Acne in adolescents

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Background

Acne vulgaris affects more than 90% of Australian adolescents aged 16–18 years. It may have a significantly deleterious effect on their self-esteem and emotional state. Moderate-to-severe acne can lead to scarring. There are many treatment options available. Most teenagers obtain information from their peers or from the internet.

Objective

The aim of this article is to inform general practitioners (GPs) of the pathogenesis, physiology and description of acne, as well as therapeutic options, including topical and systemic therapies. Skin care, diet and other factors of importance are also discussed.

Discussion

The first point of contact with patients is in general practice. GPs effectively manage most patients with acne. Treatment choice is guided by experience, with many clinical acne treatment guidelines available. The most common reason for treatment failure is insufficient duration of therapy. Successful treatments require months of topical agents and, in many cases, additional systemic therapies. Internationally, there is a resurgence in the basic research of acne vulgaris, leading to new topical and systemic treatments.

Acne vulgaris (vulgaris meaning common in Latin) affects more than 90% of Australian adolescents aged 16–18 years. In most cases, it is a self-limiting complaint.[1] However, it takes several years for acne to naturally resolve in this patient group. It has a profound impact on self-esteem, mood and psychological status. Moderate-to-severe acne has the potential to cause permanent scarring.[2]

The thrust of this article is inflammatory acne in young people. Although parents and most doctors consider acne to be a disease of puberty, increasingly, comedonal acne is now seen in children under the age of 10 years. The reasons for this include that children are maturing earlier and are generally of a larger size than previous generations. The belief that acne is caused by poor hygiene, excessive consumption of fatty foods and chocolate has not been validated by extensive research.[3,4]

It is important to realise that your patients have received extensive information from commercial sources via the internet where cosmetic and other companies have extensively marketed products, many of which make no logical or medical sense. As in all aspects of medicine, our patients withhold or disguise such information. This is especially important in the atopic group, who already have a fragile epidermal barrier. Excessive washing, scrubbing and the use of extensive topical agents makes the use of prescription therapies, especially retinoids, problematic.

Often in tertiary practice, quite adequate medications have been prescribed, but poor compliance by the patient has resulted in an equally poor outcome. Patient explanation at the first consultation, with realistic time lines of treatment duration, is paramount. Not infrequently, patients become confused by excessive and often conflicting advice from pharmacists, paramedical services and, especially, the internet. In some pharmacies, there is a tendency to upsell non-prescription and unnecessary agents, from washes and scrubs through to probiotics. This increases the expense of their pharmacy experience. From clinical experience, one result is that patients do not purchase the necessary prescribed treatments. Acne vulgaris is readily treatable, with general practice as the point of first contact. Most acne is ably managed and stays in this location.

Pathophysiology of inflammatory acne

Four main factors are involved in the development of acne:

1. Abnormal follicular keratinocyte hyperproliferation, leading to the formation of a follicular plug
2. Increased sebum production within sebaceous follicles
3. Proliferation of microorganisms (eg *Propionibacterium acnes*) in the retained sebum
4. Inflammation

There is a strong genetic element in many patients. All acne, including comedonal acne, has an inflammatory basis.

Clinical features

Acne lesions are clinically classified as comedones, pustules, nodules, cysts and scars. Comedones are the distinguishing features between acne rosacea and acne vulgaris. They are keratin-filled plugs that can be described as open or closed. Open comedones are commonly referred to as blackheads; the black appearance is due to oxidisation of keratin plugs. Closed comedones are whiteheads. Pustules occur when follicular inflammation is such that large collections of neutrophils collect. Cysts are follicular-lined keratin-filled structures that dilate. Nodules occur when there is further inflammation. These are clinically red, tender, palpable lesions. This is where the follicular structures have ruptured. Scarring can be the final outcome once healed.

Scars

Many variations of scarring occur in acne. These include ice-pick (narrow and deep), hypertrophic (heaped and smooth) and atrophic scars (flat and slightly depressed) with a thinner epidermal surface. Finally, keloids and hypertrophic scars extend well beyond the site of original inflammation. These occur in the more severe forms of acne and once present they are permanent. Physical treatment modalities may help reduce such scarring but do so poorly.[5] Patients usually present with a range of clinical lesions from comedones through to cysts. Equally, when scarring is present there is usually a variety of different clinical scars.

