

TREATMENT OF ACNE VULGARIS

Summary

- ☐ Acne vulgaris is a chronic, treatable disease but response to treatment may be delayed.
- ☐ Topical agents are useful as monotherapy for mild acne and in combination with systemic therapies for moderate acne.
- ☐ Oxytetracycline is the systemic treatment of choice for moderate acne in non pregnant patients and adolescents.
- ☐ Erythromycin is the systemic treatment of choice in pregnant patients and children under 12 years.
- ☐ Patients with severe or frequently relapsing acne should be referred to a dermatologist for isotretinoin therapy.

INTRODUCTION

Acne vulgaris is a multifactorial disease of the pilosebaceous unit of the skin. The face, back and chest are the areas most commonly affected as they possess a large number of sebaceous glands. Acne affects the sexes equally with a peak incidence at 14-17 years for girls and 16-19 years for boys.¹ However, 80% of the population between the ages of 11 and 30 years will be affected by acne vulgaris at some time.² The real misery should not be underestimated; self confidence is undermined and repercussions such as the higher unemployment rate of sufferers have been documented.¹ Furthermore any disorder which causes scarring, particularly of the face, should not be classed as trivial, as is often the case with teenage acne.

CLASSIFICATION

- Mild acne:** Open and closed comedones present, perhaps accompanied by a few superficial inflammatory lesions.
- Moderate acne:** Many inflammatory lesions present, largely superficial, but more deep seated pustules evident. Tendency of these lesions to scar with time.
- Severe acne:** Consists of nodules and cysts with marked scarring evident which may be keloidal in some cases. Has often spread to the chest, back and down the arms.^{1,3}

PATHOPHYSIOLOGY

Acne vulgaris is the result of the obstruction of sebaceous follicles. These are located primarily on the face and trunk.²

The causative factors are:

- Increased sebum production -leading to in some cases a greasy appearance. Hormonal therapy and systemic isotretinoin act here.^{4,5}
- Follicular plugging in the pilosebaceous unit - due to hypercornification of the duct. Blackheads (*open comedones*) and whiteheads (*closed comedones*) result. Benzoyl peroxide, topical and systemic retinoids act here.
- Bacterial colonisation of pilosebaceous unit - commonly due to *Propionibacterium acnes* (P.acnes) and to lesser extent *Staphylococcus epidermis*- an inflammatory response results. Benzoyl peroxide, topical and systemic antibiotics and systemic isotretinoin act here.

- Inflammation - *superficial* - red papules plus superficial pustules.
- *deep* - pustules, nodules and cysts, often lead to scarring if not treated adequately.^{1,6} Topical and systemic antibiotics and systemic isotretinoin act here.

AIMS OF TREATMENT

- to prevent scarring by starting treatment at an early stage.⁷
- to limit disease duration.
- to reduce psychological stress that may affect most sufferers.

TREATMENT

TOPICAL AGENTS

Topical agents are the mainstay of treatment for mild acne. Application is to all of the involved area and not merely to the individual lesions. The frequency of application is determined by individual tolerance. Counselling the patient is vital to aid compliance as clinical improvement may not be apparent for six to eight weeks.^{3,9}

Benzoyl Peroxide

Benzoyl peroxide is a potent bacteriostatic and comedolytic agent that has been in use for many years.⁹ It is an excellent first line therapy for both inflammatory and non-inflammatory lesions.⁷ Benzoyl peroxide is available in Ireland in the form of gels, creams and lotions and is used in concentrations of 5 and 10%. Gels are more effective in releasing the active substance than creams or lotions but can also be more irritating. For large affected areas, lotions may be more convenient for the patient to apply.¹⁰

Benzoyl peroxide does not induce any changes in the resistance pattern of aerobic bacteria to antibiotics and it also prevents such resistance when used concomitantly with topical erythromycin.³ Irritant reactions e.g. mild redness and peeling of skin are the most common side effects. These reactions may be minimised by starting with a low concentration preparation used on alternate days and then increasing both the strength of preparation and frequency of application as tolerated.¹⁰ Washing with soap and water 20-30 minutes before application greatly enhances efficacy. Patients should also be warned that benzoyl peroxide can bleach hair and clothing.^{10,11}

Topical Retinoids

Tretinoin and isotretinoin are retinoid derivatives for topical use.⁹ Tretinoin is available in a variety of formulations eg cream, gel or lotion 0.01-0.025% and isotretinoin as a 0.05% gel. Therapy may be tailored to the sensitivity of the patient's skin eg creams are preferred as they tend to be less irritant than gel preparations.^{2,12}

Topical retinoids do not possess antibacterial activity and so may be used in combination with benzoyl peroxide or topical antibiotics. Tretinoin and benzoyl peroxide however may inactivate one another if applied simultaneously and so these agents should be applied at different times of the day if prescribed concomitantly.^{9,10,11}

To enhance patient compliance it is important to stress several points when counselling the patient namely:

- A flare up of acne may develop in the early weeks of treatment. This is due to eruption of existing microcomedones. Maximum improvement may not be evident for 3-4 months^{2,10,12,13}

