Management of mild to moderate acne vulgaris

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Abstract
Acne is a chronic inflammatory disease of the pilosebaceous units. It is the most common diagnosis in dermatology and regularly affects adolescents and young adults. Acne can be mild, moderate or severe. Treatment includes topical keratolytics, topical retinoids, antibiotics, hormonal therapy and systemic retinoids in severe cases.

Introduction
Acne is a common skin condition with substantial cutaneous and psychological disease burden. Usually, it starts in adolescence and resolves by the mid-20s, but can continue up to 40 years of age in some people.
Active sebaceous glands and increased sebum production are implicated in the development of acne. Affected patients present with seborrhoea (greasy skin). There are comedones, papules, pustules and nodules in severe cases.

Discussion
The pathophysiology of acne involves increased sebum production, increased keratinisation of the pilosebaceous duct, proliferation of microbial flora like Propionibacterium acnes, Staphylococcus epidermidis and inflammation. P. acnes is a normal component of the cutaneous flora which inhabits the pilosebaceous units and uses lipid-rich sebum as a nutrient source.
Usually, acne in teenagers is caused by a hormonal imbalance that is associated with increased androgen levels at the onset of puberty. Genetic factors also influence susceptibility to acne. This is confirmed by the very high concordance between monzygotic twins, in which the extent and severity of acne and sebum excretion rate are virtually identical.
Other secondary precipitators of acne include stress, the use of comedogenic cosmetics, drugs such as systemic steroids, endocrine diseases and polycystic ovarian syndrome.
Premenstrual flares occur in approximately 70% of females with acne. Possibly, this relates to premenstrual changes in the hydration of the pilosebaceous epithelium. Clinically, the lesions of acne are polymorphic. There may be open comedones (black heads) closed comedones (white heads), papules, pustules or in severe cases, nodules.
Commonly, lesions occur on the face (in 99% of cases) and less so on the back (60%) and chest (15%). Itching is a rare symptom of acne, but may relate to the release of histamine-like compounds by P. acnes. Pain may be associated with secondary infection of the lesions by other bacteria.
It is important to grade acne according to severity before planning treatment. There are many acne-grading systems in existence, but there is no gold standard, nor standardised system, that is consistently used in clinical practice. Also, no method has yet gained universal acceptance.
Acne can be graded on a scale of 1-10 as mild, moderate or severe. The other grading system is based on the morphology of lesions where mild acne consists of open and closed comedones and some papules and pustules. Moderate acne features more frequent papules and pustules with mild scarring. Severe disease contains all of the above, plus nodules and abscesses and more scarring (Figures 1-4).

Table I: Acne grading

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>Comedones only</td>
</tr>
<tr>
<td>2</td>
<td>Inflammatory papules in addition to comedones</td>
</tr>
<tr>
<td>3</td>
<td>Pustules that are present in addition to either of the above</td>
</tr>
<tr>
<td>4</td>
<td>Nodules, cysts, conglobate lesions or ulcers that are present in addition to any of the above</td>
</tr>
</tbody>
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Acne has a psychosocial effect on sufferers. One study has shown that they experience shame, embarrassment,
anxiety, loss of self-esteem, impaired social contact and depression.9 Disease-specific questionnaires that are used to assess the psychosocial impact of acne include the Cardiff Acne Disability Index, Assessment of the Psychosocial Effects of Acne and the Acne Quality of Life Scale.10

Diet and acne

The role of diet in the development of acne is highly controversial. Patients and clinicians often suggest that fatty foods, sweets and chocolates are aggravating factors that cause acne, but previous older studies have failed to prove a causal relationship between diet and acne.4 However, more recent studies have demonstrated compelling evidence that high glycaemic-load diets may exacerbate acne.11 Some studies suggest that dairy intake increases acne risk.1 Further studies are needed to explore the effects of diet on acne.

Acne variants

There are several clinical variants of acne.

Acne excorées

Acne excorées is a form of acne that results when patients pick at and tamper with the lesions. Such lesions become excoriated (Figure 5). Usually, there is an underlying personality issue, psychosocial problem or obsessive compulsive disorder in such patients.
Drug-induced acne

Drug-induced acne occurs following the intake of drugs such as corticosteroids, both orally and topically. The lesions of steroid-induced acne are more monomorphic. Antiepileptic drugs, like phenytoin and phenobarbitone; antituberculosis drugs, such as isoniazid and rifampicin; and halogens like iodides and halothane, can trigger acne or form acne eruptions. Other implicated drugs include lithium, quinine, sulphur and disulfiram.2

Acne cosmetica

Acne cosmetica is caused by the use of comedogenic cosmetics. Characteristically, lesions occur in the perioral area in females, especially those who had acne as adolescents and who have used cosmetics for a long time.2

Pomade acne

Pomade acne is due to the use of pomades. These are greasy preparations that are used to straighten curly hair. Lesions are noninflammed and occur on the forehead and other areas where greasy pomades may be in contact with hairless skin.

Chloracne

Chloracne occurs following exposure to certain toxic chlorinated hydrocarbons. The lesions comprise multiple comedones on both sides of the face. The lesions may occur on other parts of the body in severe cases.2

Severe acne variants are pyoderma faciale, acne conglobata and acne fulminans.

Treatment

Treatment aims to alleviate symptoms, clear up existing lesions, limit disease activity, prevent the development of scars and improve quality of life.

