The role of benzoyl peroxide in the management of acne vulgaris

Benzoyl peroxide is a common ingredient in over-the-counter preparations for acne but its side effects mean patients may reject it. In this article, Rod Tucker and Shernaz Walton review the evidence for its effectiveness and provide tips for pharmacists to help patients get the most from it

Acne vulgaris is an extremely common and distressing condition that affects over 90 per cent of adolescents between the age of 16 and 18 years.[1] Of these, approximately 15 per cent require medical intervention.[2] Furthermore, research has shown that acne has a negative impact on patients' quality of life that is comparable to that caused by conditions such as asthma and epilepsy.[3] Although predominately a teenage problem, acne can and does persist into adult life and still affects roughly 1 per cent of women and 5 per cent of men at the age of 40 years.[4]

There is a wide range of over-the-counter products available to treat acne. In many of these preparations, benzoyl peroxide is a common ingredient. Unfortunately, benzoyl peroxide-based products are often rejected by patients after a few days' use, once their skin starts to flake or become inflamed. These side effects are so common that patients who claim not to experience them are likely to be non-compliant. Compliance is further reduced by the bleaching effects on clothing, towels and bed-linen. Nevertheless, providing patients with adequate advice and information about these side effects and how to minimise them usually results in greater perseverance with treatment and ultimately an improvement in their acne.

This article reviews the evidence for the benefits of benzoyl peroxide and provides useful advice and tips for pharmacists to convey to patients using such products to ensure that they derive maximum benefit from it.

History of benzoyl peroxide

Benzoyl peroxide is not a new drug. As early as 1905 Loevenhart and Kastle described the use of benzoyl peroxide in research on potatoes[5] and Loevenhart also noted the benefits on burns and chronic varicose leg tumours. In 1929, the value of benzoyl peroxide in treating wounds and burns was reported by Lyon and Reynolds[6] and, in 1934, benzoyl peroxide was shown to be effective in a case of acne vulgaris.[7] By 1948 there were many benzoyl peroxide products available for treating wounds and varicose leg ulcers. However, the use of the drug in acne was not explored in any detail until the 1960s when William Pace began treating acne patients with a precipitated sulphur cream that contained benzoyl peroxide.[8] During the 1970s the range of potential uses for benzoyl peroxide increased and Kligman *et al*[9] have described the use of benzoyl peroxide in the treatment of athlete's foot and tinea versicolor. Benzoyl peroxide has also been used to treat leg ulcers[10,11] and was shown to be of some benefit in patients with seborrhoeic dermatitis.[12] Today, benzoyl peroxide is mainly used in the treatment of mild to moderate acne and is often prescribed in conjunction with oral antibiotics in the treatment of moderate to severe acne.

In order to understand how benzoyl peroxide works, it is necessary to review the pathophysiology of acne.

Pathophysiology of acne vulgaris

Although the precise cause of acne is unclear it appears to be associated with at least four factors: increased sebum production, follicular keratinisation, bacterial colonisation and inflammation.[13] Of these, sebum excretion is under genetic control as shown by the similarity of sebum excretion rates in identical twins, postulating the mechanism of a genetically mediated elevation of circulating androgens.[14] Acne is a disease of the pilosebaceous follicle and, during adolescence, there is an increase in the production of sex hormones (mainly androgens) that stimulate the sebaceous glands to produce more sebum. Indeed, there is a direct relationship between the degree of seborrhoea and the severity of the acne[15] and sebum itself is comedogenic (comedone-forming) and causes inflammation if cutaneously injected.[16] The epithelial cells lining the pilosebaceous follicle are normally desquamated (shed) and carried to the surface of the skin in the sebum. In acne, there is an increase in the production of epithelial cells lining the follicle, a process termed "ductal hypercornification", which can lead to the blockage of the follicle. When the blockage occurs close to the surface of the skin, pigment in the desquamated cells reacts with the atmosphere and turns black. This produces an open comedone or blackhead, which is the primary acne lesion.[17] The mechanism that initiates hypercornification is now thought to be an inflammatory process. Research by Jeremy *et al*[18] demonstrated the presence of significant inflammatory factors such as CD3+ and CD4+ T cells and large macrophages around clinically normal follicles before hypercornification. In addition, Guy and Kealey[19] observed that *in vitro*, the pro-inflammatory cytokine interleukin-1a (IL-1a) was able to induce comedonal features such as hyperproliferation and abnormal differentiation in isolated pilosebaceous follicles. In an *in vivo* study by Aldana *et al*,[20] comedones were found to contain sufficient IL-1a to initiate a non-specific inflammatory response if released into the dermis. However, what remains unclear is the specific trigger for increased production of 1L-1a. It has been suggested by Jeremy[18] that since follicular keratinocytes in acne are known to be deficient in the essential fatty acid linolenic acid, this could provide the necessary trigger for the increased production of IL-1a. If these studies are correct, it might explain the action of many anti-inflammatory acne therapies and strengthen the argument that patients should apply treatment, not just to the inflamed lesions but to the whole of the acne-prone area.