- Dryness and erythema reported with initial use may be minimised by applying tretinoin or isotretinoin initially once every 2-3 nights and gradually increasing the frequency to once nightly, if tolerated. This allows the patient to adjust to therapy while maintaining its efficacy.^{2,10,12}
- The use of sunscreens in conjunction with topical retinoids is recommended because of their photo-irritant effect.¹²

TOPICAL ANTIBIOTICS

Topical antibiotics are very useful in the treatment of mild to moderate inflammatory acne vulgaris.¹⁴ To be effective these products must be applied once or twice daily to the clean skin surface, covering all of the affected area and not just individual lesions.^{5,15} Antibiotics available as topical preparations in Ireland are chloramphenicol, clindamycin, erythromycin and tetracycline. Disadvantages of these preparations are as follows:

Tetracycline Reports of skin discolouration. Fluoresces under UV light which could be a distinct disadvantage at the disco. May stain clothes and bedding yellow.^{1,3,15}

Clindamycin: Small risk of pseudomembranous colitis. Although more common with oral or parenteral forms, prescribers should be aware of this adverse effect.

Erythromycin: Reports of resistance to *P. acnes* - these organisms may be cross resistant to clindamycin. By combining erythromycin with benzoyl peroxide or zinc the clinical effects of such resistance may be circumvented.^{9,15}

Mild local irritation may be experienced but contact allergic dermatitis is rarely a problem with these preparations.¹⁵ A response to topical therapy may not be seen for 4-6 weeks.¹⁶ These preparations are relatively expensive and are best reserved for use in patients unable to tolerate oral antibiotics or in whom benzoyl peroxide has caused a great deal of skin irritation.^{9,15}

SYSTEMIC ANTIBIOTICS

Oral antibiotics should be considered when acne is resistant to topical antibiotics, covers large areas of the body or where large inflammatory nodules are present.^{3,5,8,9,14,17} Tetracycline, oxytetracycline, minocycline, doxycycline and erythromycin are the antibiotics currently indicated for acne vulgaris treatment. These agents must be given at full dose for at least 3-4 months before assuming failure to respond.^{3,6,19} The potential for clinically significant drug interactions should be considered prior to initiating long term antibiotic therapy. For further information please refer to NMIC Bulletins 1996 Volume 2 No's 2, 3 and 5.^{20,21,22}

Tetracyclines

Tetracycline and oxytetracycline are given in doses of 500mg twice a day, with minocycline and doxycycline in doses of 100mg/day and 50-100mg/day respectively. The tetracyclines are thought to be equally effective in the treatment of moderate to severe acne.^{1,5,9} Doxycycline and minocycline have a similar action to tetracycline and oxytetracycline but with the advantage of requiring fewer doses and lacking dietary restrictions.^{5,14,17} Duration of treatment varies from 3 months or longer depending on the patients response.

There has been some controversy recently concerning minocycline use with reports of a minocycline-induced autoimmune hepatitis, a systemic lupus erythematosus - like syndrome and minocycline induced hyperpigmentation. Prescribers should be aware of these adverse effects. Also as minocycline is expensive it should be reserved for those patients who do not improve with one of the first line drugs e.g.

oxytetracycline.^{11,23} Finally, tetracyclines are contraindicated in pregnancy and in children less than twelve years old due to a risk of abnormal bone development and tooth pigmentation.^{14,17}

Erythromycin

Erythromycin has been shown to be as effective as tetracyclines for acne. It is typically given in doses of 250-500mg twice a day. Its advantages over tetracycline are lack of photosensitivity reactions and dietary restrictions. It is also the drug of choice for acne in pregnant patients and in children under twelve years.^{1,17} A disadvantage of erythromycin is the risk of resistance to P acnes. This risk has been shown to be greater with erythromycin than tetracycline. Resistance should be suspected in patients whose response to therapy diminishes or in those patients who do not respond after 3-6 months of therapy.^{11,12} As erythromycin is widely used for systemic infections and so to avoid resistance, tetracycline or oxytetracycline are the drugs of first choice for acne.⁹

