol, and norethindrone acetate with ethinyl estradiol.

b) Spironolactone

They functions primarily as a steroidal androgen receptor blocker. It may cause hyperkalemia (when higher doses are prescribed or when there is cardiac or renal compromise), menstrual irregularities.[57,58]

c) Cyproterone acetate

It is the first androgen receptor blocking agent to be well studied and found to effective in acne in females.[59,60] Higher doses have been found to be more effective than lower dose. It is also combined (2 mg) with ethinyl estradiol (35 or 50 μg) as an oral contraceptive formulation to treat acne.

d) Flutamide

It is useful in acne when given in females with hirsuitism.[60,61]

Oral isotretinoin

Oral retinoid is indicated in severe, moderate-to-severe acne or lesser degree of acne producing physical or psychological scarring, unresponsive to adequate conventional therapy.[62,63] It is the only drug that affects all four pathogenic factors implicated in the etiology of acne.

Although there are many studies, but very large evidence-based study is lacking to confirm the dosing schedule. The approved dose is 0.5–2 mg/kg/day, which is usually given for 20 weeks.[64–66] Alternatively, lower dose can be used for longer period, with a total cumulative dose of 120 mg/kg.[65] New developments and future trends are low-dose long-term isotretinoin regimens and new isotretinoin formulations (micronized isotretinoin).[51]

Side effects include those of musculoskeletal, mucocutaneous, and ophthalmic systems, as well as headache, and central nervous system effects.[66] Most of the side effects are temporary and resolves after the drug is discontinued. Oral isotretinoin is a potent teratogen. Therefore women of child-bearing age require negative pregnancy test before treatment, strict contraceptive measures essential before, during and even 6 weeks posttherapy. Due to this, in United States, a new risk management programme (iPLEDGE) has been developed where all the patients receiving this drug have to register.[67,68]

Physical Treatment

A. Lesion removal

a) Comedones

Both open and closed comedones can be removed mechanically with comedone extractor and a fine needle or a pointed blade.[4] Preprocedure topical retinoid application makes the procedure easier. Gentle cautery and laser puncture of macrocomedones are also useful procedure.[69] The limitations of comedo extraction include incomplete extraction, refilling, and the risk of tissue damage.

b) Active deep inflammatory lesions

Aspiration of deep inflamed lesion may be needed in few cases which are followed by IL steroid injection in cysts and sinus tract.[4,70]

B. Phototherapy

a) Visible light

They are indicated for mild-to-moderate inflammatory acne. *In vitro* and *in vivo* exposure of acne bacteria to 405–420 nm of ultraviolet free *blue light* results in the photo-destruction through the effect on the porphyrin produced naturally by *P. acne*.[71] Use of limited spectrum wavelength, such as blue light (peak at 415 nm), and mixed blue and red light (peak at 415 and 660 nm) have been found to be effective in reducing acne lesions after 4–12 weeks.[72,73]

b) Photodynamic therapy

(with addition of δ-aminolevulinic acid) and pulsed dye laser (585 nm) were also effective in acne, but further trials are needed to confirm the same.[74–76]

Physical treatment of scars

Acne scar can be broadly divided into two groups, those involving tissue losses (Ice pick scar, Box scar, Rolling scar, and Follicular macular atrophy) and those involving tissue excess (hypertrophic scars or keloids). Currently available treatment for scars include simple excision, and suturing, either alone or combined with punch grafting and laser resurfacing, dermabrasion, various type of lasers, chemical peels, and fillers. For hypertrophic scars, treatment includes pressure therapy, IL corticosteroid, 5-fluorouracil and bleomycin injections, surgical excision, radiotherapy, laser therapy and cryotherapy.

All the procedures have their own merits and demerits; to be chosen carefully seeing the merit.[77–79]

Acne and diet

Dietary restriction has not been demonstrated to be benefit in the treatment of acne.[80,81] The myth that diet affects acne is widespread, but previous studies are not supporting it. Of late, various authors again claiming that there is the definite role of diet in acne but to conclude that further controlled trials are needed.[82–84] It has been shown that the prevalence of acne is lower in rural, nonindustrialized societies than in modernized western populations may be due to lower glycemic index diet, claims one trial.[85] Although not currently recognized within our dermatology standard of care, but due to "consistent and good quality patient oriented evidence", dietary management of acne appears to be accumulating.