Mangement of acne

In acne, we are treating two linked conditions. One is the physical appearance and the other is the psychological effect.[2] Unfortunately, there is frequently no obvious link between the two. Patients with quite minimal acne may be emotionally devastated and considerably impaired by their perception of their acne. Occasionally, patients with quite severe nodular cystic acne and scarring appear in the consultation to be minimally affected and have low levels of enthusiasm for treatment. Rarely, patients, predominantly young women, present with minimal acne but significant visible cutaneous damage from picking and scratching, frequently leaving many hypopigmented scars. This type of acne is known as acne excoriee. These patients compulsively pick at their skin, creating more damage than the original acne. The general practitioner (GP) has a better chance of measuring both aspects because of a longer relationship with the patients and/or their family. It is very difficult for a specialist to make a detailed assessment of the psychological effects and emotional impact of acne. There are clinical office tools that some dermatologists use as a way of recording the emotional aspects of patients' acne.[6]

There are still many misconceptions about acne.[1] In nearly all teenage patients, it is not caused by abnormal hormone levels. There is a separate subset in mature adult females known as 'hormonal acne'. This is a steadily increasing group presenting to medical practitioners. The majority of patients in this subset have developed acne in their second or later decades of life. This has a much more chronic and clinically low-grade appearance that persists for many years. The reasons for this have not been elucidated and are presently the subject of much research.[7]

Skin care

Generally, heavy cleansing, milder cheaper soaps and washes, scrubbing/exfoliating cause further irritation to the epidermis and blockage of sebaceous glands by causing damage and inflammation of the epidermal barrier. Patients with acne complain of being excessively oily. Therefore, moisturisers are not routinely needed in this group. Squeezing and picking at lesions only leads to follicular rupture and more nodular inflammatory acne. Oil-free make-up is permitted. Oil-free sunscreen is a requirement as sunburn causes swelling of the epidermis, which creates more blockage and more acne. The use of excessive volumes of sunscreen and make-up will block and aggravate acne.

Diet

Extreme dietary programs have not been shown to be of any value. A balanced, healthy diet is appropriate. Some researchers state that there is compelling evidence that diet may exacerbate acne.[8] For others the story is not so certain.[9–11] This area is still quite controversial and three major food classes – carbohydrates, milk and other dairy products, and saturated fats, including trans fats – as well as a deficiency of omega-3 polyunsaturated fatty acids, are linked to the promotion of acne.[8] The role of gamma-linoleic acid (omega-6 fatty acid), dietary fibre, antioxidants, vitamin A, zinc and iodine remains to be elucidated.[10]

Diet-induced insulin and insulin-like growth factor 1 (IGF-1) superimpose on elevated IGF-1 levels during puberty and affect sebaceous gland homeostasis.[8,10] Some researchers believe that patients should balance total calorie intake and restrict refined carbohydrates, milk, dairy, protein supplements, saturated fats and trans fats. They recommend a palaeolithic-style diet enriched in vegetables and fish.[8,9]

Topical therapies

Topical comedolytics are thought to unblock the pilosebaceous duct and/or act as antibacterial agents.[12] These products are of value in very mild acne. Benzoyl peroxide is a comedolytic and antibacterial agent and available over the counter in many

different combinations and formulations. Azaleic acid is also available over the counter. Salicylic acid and alphahydroxy acids (eg glycolic acid) act as keratolytics that open comedones.

Topical retinoids (vitamin A derivatives) are the most effective comedolytics available. They may be quite irritating to delicate skin types and are associated with the potential for photosensitivity. Hence, nightly application is required. Patients need to be instructed and counselled on how to use these agents to reduce facial erythema and cutaneous desiccation, particularly in the first couple of weeks of treatment.[13] Topical retinoids are not recommended during pregnancy, although there is no evidence of fetal harm. If a user becomes pregnant, it is quite safe to stop using these agents.[14] Topical dapsone has been released in Australia. Its mechanism of action is predominantly as an anti-inflammatory agent; it is not a topical antibiotic. It works on the inflammatory cascade that leads to erythema, nodules and cysts.[15]

Topical antibiotics are available on prescription for the treatment of acne. They are best used twice daily. Ideally, these agents should be combined with benzoyl peroxide and/or topical retinoids. These combination agents increase the potency of the clinical response. There are significant concerns about increased antibiotic resistance with the use of topical and oral antibiotics as monotherapy in acne. By using combination products, the risk of antibiotic resistance is markedly reduced.[12,16] Therefore, all acne guidelines aim to reduce the use of topical and/or systemic antibiotic therapies.[16]