HORMONAL THERAPY

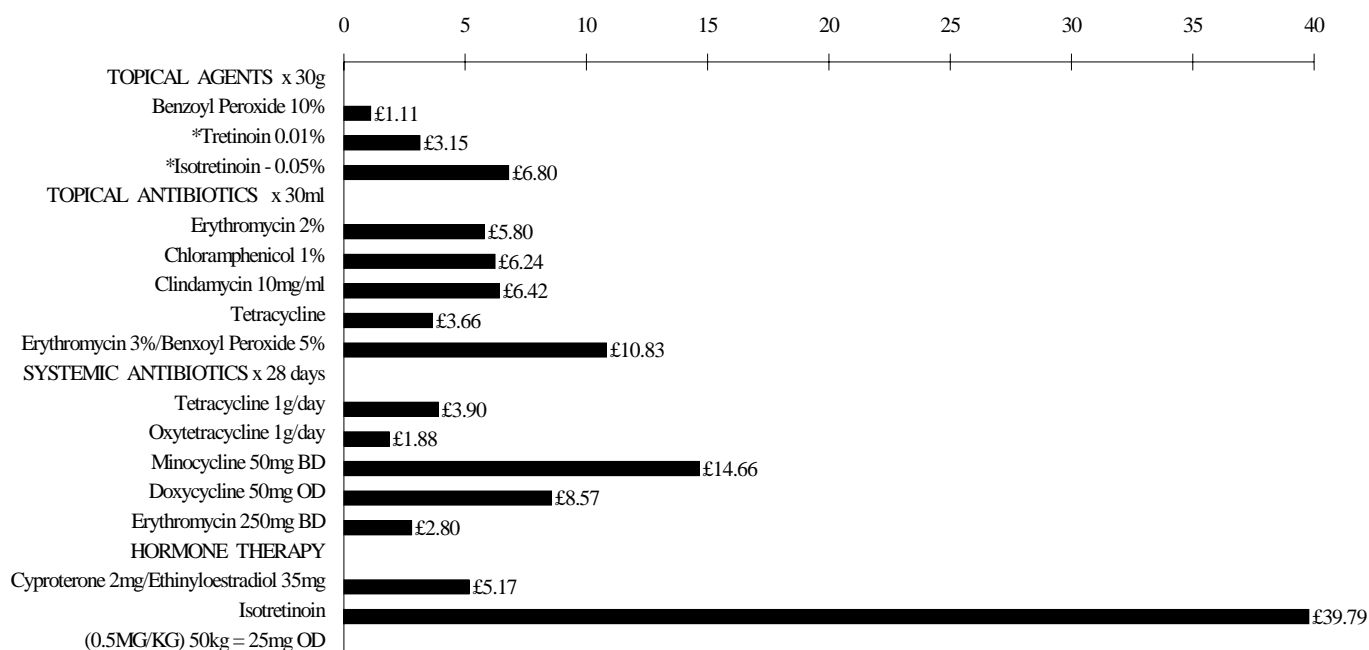
Most work has been undertaken with cyproterone and ethinyloestradiol (Dianette) at varying doses. This combination is useful for women with moderate acne who also wish to obtain adequate contraceptive cover. Response should be seen after the first six to eight weeks and treatment should be continued for at least six to twelve months.¹⁷ Topical therapy should be continued while on hormonal treatment. Oral contraceptives containing high concentrations of progestogens and combined contraceptive pills containing norethisterone or levonorgestrol may aggravate acne whereas those containing gestodene or desogestrel do not.^{3,14}

ISOTRETINOIN

Use of oral isotretinoin has revolutionised the treatment of severe or frequently relapsing acne. It is indicated for the treatment of cystic and conglobate acne and severe acne that has failed to respond to other therapies.²⁴ Doses of 0.5-1mg/kg/day are given, with treatment courses usually lasting for a period of approximately four months.

Isotretinoin is not however without side effects and for this reason it should usually be prescribed or initiated by a dermatologist.²⁴ Among the most commonly reported effects are dry skin, cheilitis, myalgias and arthralgias. Dry eyes have also been reported and contact lens wearers should be advised on the use of artificial tears.^{1,5,14,17} Monitoring of liver transaminases, triglyceride and cholesterol levels is recommended prior to treatment and at frequent intervals thereafter as elevated levels have been reported during therapy.^{14,17,19} However its most formidable side effect is teratogenicity. Reports suggest a twenty five fold increased risk of fetal abnormalities after maternal exposure to isotretinoin.¹⁰ All women of childbearing potential must practise effective contraception for at least the first four weeks before treatment, during the treatment period and for at least one month after finishing the course.^{5,9,10,17,19,24}

COST OF ONE MONTHS ACNE THERAPY - BASED ON GMS PRICES



*Based on MIMS Aug '97 price.

REFERENCES

1. Practitioner 1993;237:160-164
2. N. Eng J. Med. 1997; 336(16):1156-1162
3. BMJ 1994;308:831-3
4. J. Am. Acad. Derm. 1995;78(7):76-84
5. Postgrad. Med. 1985;78(7):76-84
6. Irish Doctor 1995;(Sept):43-46
7. Med. J. Aust. 1996;165:153-158
8. Irish Med. J. 1995;88(4):114-5
9. Int. Pharm. J. 1995; 9(1):11-13
10. Postgrad. Med. 1992;92(5):181-194
11. SMRC 1997;37:143-146
12. J. Am. Acad. Derm. 1995;32:S31-41
13. Product Info. - Retin A Cream - Janssen-Cilag. - 1997
14. Drugs 1994;48(1):59-70
15. DTB 1992;30(9):33-35
16. Product Info.-Dalacin T solution: Pharmacia & Upjohn 1997
17. Pharm. J. 1990: 729-30
18. Irish Med. J. 1997;90(3):92-93
19. Practitioner 1988;232:942-47
20. NMIC Bulletin 1996 Vol. 2, No.2
21. NMIC Bulletin 1996 Vol. 2, No. 3
22. NMIC Bulletin 1996 Vol. 2 No. 5
23. BMJ 1996;312:169-72
24. Product Info - Roaccutane - Roche pharmaceuticals '97