The benefit of dietary management in the treatment of acne has been neither demonstrated nor disproved.[85,86]

Conclusion

Various topical and systemic drugs are available to treat acne, which may sometimes confuse the treating dermatologist. To overcome this situation a panel of physicians and researchers worked together as a *"Global Alliance"* and *"Task Force"* to improve outcomes in acne treatment.[87–89] They have tried to give consensus recommendation for the treatment of acne, mostly evidence-based and inputs from various countries. Similar alliance has also been formed in India recently with their recommendations.[90]

Topical retinoid

- It should be primary treatment for most forms of acne vulgaris.
- To be applied to entire affected area.
- Antimicrobial to be added for inflammatory lesions.
- Essential part of maintenance therapy.

Combination therapy

- It works better and clearing of lesion is faster.
- Stop antibiotic if inflammatory lesion subsides.
- If withdrawal is not possible, switch to benzoyl peroxide plus an antibiotic.
- Topical retinoid can be continued to prevent remission.

Antibiotics

- Oral and topical antibiotics not to be used as monotherapy to prevent bacterial resistance.

- Helpful in moderate-to-severe acne.
- Generally oral antibiotics are well tolerated, sometimes associated with severe adverse events.
- Always use the same antibiotic if it was effective previously.
- Doxycycline and minocyclines are more effective than tetracycline.
- Do not use chemically dissimilar oral and topical antibiotic together.

Hormonal therapy

It is an excellent choice in women requiring oral contraceptive (estrogen containing) for other reason and having moderate-to-severe acne with SAHA symptoms. Oral antiandrogen like spironolactone and cyproterone acetate can be useful in the treatment of acne.

Oral isotretinoin

It is approved in severe recalcitrant nodulocystic acne. It can also be used in moderate-to-severe acne vulgaris resistant to conventional therapy, frequently relapsing, with severe psychological and physical scarring due to acne. Pre-treatment counselling, patient selection, and monitoring are critical due to its side effects like teratogenicity, and adverse psychiatric events.

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References

1. Simpson NB, Cunliffe WJ. Disorders of the sebaceous glands. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's Text book of Dermatology. 7th ed. Vol. 43. Blackwell Science; 2004. pp. 43.1–43.75.

2. Gollnick HP, Zouboulis CC, Akamatsu H, Kurokawa I, Schulte A. Pathogenesis and pathognesis-related treatment of acne. J Dermatol. 1991;18:489–99. [PubMed]

3. Leyden JJ. New understanding of the pathogenesis of acne. J Am Acad Dermatol. 1995;32:515–25.[PubMed]

4. Plewig G, Kligman AM. Acne and Rosacea. 3rd ed. New York: Springer-Verlag; 2000.

5. Cunliffe WJ, Gollnick HP. Acne: Diagnosis and management. 1st ed. London: Martin Dunitz Ltd; 2001.

6. Packman AM, Brown RH, Dunlap FE, Kraus SJ, Webster GF. Treatment of acne vulgaris: Combination of 3% erythromycin and 5% benzoyl peroxide in a gel compared to clindamycin phosphate lotion. Int J Dermatol. 1996;35:209–11. [PubMed]

7. Yang DJ, Quan LT, Hsu S. Topical antibacterial agents. In: Wolverton SE, editor. comprehensive dermatologic drug therapy. 2nd ed. Philadelphia: Saunders Elsevier; 2007. pp. 525–46.