Finally, what is the role of the skin bacterium *Propionibacterium acnes* in acne? As noted by Bojar and Holland[21] "there is no formal proof linking *P acnes* with acne". In a study by Graham *et al*,[22] it was shown that viable *P acnes* species were able to induce keratinocytes to produce IL-1a and other agents such as tumour necrosis factor *in vitro*. *P acnes* therefore might have a contributory role in comedogenesis through induction of IL-1a within keratinocytes. In addition, there is some evidence that the bacterium has T-cell mitogenic activity[23] and such activity may contribute to inflammation via activation of T cells and the release of immunological cytokines. The mechanism through which *P acnes* is able to stimulate cells to release cytokines appears to be mediated through activation of toll-like receptor 2 (TLR2) on the surface of cells.[24] The TLRs, of which several types have been identified, are pattern recognition receptors on the surface of cells that can mediate an immune response to bacterial ligands. Indeed, activation of the TLR2 suggests that this is a primary mechanism responsible for the inflammatory changes in acne.

Mode of action of benzoyl peroxide

Benzoyl peroxide has both comedolytic and antibacterial effects. Evidence for the comedolytic effect comes from several studies. Work with experimentally induced comedones by Oh and Myung[25] and Kaidbey and Kligman[26] both demonstrated that 5 per cent benzoyl peroxide was an effective comedolytic. Kligman *et al*[27] have also shown that benzoyl peroxide can reduce the size of

Rod Tucker, PhD, MRPharmS, is a pharmacist at HMP Hull. Shernaz Walton, MD, FRCP, is consultant dermatologist at Hull and East Yorkshire Hospitals NHS Trust (e-mail rodtucker@rodtucker.karoo.co.uk)

comedones by as much as 50 per cent in experimental models. Further support for the comedolytic action was provided by Cunliffe,[28] who observed that 5 per cent benzoyl peroxide increased the sebum excretion rate by 22.5 per cent, and Pierard-Franchimont,[29] who observed how an increase in sebum excretion rate with benzoyl peroxide correlated with an improvement in acne lesions. It was postulated that this increase was due to an effect on non-inflamed lesions, possibly by reducing pilosebaceous duct obstruction.

The bactericidal properties of the drug have been well documented. Bojar *et al*[30] showed that application of 5 per cent benzoyl peroxide gel significantly reduced the number of *P acnes* recovered from both the skin surface and follicles after only 48 hours. Furthermore, at the end of the study period (28 days) the acne severity was significantly reduced compared with baseline values. In another more recent study comparing benzoyl peroxide 6 per cent gel with clindamycin 1 per cent gel, benzoyl peroxide reduced the population of *P acnes* after only three days to the same extent as clindamycin did after 14 days.[31] Indeed, Kligman[32] has suggested that twice daily application of benzoyl peroxide for five days will reduce the *P acnes* population by more than 95 per cent, a feat that no antibiotic can match.