Systemic therapies

Systemic treatments are required when topical agents as monotherapy are ineffective. They are usually indicated when the clinical lesions become more papular, nodular, pustular and, especially, cystic. A number of systemic antibiotics are routinely used. It is worth stressing at this point that systemic treatments take weeks to months to become effective.[17]

The most popular systemic agent in Australia is doxycycline at a dose of 50 mg daily. The dose can be increased depending on the size of the patient. Troublesome photosensitivity is an issue, as are administration difficulties. These medications need to be taken one hour before or two hours after a meal. This is problematic when dealing with teenage patients. Minocycline 50 mg twice daily – again higher doses are given – is often preferred to doxycycline as it is not so strongly photosensitising and is easier to take. Minocycline is given with food and is well tolerated. Higher doses and/or long-term therapy can lead to pigmentation of teeth, oral mucosa and, very rarely, skin. Issues with headache and the question of intracranial hypertension still cloud the use of this medication. It is extremely rare for systemic lupus erythematosus to be induced with this family of medications.

Second-line oral therapies include erythromycin 250–400 mg once or twice daily, trimethoprim with sulfamethoxazole 80–400 mg once or twice daily, or trimethoprim 300 mg alone once or twice daily. Some of the newer antibiotic therapies (azithromycin 500 mg, clarithromycin 250 mg) have also been used in patients with very resistant acne. In situations where there is a failure of therapy despite using the correct dose for body weight for a minimum of three months, consider using an alternative approach. As a guideline, treatment with antibiotics should be reviewed every three to six months.

Combined oral contraceptives[17,18]

Combined oral contraceptives more likely to improve acne are those containing cyproterone acetate, desogesterel, dienogest, drospirenone or jestodene. Clinically, nearly all hormonal therapies are effective in the long-term control of acne; however, onset of visible improvement is very slow and clinical effects take at least three months to become apparent, with best results seen over six months. These therapies frequently complement oral antibiotic and topical treatments. Oral antibiotic and topical retinoid therapy give a faster improvement in acne at first. Then it is advisable to cease the oral antibiotic and continue with the topical and hormonal therapy in the long term. Many female teenagers can be maintained in the longer term with only their combined oral contraceptive. The age at which patients are first prescribed a combined oral contraceptive is becoming lower and is a clinical judgement best determined by the GP.

Spironolactone is a synthetic steroid and weak diuretic.[19,20] It can be prescribed as monotherapy or in conjunction with a combined oral contraceptive. In Australia, it is especially used for hypertrichosis and/or seborrhoea. The usual dose is 50–100 mg daily for at least six months. In those of slight build, the dose can be reduced by 25–50 mg. Very rarely, patients become hypotensive and there is further academic argument whether monitoring with urea and electrolytes, particularly potassium levels, is indicated. When used as monotherapy, spironolactone very rarely causes menstrual irregularities. Addition of the combined oral contraceptive pill in these patients will lead to more regular and less troublesome periods. It takes at least two to three months for a clinically apparent improvement to develop.

For particularly resistant, poorly responding acne associated with mental health issues, or severe acne, the use of oral isotretinoin is the gold standard. Prescription of isotretinoin in Australia is subject to the *Poisons Standard*. It can only be prescribed by specialist practitioners, who are predominantly dermatologists. Isotretinoin is a synthetic vitamin A derivative that is thought to reduce sebaceous gland activity. In addition, it is comedolytic and anti-inflammatory. A proper course of isotretinoin should bring long-term remission of acne in 80% of patients. It does, however, have multiple side effects, especially mucocutaneous effects. These are frequently minor but in some individuals can be quite problematic.

Of prime importance, isotretinoin is teratogenic and pregnancy must be avoided throughout treatment and for one month after cessation of therapy. The teratogenic effects predominate in very

early fetal development. The standard practice is for patients to undergo pregnancy testing and counselling prior to starting this medication. The use of isotretinoin is primarily the domain of specialists and not the remit of this article.

Key points

- In teenagers, enthusiasm for, and compliance with, therapy is paramount. It is prudent to recall that this patient group accepts most health advice from their peers or from the internet. They do not value the input of trained medical practitioners as highly as their parents.
- Compliance with topical treatments, which should contain either a retinoid or benzoyl peroxide as monotherapy or in a combination agent, is required for several months nightly, and this should suffice in minor early inflammatory and/or comedonal acne.
- Once lesions become clinically more apparent, inflammatory and papular, a systemic agent is required. Oral antibiotics as listed in this article should lead to a therapeutic improvement by six weeks. If not apparently effective by 12 weeks, alternative agents should be sought.
- Hormonal therapies in the female population and/or the use of spironolactone are much slower; however, for many patients, these therapies can be useful. They can be used in combination with topical and systemic antibiotics. Once control is obtained, cease the oral antibiotic and continue topicals with the oral contraceptive. The use of topical therapy, particularly with a retinoid, reduces the long-term risk of pigmentary dyschromia and/or deeper elastic tissue/collagen damage leading to scar formation.