8. Fyrand O, Jakobsen HB. Water-based versus alcohol-based benzoyl peroxide preparations in the treatment of acne vulgaris. Dermatologica. 1986;172:263–7. [PubMed]

9. Mills OH, Jr, Kligman AM, Pochi P, Comite H. Comparing 2.5%, 5% and 10% benzoyl peroxide on inflammatory acne vulgaris. Int J Dermatol. 1986;25:664–7. [PubMed]

10. Bojor RA, Cunliffe WJ, Holland KT. The short term treatment of acne vulgaris with benzoyl peroxide: Effects on the surface and follicular cutaneous microflora. Br J Dermatol. 1995;132:204–8. [PubMed]

11. Eady EA, Cove JH, Joanes DN, Cunliffe WJ. Topical antibiotics for the treatment of acne vulgaris: A critical evaluation of the literature on their clinical benefit and comparative efficacy. J Dermatol Treat.1990;1:215–26.

12. Krishnan G. Comparison of two concentrations of tretinoin solution in the topical treatment of acne vulgaris. Practitioner. 1976;216:106–9. [PubMed]

13. Shalita A, Weiss JS, Chalker DK, Ellis CN, Greenspan A, Katz HI, et al. A comparison of the efficacy and safety of adapalene gel 0.1% and tretinoin gel 0.025% in the treatment of acne vulgaris: A multicentric trial. J Am Acad Dermatol. 1996;34:482–5. [PubMed]

14. Leyden JJ, Shalita A, Thiboutot D, Washenik K, Webster G. Topical tretinoin in inflammatory acne: A retrospective, investigator-blinded, vehicle-controlled, photographic assessment. Clin Ther. 2005;27:216–24.[PubMed]

15. Kang S. The mechanism of topical retinoids. Cutis. 2005;75:14–24. [PubMed]

16. Njar VC, Gedia L, Purushottam P, Chopra P, Vasaitis TS, Khandelwal A, et al. Retinoic acid metabolism blocking agents (RAMBAs) for treatment of cancer and dermatological disease. Bioorg Med Chem. 2006;14:4323–40. [PubMed]

17. Krautheim A, Gollnick H. Acne; topical treatment. Clin Dermatol. 2004;22:398–407. [PubMed]

18. Jain S. Topical tretinoin or adapalene in acne vulgaris: An overview. J Dermatol Treat. 2004;15:200–7.[PubMed]

19. Galvin SA, Gilbert R, Baker M, Guibal F, Tuley MR. Comparative tolerance of adapalene 0.1% gel and six different tretinoin formulations. Br J Dermatol. 1998;139:34–40. [PubMed]

20. Shalita A, Weiss JS, Chalker DK, Ellis CN, Greenspan A, Katz HI, et al. A comparison of the efficacy and safety of adapalene 0.1% and tretinoin gel 0.025% in the treatment of acne vulgaris: A multicentric trial.J Am Acad Dermatol. 1996;34:482–5. [PubMed]

21. Percy SH. Safety and efficacy of adapalene gel 0.1% in acne vulagaris: Results of post-marketing surveillance study. Indian J Dermatol Venereol Leprol. 2003;69:277–80. [PubMed]

22. Wolfe JE. An update of recent clinical trials examining adapalene and acne. J Eur Acad Venereol.2001;15:23–9. [PubMed]

23. Johnson BA, Nunley JR. Topical therapy for acne vulgaris.How do you choose the best drug for each patient? Postgrad Med. 2000;107:73. [PubMed]

24. Dobson RL, Belknap BS. Topical erythromycin solution in acne.Results of multicentric trial. J Am Acad Dermatol. 1980;3:478–82. [PubMed]

25. Shalita AR, Smith EB, Bauer E. topical erythromycin vs clindamycin therapy for acne-A multicenter, double blind comparison. Arch Dermatol. 1984;120:351–5. [PubMed]

26. Kurokawa I, Nishijima S, Kawabata S. Antimicrobial susceptibility of *Propionibacterium acne* isolated from acne vulgaris. Eur J Dermatol. 1999;9:25–8. [PubMed]

27. Bojar RA, Eady EA, Jones CE, Cunliffe WJ, Holland KT. Inhibition of erythromycin-resistant propionibacteria on the skin of acne patients of topical erythromycin with and without zinc. Br J Dermatol.1990;130:329–36. [PubMed]

28. Cochrane RJ, Tucker SB, Flannigan SA. Topical zinc therapy for acne vulgaris. Int J Dermatol.1985;24:188–90. [PubMed]