The anti-bacterial action of benzoyl peroxide is probably related to its ability, once in the skin, to release free radical oxygen. The drug is lipophilic: it penetrates the stratum corneum and enters the pilosebaceous follicle. It is rapidly broken down to benzoic acid and hydrogen peroxide and generates free radicals that oxidise proteins in bacterial cell membranes, exerting a bactericidal action.[33] In addition, Fulton *et al*[34] and Cunliffe[35] have shown how benzoyl peroxide can reduce the free fatty acid content of sebum, which provides a useful marker for bacterial activity. Benzoyl peroxide has an anti-inflammatory action and there is evidence from *in vitro* studies to suggest that this action arises from its ability to kill polymorphonuclear leukocytes (PMN cells) in the pilosebaceous follicles and so prevent their release of reactive oxygen species (ROS) such as peroxides which enhance tissue inflammation.[36]

Effectiveness of benzoyl peroxide

One extensive review of the literature on the management of acne in 2001[37] found that, of 250 comparisons, only 14 had level A evidence (ie, based on at least two trials of acceptable quality with good statistical and meaningful clinical outcomes). This review concluded that benzoyl peroxide is superior to vehicle or placebo. A second, more recent systematic review using more rigid inclusion criteria looked at well designed randomised controlled trials from 1966 to 2004[38] and identified only one clinical trial involving benzoyl peroxide. A search of PubMed using the terms "acne vulgaris" and "benzoyl peroxide" identified several studies. The refer-

Table 1: Details of randomised, double-blind (RDB) clinical studies using benzoyl peroxide (BP) for the treatment of acne

Study details	Severity/area	Comments
Shalita *et al*[39] RDB; n = 420 10 weeks	Grade II–III (defined), face only	Combination of erythromycin 3%/BP 5% gel v individual components and vehicle. Combination produced greater reduction in inflamed lesions than BP alone but difference not significant for comedones.
Jaffe *et al*[40] RDB; n = 107 12 weeks	Severity of acne rated for individuals on back, chest and face	BP 5% cream with potassium hydroxyquinine sulphate (PHQ) v BP without PHQ v BP with 1%hydrocortusone v vehicle base. Greater improvement in scores for face, chest and back occured with 10% BP combined with PHQ compared with BP cream alone and vehicle base. Large improvements noted with vehicle alone.
Leyden *et al*[41] RDB; n = 480 10 weeks	Moderate – moderately severe acne (defined), face only	BP 5%/clindamycin 1% combination gel v separate components v placebo. Combination of BP 5%/clindamycin 1 % produced statistically greater reduction in inflamed and total lesions (inflamed and non-inflamed compared with BP alone at week 6. Improvements in acne grade occurred in 46% in combination group and 31% in BP group. Adverse effects were similar in all groups.
Hunt *et al*[42] RDB; n = 150 12 weeks	Mild to moderate (not defined), face only	Significant reduction in both non-inflamed and inflamed lesions with 5% BP lotion compared with gluconolactone 14 %. No patient perception data reported.
Tschen *et al*[43] RDB; n = 287 10 weeks	Grade II – III (defined), face only	Study as Leyden above.[41] Combination of clindamycin 1%/BP5% produced significantly greater reductions in inflamed lesions than BP at week 8. The reductions in non-inflamed lesions and global improvements were similar for the combination and BP.
Lookingbill *et al*[44] RDB; n = 334 12 weeks	Moderate – severe, face only	Clindamycin 1%/BP 5% gel combination v separate components v vehicle. Greater reduction in inflamed lesions with combination. Similar reduction in non-inflamed lesions to BP alone.
Norris *et al*[45] RDB; n = 69 12 weeks	Mild – moderate (defined), face, chest, and back	Oxytetracycline 500mg daily v BP 5% gel v tetracycline topical gel. All treatments produced significant improvements. However there was no significant difference between any of the treatments.
Borglund *et al*[46] RDB; n = 106 10 weeks	More than 10 papules/pustules, face only	Topical meclocycline v BP 5% gel v combination of the two. BP more effective than either single agent or combination.
Dunlop *et al*[47] BD; n = 70 12 weeks	Mild – moderate (defined) Area – not defined	Isolutrol vs BP 5% lotion. No difference in the reduction of inflamed lesions, but BP significantly better at reducing non-inflamed lesions. Greater incidence of unwanted effects with BP.
Burke *et al*[48] RDB; n = 94 8 weeks	Mild – moderate (defined), area unknown	Erythromycin 1.5% v BP 5% gel v erythromycin vehicle. Equally effective at reducing inflamed lesions but BP much better at reducing non-inflamed lesions.
Boutli *et al*[49] RDB; n = 37 12 weeks	Grade II (defined), face only	Chloroxylenol and salicyclic acid 2% v BP 5% gel. No difference between groups but both showed a significant improvement in all lesion types. Adverse effects greater in BP group.
Papageorgiou *et al*[50] RDB; n = 41 8 weeks	Grade I, face only	Chloroxylenol and zinc oxide v BP 5% cream. Significant reduction in both types of lesions but no difference between treatments.
Swinyer *et al*[51] RDB; n = 60 12 weeks	More than 20 facial lesions, face only	BP 5% gel v clindamycin 1%. Greater reduction in total lesions by BP.
Milani *et al*[52] RDB; n = 60 8 weeks	Mild – moderate acne (defined), face only	BP 4% gel v hydrogen peroxide 1%. No difference in reduction of lesions however, hydrogen peroxide gel had better tolerability profile.
Hughes *et al*[53] RDB; n = 77 12 weeks	Mild – moderate acne (defined), face only	BP 5% gel v isotretinoin gel 0.05% v placebo. BP effective earlier than isotretinoin and had a greater effect on inflamed lesions. Little difference in adverse effects.
Chalker *et al*[54] RBD; n = 165 10 weeks	Grade III (defined), face only	BP 5%/erythromycin 3% combination v 5% BP gel v 3% erythromycin gel v vehicle gel. Combination not different to BP for comedone reduction or for papules and pustules.

