Acne

Acne vulgaris is largely a condition of young people and resolves in the majority of patients by the age of 25 years. It is believed to be nearly universal in adolescents. From a medical point of view, acne vulgaris is a minor problem in most cases. However, its psychological impact on sufferers can be enormous, given that it affects young people at a stage in their lives when they are especially sensitive about their appearance. Patients are often anxious to find a cure for what they consider to be a highly embarrassing problem. About 60% of teenagers consider their condition sufficiently serious to either self-treat with non-prescription products or to seek medical advice. Several effective products for mild-to-moderate acne are available without prescription, although correct use and persistence are necessary to increase the chance of success.

CAUSES

Acne vulgaris is the result of a combination of several factors. The main processes involved are as follows.

- The pilosebaceous units in the dermis of the skin consist of a hair follicle and associated sebaceous glands. These glands secrete sebum – a mixture of fats and waxes – the function of which is to protect the skin and hair by retarding water loss and forming a barrier against external agents. The hair follicle is lined with epithelial cells which become keratinised as they mature.
- During puberty, the production of androgenic hormones increases in both sexes and levels of testosterone rise. Testosterone is taken up into the sebaceous glands, where it is converted into dihydrotestosterone, stimulating the glands to secrete increased amounts of sebum.
- At the same time, the keratin in the follicular epithelial walls becomes unusually cohesive; sebum accumulates within it, forming keratin plugs. These block the openings of the follicles in the epidermis and cause them to dilate beneath the surface of the skin.

- If the orifice of the follicular canal opens sufficiently, the keratinous material is extruded through it and an open comedone results. This is also known as a blackhead because the keratinous material is dark in colour. Because this material can escape, the comedone does not become inflamed. If the follicular orifice does not open sufficiently, a closed comedone (whitehead) results, in which inflammation can occur. Most acne sufferers have a combination of both types of comedone.
- The actions of microorganisms, principally *Propionibacterium acnes*, cause the follicular wall of closed comedones to disrupt and collapse, spilling their contents into the surrounding tissue and provoking an inflammatory response. In addition, bacterial enzymes bring about the decomposition of triglycerides in the sebum to produce free fatty acids, which also cause inflammation. In the more common milder form of acne, this process leads to the formation of papules around the follicular openings; in the more severe form it leads to cyst formation in the deeper layers of the skin.

TREATMENT

Only topical products are available without prescription for the treatment of mild-to-moderate acne. Antibiotics – both systemic and topical – are available on prescription for more severe conditions. The overall aims of topical therapy are to remove follicular plugs, allowing sebum to flow freely, and to minimise bacterial colonisation of the skin. Four main types of preparation are available without prescription:

- keratolytics (also known as comedolytics in relation to acne)
- antimicrobials
- anti-inflammatory agents
- abrasives.

Keratolytics

Compounds available

The compounds available are:

- benzoyl peroxide
- salicylic acid
- sulphur
- resorcinol.

Mode of action

Keratolytic agents promote shedding of the keratinised epithelial cells on the surface of the skin, preventing closure of the pilosebaceous orifice and formation of follicular plugs, and facilitating the flow of sebum. The various compounds cause this effect via different mechanisms. The keratolytic agents also possess varying levels of antimicrobial activity, which contributes to their effectiveness.

Benzoyl peroxide has been in use for the treatment of acne for more than 60 years. It is generally accepted as the most effective topical treatment for mild conditions and there is good evidence to support this.[1–5] There is some difference of opinion over the principal mechanism of action of benzoyl peroxide. It was generally thought that its activity is mainly a comedolytic effect through an irritant action, leading to an increased turnover of the epithelial cells lining the follicular duct and increasing sloughing.[6] More recently, however, its principal mode of action has been suggested to be as a bactericide against *P. acnes*. Benzoyl peroxide is lipophilic and therefore penetrates the follicle well. Once absorbed, it releases oxygen, which suppresses the bacteria, thereby reducing the production of irritant free fatty acids.[7]

Quinoderm (Ferndale) contains potassium hydroxyquinoline sulphate, which has both antibacterial and keratolytic properties, in addition to benzoyl peroxide. A comparison[8] showed this combination to be more effective than benzoyl peroxide alone.

Salicylic acid is used in concentrations of up to 2% for acne. It exerts its keratolytic effect by increasing the hydration of epithelial cells, and it may also have some bacteriostatic activity and a direct anti-inflammatory effect on lesions. It is also believed to enhance penetration into the skin of other medicaments, and is combined with sulphur in some formulary preparations.