29. Sardesai VR, Kambli VM. Comparison of efficacy of topical clindamycin and nicotinamide combination with plain clindamycin for the treatment of acne vulgaris and

acne resistant to topical antibiotics. Indian J Dermatol Venereol Leprol. 2003;69:138–9. [PubMed]

30. Parry MF, Rha CK. Pseudomembranous colitis caused by topical clindamycin phosphate. Arch Dermatol. 1986;122:583–4. [PubMed]

31. Lyon RE. Comparative effectiveness of benzoyl peroxide and tretinoin in acne vulgaris. Int J Dermatol.1978;17:246–51. [PubMed]

32. Chu A, Huber FJ, Plott RT. The comparative efficacy of benzoyl peroxide 5%/ erythromycin 3% gel and erythromycin 4%/ zinc 1.2% solution in the treatment of acne vulgaris. Br J Deramtol. 1997;136:235–8.[PubMed]

33. Leyden JJ, Berger RS, Dunlap FE, Ellis CN, Connolly MA, Levy SF. Comparison of the efficacy and safety of a combination topical gel formulation of benzoyl peroxide and clindamycin with benzoyl peroxide, clindamycin and vehicle gel in the treatment of acne vulgaris. Am J Clin Dermatol. 2001;2:33–9. [PubMed]

34. DelRosso JQ. Combination topical therapy in the treatment of acne. Cutis. 2006;78:5–12. [PubMed]

35. Handojo I. The combined use of topical benzoyl peroxide and tretinoin in the treatment of acne vulgaris.Int J Dermatol. 1979;18:489–96. [PubMed]

36. Zouboulis CC, Derumeaux L, Decroix J, Maciejewska-Udziela B, Cambazard F, Stuhlert A. A multicentric, single- blind, randomized comparison of fixed clindamycin phosphate/tretinoin gel formulation (Velac) applied once daily and a clindamycin lotion formulation (Dalacin T) applied twice daily in the treatment of acne vulgaris. Br J Dermatol. 2000;143:498–505. [PubMed]

37. Katsamba A, Dessinioti C. New and emerging treatments in dermatology: Acne. Dermatol Ther.2008;21:86–95. [PubMed]

38. Shalita AR. Treatment of mild and moderate acne vulgaris with salicylic acid in an alcohol-detergent vehicle. Cutis. 1981;28:556–8, 561. [PubMed]

39. Cunliffe WJ, Holland KT. Clinical and laboratory studies on treatment with 20% azelaic acid cream for acne. Acta Derm Venereol Suppl (Stockh) 1989;143:31–4. [PubMed]

40. Iraji F, Sadeghinia A, Shahmoradi Z, Siadat AH, Jooya A. Efficacy of topical azelaic acid gel in the treatment of mild-moderate acne vulgaris. Indian J Dermatol Venereol Leprol. 2007;73:94–6. [PubMed]

41. Garg T, Ramam M, Pasricha JS, Verma KK. Long term topical application of lactic acid/ lactate lotion as a preventive treatment for acne vulgaris. Indian J Dermatol Venereol Leprol. 2002;68:137–9. [PubMed]

42. Enshaieh S, Jooya A, Siadat AH, Iraji F. The efficacy of 5% topical tea tree oil gel in mild to moderate acne vulgaris: A randomized, double-blind placebo controlled study. Indian J Dermatol Venereol Leprol.2007;73:22–5. [PubMed]

43. Heffernan MP, Nelsoa MM, Anadkat MJ. A pilot study of the safety and efficacy of picolinic acid gel in the treatment of acne vulgaris. Br J Dermatol. 2007;136:548–52. [PubMed]

44. DelRosso JQ. New topical therapies for the treatment of acne vulgaris. Cutis. 2007;80:400–10.[PubMed]

45. Mernadier J, Alirezai M. Systemic antibiotics for acne. Dermatology. 1998;196:135–9. [PubMed]

46. Harrison PV. A comparison of doxycycline and minocycline in the treatment of acne vulgaris. Clin Exp Dermatol. 2003;139:459–64.