Table 2: Details of clinical studies using benzoyl peroxide (BP) for the treatment of acne that were not randomised or double-blind

Study details	Severity/area	Comments
Bucknall *et al*[55] Single blind; n = 44 12 weeks	Severity – not reported, face only	BP 5% lotion and tretinoin 0.025% lotion. Greater improvement, based on lesion counts and both clinician and patient-rated opinion, for tretinoin.
Belknapp[56] Parallel group comparison; n = 69 8 weeks	Grade II – III, face only	BP 5% gel v retinoic acid 0.05% cream. Significantly more patients in BP experienced overall excellent results.
Lyons[57] Controlled, randomised n = 147 8 weeks	Grade I – III, area not reported	BP 5% gel v tretinoin cream 0.1%. Patients changed after 4 weeks to 10% BP. No significant differences in total lesion count but BP significantly better at reducing inflamed lesions and as good at reducing non-inflamed lesions.
Korkut *et al*[58] Open labelled, prospective; n = 105 6 months	Severity not reported, face only	BP 5% lotion v adapalene 0.1% v combination. No significant difference (based on lesion counts) between all three groups at follow-up. Concluded that combination therapy is no more effective than monotherapy.
Bassett *et al*[59] Randomised single blind (RSB); n = 124 12 weeks	Mild – moderate, area not recorded	BP 5% lotion v 5% tea-tree oil lotion. Both therapies equally effective, in terms of lesion reduction but onset of action of tea-tree oil was slower.
Nascimento *et al*[60] RSB; n = 178 11 weeks	12 inflamed, 12 non-inflamed lesions, face only	BP 4% gel v adapalene 0.1% gel. No difference between the groups. Results based on lesion counts.
Gold[61] Non-randomised, open label; n = 963 4 weeks	Severity not reported, face only	BP 4.5 or 8.5% in 10% urea cream or gel and cleanser only, BP preparation and oral doxycycline and BP preparation and oral minocycline. Patients prescribed cleanser or gel at equal strengths. Greatest reduction in lesions for BP and doxycycline (52%). BP combination alone produced 44% reduction in total lesions.
Sawleshwarkar *et al*[62] Open label, non-comparative; n = 630 6 weeks	Grade I – III (defined), face only	BP 4% in hydrophase base. Physician assessment showed 85% had good to very good effect, patient's rated satisfaction was 72% after 6 weeks. No data on lesion counts.
Devillez[63] RSB; n = 30 11 weeks	Minimum 12 inflammed lesions, face only	BP 4% gel v benzyamcin gel. No significant difference between groups. BP faster onset of action. Measurement based on inflamed lesions only.
Tucker *et al*[64] RSB; n = 79	Mild to moderate, face only	BP 5% gel plus clindamycin 1% gel v BP and clindamycin gels alone. Combined use of two agents superior to either agent alone.
Leyden *et al*[65] RSB; n = 492 10 weeks	Grade II – III (defined), face only	BP 5%/clindamycin 1% gel v BP 5% gel v BP5%/erythromycin 3% gel. No significant difference in comedone reduction between groups. Significant ($P = 0.04$) difference in reduction of inflamed lesions between BP/clindamycin v BP alone
Dogra *et al*[66] Type not defined; n = 100 6 weeks	Not defined	BP 10% cream, retinoic acid 0.05% cream, erythromycin 2% lotion, glycerine in methylated spirits 50%. Based on lesion counting. Reductions in non-inflamed and inflamed lesions similar for BP and retinoic acid and similar to erythromycin for inflamed lesions only.