Sulphur is claimed to possess keratolytic and antiseptic properties, although this is debatable; it does, however, appear to hasten the resolution of inflammatory pustular lesions.

Some authorities consider preparations based on salicylic acid or sulphur to be obsolete for the treatment of acne, and in the *British National Formulary* they are regarded as a second-line choice. There is little evidence for the effectiveness of salicylic acid in the treatment of acne. Some studies have found proprietary preparations containing salicylic acid to be more effective than benzoyl peroxide, but these studies appear to have been conducted or sponsored by the manufacturer.[9,10]

Resorcinol is only found in combination with sulphur in a single proprietary preparation. It is not regarded as efficacious, has several drawbacks and is not recommended.

Adverse effects, cautions and use

Benzoyl peroxide is mildly irritant and may cause redness, stinging and peeling, especially at the start of treatment, but tolerance usually develops with continued use. To minimise these effects, the lowest available strength (usually 5%) should be used and applied at night for the first week so that any erythema subsides by the next morning. If there is no adverse reaction, application can be twice daily. Several weeks of regular application are usually required to produce real benefit; if the lower strength is ineffective, the higher strength (10%) can be tried. Treatment should not be prolonged beyond 3 months with the 5% preparations or beyond 2 months with the 10% preparations.

True allergy occurs in a very small minority of patients, but allergic contact dermatitis is more common. If troublesome skin irritation

occurs, application should be stopped for a day or two; if the same reaction occurs when the product is used again, it should be discontinued. Care should be taken to keep all keratolytics away from the eyes, mouth and other mucous membranes. Benzoyl peroxide is an oxidising agent and may bleach clothing and bedclothes. Concerns were expressed some years ago because animal studies showed that benzoyl peroxide, although not a carcinogen, may promote the growth of tumours.[11] No such fears have been expressed by medicine safety or regulatory bodies in the UK, and benzoyl peroxide is considered safe for human use. A case–control study in England[12] found no significant association between the use of benzoyl peroxide and the occurrence of malignant melanoma.

Salicylic acid is a mild irritant and similar precautions should be adopted as for benzoyl peroxide. Preparations are applied twice or three times a day. Salicylic acid is absorbed readily through the skin and is excreted slowly. Salicylate poisoning can occur if preparations are applied frequently, in large amounts and over large areas.[13] Patients who are sensitive to aspirin should avoid preparations containing salicylic acid.

Resorcinol should not be applied over large areas of skin or for long periods, as it is absorbed and can interfere with thyroid function or cause methaemoglobinaemia. Resorcinol may cause dark-brown scaling on the skin in darker-skinned individuals. Both sulphur and resorcinol can cause skin irritation and sensitisation.

Formulations

Benzoyl peroxide is available in the form of creams, lotions, gels and washes, and in concentrations of 2.5, 5 and 10%. There is little difference in clinical response to the three concentrations in terms of reducing the number of inflammatory lesions, but formulation appears to make a difference.[4] The drying effect of an alcoholic-gel base enhances the effectiveness of the active constituent, and this formulation is more effective than a lotion of the same concentration. However, gels have a greater potential for causing drying of the skin and irritation than preparations in aqueous bland bases. Washes

containing benzoyl peroxide have been found to have little or no comedolytic effect, although in a small-scale trial[14] a skin wash containing 2% salicylic acid was found to be more effective than a 10% benzoyl peroxide wash. Brevoxyl (Stiefel) contains 4% benzoyl peroxide formulated in a hydrophase base. The manufacturer claims that the formulation holds the benzoyl peroxide in solution, increasing its bioavailability compared with traditional formulations and preventing the crystallisation of benzoyl peroxide on the skin, which leads to particulate irritation. The manufacturer's own (unpublished) studies show that this formulation is as effective as 10% benzoyl peroxide, but with no more irritant effect than a 2.5% preparation.

Some bases, particularly those of the older formulary products, may reduce the effectiveness of acne products by making the skin more greasy.