47. Goulden V, Glass D, Cunliffe WJ. Safety of long term high dose minocycline in the treatment of acne.Br J Dermatol. 1996;134:693–5. [PubMed]

48. Parsad D, Pandhi R, Nagpal R, Negi KS. Azithromyin monthly pulse vs daily doxycyline in the treatment of acne vulgaris. J Dermatol. 2000;;28:1–4. [PubMed]

49. Singhi MK, Ghiya DC, Dhabai RK. Comparison of oral azithromycin pulse with daily doxycycline in the treatment of acne vulgaris. Indian J Dermatol Venereol Leprol. 2003;69:274–6. [PubMed]

50. Bardazzi F, Savoia F, Parente G, Tabanelli M, Balestri R, Spadola G, et al. Azithromycin, a new therapeutic strategy for acne in adolscents. Dermatol Online J. 2007;13:4. [PubMed]

51. Del Rosso JQ. Recently approved systemic therapies for acne vulgaris and rosacea. Cutis. 2007;80:113–20. [PubMed]

52. Espersen F. Resistance to antibiotics used in dermatological practice. Br J Dermatol. 1998;139:4–8.[PubMed]

53. Eady EA, Jones CE, Tipper JL, Cove JH, Cunliffe WJ, Layton AM. Antibiotic resistant propionibacterium in acne: Need for policies to modify antibiotic usage. Br Med J. 1993;306:555–6.[PMC free article] [PubMed]

54. Margolis DJ, Bowe WP, Hoffstad O, Berlin JA. Antibiotis treatment of acne may be associated with upper respiratory tract infection. Arch Dermatol. 2005;141:1132–6. [PubMed]

55. Thorneycroft H, Gollnick H, Schellschmidt I. Superiority of combined contraceptive containing drospirenone to a triphasic preparation containing norgestimate in acne treatment. Cutis. 2004;74:123–30.[PubMed]

56. Huber J, Walch K. Treating acne with oral contraceptives use of lower doses. Contraception.2006;73:23–9. [PubMed]

57. Muhlemann MF, Carter GD, Cream JJ, Wise P. Oral spironolactone: An effective treatment for acne vulgaris in women. Br J Dermatol. 1986;115:227–32. [PubMed]

58. Hatwal A, Bhatt RP, Agrawal JK, Singh G, Bajpai HS. Spironolactone and cimetidine in treatment of acne. Acta Derm Venereol. 1988;68:84–7. [PubMed]

59. Fugère P, Percival-Smith RK, Lussier-Cacan S, Davignon J, Farquhar D. Cypoterone acetate/ ethinyl estradiol in the treatment of acne.A comparative dose-response study of estrogen component. Contraception.1990;42:225–34. [PubMed]

60. Shaw JC. Hormonal therapy in acne. Dermatol Clin. 2001;19:169–78. [PubMed]

61. 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;197:351–7. [PubMed]

62. Dhir R, Gehi NP, Agarwal R, More YE. Oral isotretinoin is as effective as a combination of oral isotretinoin and topical anti-acne agents in nodulocystic acne. Indian J Dermatol Venereol Leprol.2008;74:187. [PubMed]

63. Sheth R. Isotretinoin: An Indian experience. Indian J Dermatol Venereol Leprol. 2001;67:180–2.[PubMed]

64. 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. [PubMed]

65. Amichai B, Shemar A, Grunwald MH. Low-dose isotretinoin in the treatment of acne vulgaris. J Am Acad Dermatol. 2006;54:644–6. [PubMed]

66. Di Giovanna JJ. Systemic retinoid therapy. Dermatol Clin. 2001;19:161–7. [PubMed]

67. Milchell AA, Van Bennekom CM, Louik C. A pregnancy prevention programme in women of child bearing age receiving isotretinoin. N Eng J Med. 1995;333:101–6. [PubMed]

68. Dai WS, LaBraivo JM, Stern RS. Epidemiology of isotretinoin exposure during pregnancy. J Am Acad Dermatol. 1992;26:599–606. [PubMed]

69. Pepall LM, Cosgrove MP, Cunliffe WJ. Ablation of white-heads by cautery under topical anaesthesia. Br J Dermatol. 1991;125:256–9. [PubMed]