Table 3: Reduction in lesions with benzoyl peroxide reported in trials

Study reference	Reduction in lesions	
	Inflamed	Non-inflamed
Shalita *et al*[39]	37	11
Tschen *et al*[43]	53	50
Lookingbill *et al*[44]	39	30
Norris *et al*[45]	60	58
Burke *et al*[48]	37	29
Boutli *et al*[49]	40	46
Swinyer *et al*[51]	52	63
Milani *et al*[52]	71	62
Bucknall and Murdoch[55]	38	53
Lyons[57]	56	62
Korkut and Piskin[58]	72	70
Do Nascimento *et al*[60]	58	46
Tucker *et al*[64]	37	14
Leyden *et al*[65]	32	30
Dogra *et al*[66]	64	70

ence lists from these studies were reviewed from which further studies were identified. The randomised, double-blind, controlled trial is considered to be the gold standard and Table 1 gives details of the randomised trials (published in English only) which involve comparisons with benzoyl peroxide. There are a number of other trials with benzoyl peroxide which were not double-blind but report changes in lesion counts as the primary measure of efficacy and these studies are described in Table 2. Studies with benzoyl peroxide before 1980 have been reviewed by Cotterill[6] and although all showed improvements, the studies were uncontrolled. The studies in Table 1 all used changes in lesion count as the primary measure of efficacy and measured the severity of acne with either a recognised grading system or a system clearly specified by the authors. In addition, studies were conducted for a minimum of eight weeks with most lasting for 10 to 12 weeks. Unfortunately, there were some noticeable drawbacks with the studies. Acne predominately affects the face, chest and back, and only one study considered the impact of treatment on all three areas; all the other trials considered only facial acne. The different vehicles for benzoyl peroxide, such as creams, gels and lotions, make comparisons between studies more difficult although, as can be seen from Table 1, most studies have used a gel preparation.

Despite these drawbacks, the data in Tables 1 and 2 provide sufficient information to draw some conclusions about the efficacy of benzoyl peroxide. First, the drug is effective compared with placebo and, secondly, it is effective against inflamed and non-inflamed lesions. Furthermore, combining benzoyl peroxide with an antibiotic, such as erythromycin or clindamycin, appears to improve the efficacy against inflamed lesions although the effect on non-inflamed lesions is no better than benzoyl peroxide alone. Furthermore, the adverse effect profile is also similar to benzoyl peroxide alone. Finally, of the five studies in which benzoyl peroxide is compared with a topical retinoid, only one study demonstrated a superior response for the retinoid with the others either showing either no difference or that benzoyl peroxide was slightly better.