Products

- Benzoyl peroxide

  Creams

  — Brevoxyl (4% in hydrophase base)
  Stiefel

  — Oxy On-the-Spot (2.5%)
  Mentholatum

  — PanOxyl 5
  Stiefel

  — Quinoderm cream (10% with 0.5% potassium hydroxyquinoline sulphate)
  Ferndale

  — Quinoderm 5 cream (5% with 0.5% potassium hydroxyquinoline sulphate)
  Ferndale

  Lotions

  — Oxy 10 (10% benzoyl peroxide)
  Mentholatum

Gels

— Acnecide
Galderma
— PanOxyl 5 Acne Gel (5%)
— PanOxyl 10 Acne Gel (10%)
— PanOxyl Aquagel (2.5%)
all *Stiefel*

Wash

— PanOxyl Wash 10 (10%)
Stiefel

- Salicylic acid
  — Acnisal face wash (2%)
  DermaPharm
  — Salicylic Acid and Sulphur Cream BP 1980 (2% salicylic acid and 2% sulphur)
  — Salicylic Acid and Sulphur Ointment BPC 1973 (3% salicylic acid and 3% sulphur)

- Resorcinol
  — Eskamel cream (2% with 8% sulphur)
  Goldshield

Antimicrobials

Compounds available

Compounds available are:

- cetrimide
- chlorhexidine
- povidone-iodine
- triclocarban
- triclosan.

Mode of action

Two of the factors contributing to acne are increased sebum production and *P. acnes*, so a logical approach to treatment is to remove excess sebum from the skin and reduce the bacterial count. To this end, several products containing antibacterial or antiseptic ingredients are available formulated as astringent lotions and detergent-based washes; there are also some antimicrobial creams. There is some evidence to support the effectiveness of antimicrobials. Part of any value of these products may lie in the placebo effect, generated by patients participating in an active routine to deal with their problem.[15,16]

Products

- Cetrimide
  - — Torbetol (0.7% with 0.75% chlorhexidine)
    Torbet

- Chlorhexidine
  - — Cepton lotion (0.1%)
  - — Cepton medicated skin wash (1%)
  - — Cepton medicated clear gel (2.5%)
    all *LPC*

- Povidone-iodine
  - — Betadine skin cleanser (4%)
    Medlock Medical

- Triclocarban
  - — Valderma soap (1%)
    Ransom

- Triclosan
  - — Clearasil treatment cream regular (0.1% with 8% sulphur)
    Crookes

Abrasives

Product

There is one product:

- Brasivol No. 1 (fused synthetic aluminium oxide particles in a soap-detergent base)
  Stiefel

Mode of action, use and cautions

This formulation contains small, gritty particles in a skin wash, intended to remove follicular plugs mechanically. However, there is little evidence of the effectiveness of abrasive preparations in acne.[17,18] Recommended use is 1–3 times daily for a duration of 15–20 seconds. The product is contraindicated in the presence of superficial venules or capillaries (telangiectasia), and over-enthusiastic use can cause irritation.

Anti-inflammatory agents

Compounds and products available

Nicotinamide is the only compound available:

— Freederm Gel (4%)
— Freederm Lotion (10%)
both *Dendron*

— Nicam Gel (4%)
Dermal

Mode of action and use

Nicotinamide is the physiologically active amide of nicotinic acid and its deficiency in the diet can lead to a range of symptoms, including skin problems. In the topical treatment of acne it is claimed to have anti-inflammatory activity, although its mechanism of action is unknown. It is postulated that nicotinamide might act directly on inflammatory mediators, perhaps through inhibition of neutrophil chemotaxis. In a double-blind clinical trial it was found to be as effective as 1% clindamycin gel in the treatment of mild-to-moderate acne.[19] It does not appear to have been compared directly with benzoyl peroxide. It is applied twice daily. Side-effects include dryness, peeling and irritation similar to those produced by benzoyl peroxide; the same precautions in use should therefore be taken.

PRODUCT SELECTION POINTS

- Benzoyl peroxide is the first-line treatment for mild-to-moderate acne. It has a proven record of efficacy and few drawbacks. A higher strength (10%) formulation of benzoyl peroxide should only be used if 3–4 weeks' treatment with a 5% formulation produces no improvement.
- Alcoholic or astringent gel formulations of benzoyl peroxide are more effective than lotions or creams. However, water-based formulations are less likely to cause skin drying and irritation, and may improve compliance. Washes containing benzoyl peroxide have been found to have little comedolytic effect.
- There is some evidence for the effectiveness of antibacterial preparations.
- All acne treatments must be used regularly for up to 3 months to produce real benefits.

PRODUCT RECOMMENDATIONS

- First choice of treatment for mild-to-moderate acne should be an alcohol- or astringent-based gel containing 5% benzoyl peroxide.
- An aqueous cream or lotion formulation may be preferred by patients with more sensitive skin.

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