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References

1. Marks R, Plunkett A, Merlin K, Jenner N. Atlas of common skin diseases in Australia. Melbourne: Department of Dermatology, St Vincents Hospital, 1999.
2. Koo J. The psychosocial impact of acne: Patients' perceptions. J Am Acad Dermatol 1995;32(5 Pt 3):S26–30.
3. Goldberg JL, Dabade TS, Davis SA, Feldman SR, Krowchuk DP, Fleischer AB. Changing age of acne vulgaris visits: Another sign of earlier puberty? Pediatr Dermatol 2011;28(6):645–48.
4. Bhate K, Williams HC. Epidemiology of acne vulgaris. Br J Dermatol 2013;168(3):474–85.
5. Layton AM. Acne scarring – Reviewing the need for early treatment of acne. J Dermatol Treat 2000;11:3–6.
6. Agnew T, Furber G, Leach M, Segal L. A comprehensive critique and review of published measures of acne severity. J Clin Aesthet Dermatol 2016;9(7):40–52.
7. Pitashny M, Martinez de Morentin H, Brenner S. Oral contraceptives: Their mode of action and dermatological applications. Skinmed 2005;4(2):101–06.
8. Melnik BC. Linking diet to acne metabolomics, inflammation and comedogenesis: An update. Clin Cosmet Investig Dermatol 2015;8:371–88.
9. 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-masked, controlled trial. J Am Acad Dermatol 2007;57(2):247–56.
10. Kucharska A, Szmurło A, Sińska B. Significance of diet in treated and untreated acne vulgaris. Postepy Dermatol Alergol 2016;33(2):81–86.
11. Romańska-Gocka K, Woźniak M, Kaczmarek-Skamira E, Zegarska B. The possible role of diet in the pathogenesis of adult female acne. Postepy Dermatol Alergol 2016;33(6):416–20.
12. Berson DS, Shalita AR. The treatment of acne: The role of combination therapies. J Am Acad Dermatol 1995;32(5 Pt 3):S31–41.
13. Akomeah FK. Topical dermatological drug delivery: Quo vadis? Curr Drug Deliv 2010;7(4):283–96.
14. Kaplan YC, Ozsarfati J, Etwel F, Nickel C, Nulman I, Koren G. Pregnancy outcomes following first-trimester exposure to topical retinoids: A systematic review and meta-analysis. Br J Dermatol 2015;173(5):1132–41.
15. Tanghetti E, Harper JC, Oefelein MG. The efficacy and tolerability of dapsone 5% gel in female vs male patients with facial acne vulgaris: Gender as a clinically relevant outcome variable. J Drugs Dermatol 2012;11(12):1417–21.
16. Zeichner JA, Patel RV, Haddican M, Wong V. Efficacy and safety of a ceramide containing moisturizer followed by a fixed-dose clindamycin phosphate 1.2%/benzoyl peroxide 2.5% gel in the morning in combination with a ceramide containing moisturizer followed by tretinoin 0.05% gel in the evening for the treatment of facial acne vulgaris. J Drugs Dermatol 2012;11(6):748–52.
17. Koo EB, Petersen TD, Kimball AB. Meta-analysis comparing efficacy of antibiotics versus oral contraceptives in acne vulgaris. J Am Acad Dermatol 2014;71(3):450–59.
18. Arowojolu AO, Gallo MF, Lopez LM, Grimes DA. Combined oral contraceptive pills for treatment of acne. Cochrane Database Syst Rev 2012;(7):CD004425.
19. Brown J, Farquhar C, Lee O, Toomath R, Jepson RG. Spironlocatone versus placebo or in combination with steroids for hirsutism and/or acne. Cochrane Database Syst Rev 2009;(2):CD000194.
20. Layton AM, Eady EA, Whitehouse H, Del Rosso JQ, Fedorowicz Z, van Zuuren EJ. Oral spironolactone for acne vulgaris in adult females: A hybrid systematic review. Am J Clin Dermatol 2017;18(2):169–91.

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