Despite this apparent lack of difference, clinical guidelines on the management of acne[67,68] recommend that topical retinoids rather than benzoyl peroxide should be first-line therapy for comedonal acne. In fact, a recent study on health volunteers found that the keratolytic properties of benzoyl peroxide was similar to both salicylic acid and retinoic acid,[69] which suggests that benzoyl peroxide is more keratolytic than previously thought and offers support for the comedolytic action of the drug observed in the trials.

The mean reduction in lesion counts for both inflamed and non-inflamed lesions (where reported in studies) are illustrated in Table 3. One of the most striking features of Table 3 is the large variation in the effect on non-inflamed lesions — between 11 and 70 per cent. The data in Table 3 are derived from eight randomised, double-blind studies, three randomised, single-blind studies and four

others. There is no obvious explanation for this variation since all but three of the studies used a gel formulation and it has been suggested that gel formulations give rise to the greatest bioavailability.[70] Furthermore, two studies comparing different benzoyl peroxide formulations found no difference in efficacy when lesion counts were used as the primary end-point.[71,72] It is possible that some of the variation might be explained by differences in the lesion-counting techniques used in the trials. Nonetheless, variations in the extent of lesion reduction have been observed by Haider and Shaw[38] in a review of randomised, controlled trials of acne therapies. The average percentage reduction in lesions based on the data in Table 3 is 50 and 46 per cent for inflamed and non-inflamed lesions, respectively. This is greater than a value of 35 per cent for non-inflamed lesions reported by Cunliffe.[73]

Finally, the value of benzoyl peroxide in acne has been recently highlighted in a randomised, controlled study in primary care comparing a range of oral and topical treatments in facial acne. It concluded that "benzoyl peroxide alone was the most cost-effective regimen for mild to moderate facial acne.[74]

Practical advice for managing acne

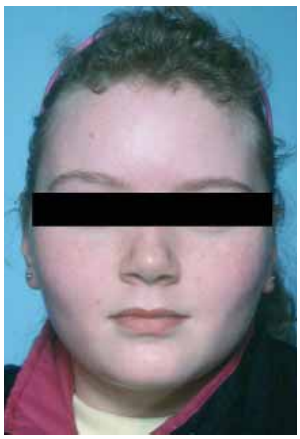
It is important that pharmacists have some appreciation of how acne severity is assessed before recommending or initiating therapy. Although several assessment scales are available these are more suited to clinical trials. In general, acne is assessed as being mild, moderate or severe (Figures 1–3), and pharmacists should identify the types of lesions present and make a broad assessment of the acne severity:

- Mild acne consists mainly of non-inflamed lesions (comedones)
- Moderate acne consists of a mixture of both inflamed lesions, ie, papules and pustules, in addition to comedones
- Severe acne consists of inflammatory papules, pustules as well as nodules and cysts

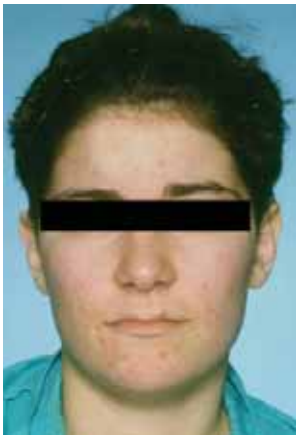
Benzoyl peroxide is licensed for the treatment of mild to moderate acne so pharmacists can treat a patient's acne if it falls within either or these categories.

Benzoyl peroxide is available in a range of strengths and one study comparing the efficacy of all three commonly used strengths (2.5, 5.0 and 10 per cent) found no difference in efficacy.[75] Another small study with 50 patients reported on the use of three concentrations of benzoyl peroxide 3 per cent (not available in the UK), 5 per cent and 10 per cent in moderately severe acne, and the authors noted that there was no real difference between the three groups.[76]

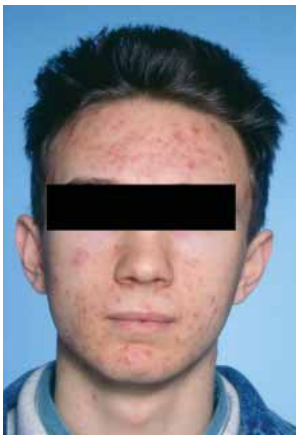
As shown in Tables 1 and 2 most of the clinical evidence is based on 5 per cent benzoyl peroxide and there seems little to be gained by using the 10 per cent preparation. Benzoyl peroxide is also available in various