The treatment of mild to moderate acne includes general measures, topical therapy, oral antibiotics and hormonal therapy.

Topical therapy alone may suffice in treating mild acne, while oral or topical therapies may be needed for moderate acne. Treatment of severe acne will not be dealt with in this article.

Topical therapies

The most commonly used topical therapies are benzoyl peroxide, topical retinoids, azelaic acid and topical antibiotics, either as monotherapy or in combination. Benzoyl peroxide is available in concentrations of 2.5%, 5% and 10%. It has antimicrobial activity, anti-inflammatory and keratinolytic activity.4

Benzoyl peroxide eliminates both surface and ductal P. acnes by releasing oxygen into the anaerobic follicular micro-environment. Bacteria cannot develop resistance to this mode of action.12,13

Commonly used topical retinoids are isotretinoin 0.05% gel and adapalene 0.1% cream or gel. Topical retinoids have significant and rapid anti-inflammatory activity and can regulate follicular keratinisation as well.5,14 Retinoids are derivatives of vitamin A.

There have been reports of teratogenicity in women who have used topical retinoids during early pregnancy. One study suggested a relative risk of 0.7 of having a baby with major congenital anomaly after using topical retinoids in pregnancy. Therefore, these products are better avoided during this time.8

Topical antibiotics can also be used to treat mild to moderate acne. They include erythromycin and clindamycin, usually in a cream or lotion base.4 Topical antibiotics reduce colonisation by P. acnes and also have direct anti-inflammatory effects by way of antioxidant effects on leukocytes action. The resistance of P. acnes to erythromycin has been reported. This has reduced the usefulness of topical erythromycin in the treatment of acne.15

Topical azelaic acid is also useful in treating mild to moderate acne. It reduces comedones by normalising the disturbed terminal differentiation of keratinocytes in the follicle infundibulum.7 It also has an anti-inflammatory effect. According to the recommendations of the Global Alliance to Improve Outcomes in Acne, topical antibiotics should never be used as monotherapy in the treatment of acne.5

Oral antibiotics

Oral antibiotics, in combination with topical therapies such as retinoids and benzoyl peroxide, can be highly effective in treating acne. Oral antibiotics are indicated in patients with moderate to severe inflammatory acne, patients who do not improve on topical therapy alone, and patients whose acne covers a large surface area, thus making topical therapy
impractical.\textsuperscript{16} Commonly used oral antibiotics are macrolides such as erythromycin and clindamycin; tetracyclines like doxycycline, minocycline and lymecycline; as well as sulphonamides such as trimethoprim-sulphamethoxazole.

There are several important points to remember when prescribing these antibiotics. Oral erythromycin is safe in pregnancy, but erythromycin estolate should be avoided as it can cause cholestatic jaundice in pregnant patients. As an inhibitor of cytochrome P450, it can reduce the clearance of theophyllin, warfarin, carbamazepine and cyclosporine.

Oral clindamycin may cause diarrhoea and may promote the overgrowth of \textit{Clostridium difficile} in the gastrointestinal tract, causing pseudomembranous colitis.\textsuperscript{16}

Tetracyclines must be taken on an empty stomach (one hour before meals or two hours after meals), as ingestion with food, especially dairy products, can block the absorption of tetracyclines. Minocycline can cause a blue-grey discoloration of the skin, especially on scars and sun-exposed areas. It can also cross the blood-brain barrier, causing vestibular disturbances such as vertigo, dizziness and ataxia.

Tetracyclines can inhibit skeletal growth in the foetus. Therefore, they should not be given to pregnant women, lactating mothers and children who are younger than nine years of age.\textsuperscript{16}

The Global Alliance to Improve Outcomes in Acne recommends a combination therapy of oral antibiotics, topical retinoids at night and benzoyl peroxide in the morning, for the treatment of mild to moderate acne.\textsuperscript{5}

It is recommended that oral antibiotics are given for a maximum of four months when they are used to treat acne. Treatment for longer periods results in antibiotic resistance.\textsuperscript{5}

After stopping antibiotics, maintenance therapy with topical retinoids and benzoyl peroxide should be continued to prevent relapses.

\textbf{Hormonal therapy}

Hormonal therapy is used in female patients with mild to moderate acne to reduce seborrhoea and premenstrual flares. It is also useful in cases where the treatment of acne and contraception are needed concomitantly. It should be considered in female patients with acne that is refractory to oral antibiotic therapy too.\textsuperscript{4} Hormonal therapy for acne includes inhibitors of ovarian androgen production, such as the combined oral contraceptive (COC) pill that contains ethinyl-oestradiol and progesterone, as well as androgen receptor blockers, such as cyproterone acetate.\textsuperscript{4,17} Antiandrogens suppress sebum production.\textsuperscript{4}

COCs are often effective in treating mild forms of acne, but antiandrogens must be used\textsuperscript{4} for the more severe forms.

Progesterone-only contraceptives often worsen acne and should be avoided in women who have no contraindication to oestrogen-containing preparations.\textsuperscript{17} All hormonal therapies should be combined with appropriate topical therapies.\textsuperscript{4} Contraindications to the oral contraceptive pill include a family history or personal history of breast cancer, ovarian cancer, hypertension, venous thrombosis, smoking and other cardiac risk factors.\textsuperscript{16}

\textbf{References}