70. Levine RM, Rasmussen JE. Intralesional corticostaeroids in the treatment of nodulo-cystic acne. Arch Dermatol. 1983;119:480–1. [PubMed]

71. Elman M, Lebzelter J. Light therapy in the treatment of acne vulgaris. Dermatol Surg. 2004;30:139–46.[PubMed]

72. Papageorgiou P, Katsambas A, Chu A. Phototherapy with blue (415 nm) and red (660nm) light in the treatment of acne vulgaris. Br J Dermatol. 2000;142:973–8. [PubMed]

73. Cunliffe WJ, Goulden V. Phototherapy and acne vulgaris. Br J Dermatol. 2000;142:855–6. [PubMed]

74. Itoh Y, Ninomiya Y, Tajima S, Ishibashi A. Photodynamic therapy of acne vulgaris with topical delta-aminolaevulinic acid and incoherent light in Japanese patients. Br J Dermatol. 2001;144:575–9. [PubMed]

75. Seaton ED, Charakida A, Mouser PE, Grace I, Clement RM, Chu AC. Pulsed- dye laser treatment for inflammatory acne vulgaris: Randomized controlled trial. Lancet. 2003;362:1347–52. [PubMed]

76. Gold MH. Acne vulgaris: Lasers, light sources and photodynamic therapy- an update 2007. Expert Rev Anti Infect Ther. 2007;5:1059–69. [PubMed]

77. Jemec GBE, Jemec B. Acne: Treatment of scar. Clin Dermatol. 2004;22:434–8. [PubMed]

78. Drino B. Acne: Physical treatment. Clin Dermatol. 2004;22:429–33. [PubMed]

79. Goodman G. Postacne scarring: A review. J Cosmet Laser Ther. 2003;5:77–95. [PubMed]

80. Bett DG, Morland J, Yudkin T. Sugar consumption in acne vulgaris and seborrhoeic dermatitis. Br Med J. 1967;3:153–5. [PMC free article] [PubMed]

81. Fulton JE, Jr, Plewig G, Kligman AM. Effects of chocolate on acne vulgaris. JAMA. 1969;210:2071–4.[PubMed]

82. Cordain L. Implications for the role of diet in acne. Semin Cutan Med Surg. 2005;24:84–91. [PubMed]

83. Treloar V. Diet and acne redux. Arch Dermatol. 2003;139:941. [PubMed]

84. Danby FW. Acne and milk, the diet myth, and beyond. J Am Acad Dermatol. 2005;52:360–2. [PubMed]

85. Smith RN, Mann NJ, Braue A, Mäkeläinen H, Varigos GA. The effect of a high-protein, low glycemic-load diet versus a conventional, high glycemic-load diet on biochemical parameters associated with acne vulgaris: A randomized, investigator marked, controlled trial. J Am Acad Dermatol. 2007;57:247–56.[PubMed]

86. Logan AC. Dietary fat, fibre, and acne vulgaris. J Am Acad Dermatol. 2007;57:1092–3. [PubMed]

87. Gollnick H, Cunliffe W, Berson D, Dreno B, Finlay A, Leyden JJ, et al. Management of acne: A report from a global alliance to improve outcomes in acne. J Am Acad Dermatol. 2003;49:s1–38. [PubMed]

88. Strauss JS, Krowchuk DP, Leyden JJ, Lucky AW, Shalita AR, Siegfried EC, et al. Guidelines of care for acne vulgaris management. J Am Acad Dermatol. 2007;56:651–63. [PubMed]

89. Thiboutot D, Gollnick H, Bettoli V, Dréno B, Kang S, Leyden JJ, et al. New insights into the management of acne: An update from the Global Alliance to improve outcomes in Acne Group. J Am Acad Dermatol. 2009;60:S1–50. [PubMed]

90. Kubba R, Bajaj AK, Thappa DM, Sharma R, Vedamurthy M, Dhar S, et al. Acne in India: Guidelines for management - IAA Consensus Document. Indian J Dermatol Venereol Leprol. 2009;75:1–64. [PubMed]