Mild acne



Moderate acne



Severe acne

Case study: Danny

Danny is a 15-year-old boy who comes to the pharmacy one afternoon with his mother, who asks for advice and something to treat his blackheads. On examination you notice that he has a number of open and closed comedones with a few small papules. He also complains that his skin feels greasy. He has not tried anything for his acne. What treatment would be suitable?

Danny has predominately mild acne and so would benefit from the use of a cleanser and benzoyl peroxide alone. It is necessary to advise him that it can take up to six weeks before assessing the effect of treatment. It does not really matter which cleanser is used — in fact there is little evidence that cleaners are effective (see text for details). Some authorities recommend that soap and lukewarm (not too hot or cold) water is all that is needed. Cleansing the skin will remove excessive sebum which is a substrate for *Propionibacterium acnes*. He should dry his skin and wait about 20 minutes before applying his benzoyl peroxide preparation to reduce irritation. He also needs to allow the benzoyl peroxide preparation to dry before going to bed to avoid bleaching of bed linen.

Case study: Cheryl

Cheryl is a 17-year-old trainee hairdresser who pops in late one evening after work to ask for your advice about her acne. She has had it for about a year and says that it was not really troubling her until now. She wears heavy make-up to cover her spots. She tells you that she has tried a cream from the Oxy-range which she purchased from a supermarket but cannot remember exactly what it was. She said that it made her skin sore and dry so she stopped using it after a few weeks. What advice would you give her?

Cheryl's acne is unlikely to respond to a different benzoyl peroxide preparation and it would be prudent to refer her to the GP. The GP would probably prescribe a topical retinoid drug which would target the formation of comedones which are the precursor of acne lesions. Cheryl can also use a commercial cleanser or soap and water if she prefers. It is worth telling Cheryl to apply the treatment to the whole of the affected area rather than just the individual spots. She also needs to be aware that her acne might worsen in the early stages (a common problem with retinoids) and she should be advised to continue as the acne will improve over time.

Case study: Matthew

Mathew is a 19-year-old student who has suffered from acne for several years but has not really bothered to do anything about it. You invite him into the consultation room and he removes his tee-shirt to show you the acne on his chest and back ,which is widespread. He also has a number of papules on his face and wants to know if he can have some cream to get rid of his spots. What would you suggest to him.

Mathew has moderate to severe and widespread acne that will not respond effectively to topical therapy alone. He needs to have oral antibiotic therapy and so needs to be referred to his GP to start treatment. Oral antibiotics can be used in conjunction with topical therapy such as benzoyl peroxide or topical retinoids. Benzoyl peroxide is a useful adjunct treatment if oral therapy is continued as it does not cause bacterial resistance.

washes although there is little evidence to recommend these. Indeed, one recent open label study with a benzoyl peroxide 3 per cent wash (not available in the UK) found that it produced a small reduction in both inflamed and non-inflamed lesions,[77] which is much less than the reductions observed for topical, leave-on products.

Benzoyl peroxide is available in different formulations, such as gels, aquagels, creams and lotions, and is available in many OTC as well as prescription products although it is often combined with antibiotics in prescription-only preparations. On a practical level, it has been suggested that the type of formulation used should be matched to a patient's skin type although there is no clinical evidence to support this. For instance, patients with oily skin might benefit from the application of a gel, wash or solution, which tends to exert a drying effect on the skin.[78] Those with dry or sensitive skin may benefit from the application of a cream, which has a moisturising effect. The general advice on using a benzoyl peroxide product is to start with a low concentration to minimise adverse effects. Sensitivity problems with benzoyl peroxide are reported to occur in around 1 to 2.5 per cent of patients.[79] They are often more likely in females and in those with dark skin, so low concentrations should be used initially with these patients. Nevertheless, it is important to emphasise to patients that the adverse effects are short-lived (one to two weeks only). It has been recommended that benzoyl peroxide is initially left on the skin for 15 minutes and then washed off and the exposure time increased gradually by 15 minutes until the drug can be tolerated for two hours.[80] In addition, it is helpful to advise patients that the irritating and drying effects of some formulations can be reduced by applying a non-comedogenic, water-based emollient, provided a suitable period is left between applications. Pharmacists should tell patients to avoid the use of ointments or oil-rich creams, which will block pores.

Irrespective of the type of formulation, benzoyl peroxide is a bleaching agent and patients need to be informed that clothes, towels, pillow cases etc can be affected. Patients should wash their hands after applying benzoyl peroxide.

Female patients wondering about the use of make-up and topical acne therapies can be advised to use light or oil-free (sometimes labelled as "non-comedogenic") make-up if needed during the day and to use their topical preparations only at night when they have removed their make-up.

It is also important that patients are informed that topical preparations should be applied sparingly, a pea-sized amount is sufficient to treat the face. More is not better: in fact, applying too much preparation is likely to increase irritation. In addition the whole of the affected areas should be treated not just the individual lesions. This is because most topical therapies (including benzoyl peroxide) have a preventive action against new lesions, rather than being effective against existing lesions. Pharmacists should tell patients to persevere with therapy. Acne responds slowly to treatment and requires at least six weeks before the efficacy of a preparation should be assessed although some degree of improvement should be apparent before the end of the six weeks. If the treatment is effective, there is no consensus on the continued length of application. Indeed, benzoyl peroxide can be used indefinitely, provided it is tolerated, although the frequency of application can be reduced once the acne has cleared. If patients find that treatment with benzoyl peroxide is not effective after six weeks, changing the strength or formulation is unlikely to be effective unless the patient has experienced compliance problems and alternative treatments should be sought, probably from their GP. Benzoyl peroxide can also be used in conjunction with other topical preparations such as retinoids. In such cases, pharmacists should advise patients to use the benzoyl peroxide in the morning and the retinoid 12 hours later.

Women with mild acne who are pregnant can be treated with benzoyl peroxide although if the condition has significant inflammation then benzoyl peroxide is best combined with topical erythromycin, for which pharmacists should refer patients to their GP. It is worth noting that topical retinoids should be avoided in pregnancy. Examples of cases that pharmacists might encounter in practice are outlined in the Panel.

OTC alternatives to benzoyl peroxide

If patients find benzoyl peroxide too irritating or ineffective, what are the options for pharmacists? There are at least three agents available OTC which can also be used to treat mild to moderate acne: salicyclic acid, nicotinamide, and cleansing washes containing chlorhexidene and povidone-iodine. One recent systematic review of the evidence for the myths and misconceptions in acne management found some, albeit weak, evidence for the role of facial washes containing chlorhexidene and povidone-iodine.[81] One review of four clinical trials with salicyclic acid-based solutions found some evidence to support the effectiveness of the drug with the greatest effect from a 2 per cent solution.[82] A further study using a facial wash containing 2 per cent salicyclic acid has also shown benefits.[83] The best evidence is therefore for a 2 per cent solution and pharmacists should advise patients to use only preparations that contain the drug at this strength. There has been one, randomised controlled trial with nicotinamide and topical clindamycin that showed nicotinamide to be equally effective.[84]

Conclusion

In conclusion, all the available evidence suggests that benzoyl peroxide is an effective drug in the management of mild to moderate acne. Pharmacists presented with requests for treatment for acne can recommend a benzoyl peroxide preparation in the knowledge that the drug is comparable in efficacy to therapies available on prescription. They should help patients to select a product based on their skin type as well as offering advice on how to use the product. With the increasing emergence of bacterial resistance to antibiotics, patients can be reassured that there is no reported evidence of resistance to benzoyl peroxide. It is 26 years since Melski and Arndt concluded that "the benzoyl peroxide preparations are the single most useful group of topical agents and agents of choice for most patients"[85] and it would seem that this statement is still valid today.

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