Section 13.4 Dermatological medicines (topical) – Medicines affecting skin differentiation and proliferation

Benzoyl peroxide

Review submitted by
The International League of Dermatology Societies.
Question raised by the 18th Expert Committee on Selection and Use of Essential medicines

Should adults and children with mild to moderate acne be treated with benzyl peroxide compared to other topical preparations for acne?

Summary of review

It is the view of the ILDS working party that benzoyl peroxide should be retained on the WHO list of essential medicines for both adults and children. It is the first line treatment for acne, one of the common skin conditions, mostly affecting younger age group. It is effective, safe and easily available worldwide for topical treatment of acne. Other treatments for acne listed on the essential medicines lists include tetracycline (oral).

Public health need

Acne vulgaris is a very common skin condition affecting the pilosebaceous unit. Estimates of prevalence indicate that between 50-80% of teenagers between 14-16 year of age have this condition, which can affect the quality of life. Acne also occurs, but is rare, in children below the age of 10. The prevalence declines in individuals above the age of 25, although it occurs regularly in those between the ages of 25-40. It is rare in individuals above the age of 50. It is a disease that is seen in otherwise healthy individuals, but can occur in women with underlying disorders of androgen metabolism such as polycystic ovary syndrome. These constitute a minority of patients, who would need disease specific treatment as well.

Evidence on efficacy and safety

Benzoyl peroxide is a comparatively old medication that has been in use in different formulations for over 50 years. It is still the first line choice of treatment for mild to moderate acne being effective and inexpensive. It is listed as first line treatment in a large number of national treatment guidelines eg USA (http://emedicine.medscape.com/article/1069804-treatment), International paediatric (http://pediatrics.aappublications.org/content/118/3/1188.full.html), UK GPs (http://www.equidelines.co.uk/equidelinesmain/gip/vol_14/oct_11/poyner_acne_oct11.php)

Two systematic reviews comparing benzoyl peroxide (BP) versus placebo in 1999 [1] and 2004 [2] both rated the treatment as effective with a low level of adverse events which were mainly erythema, peeling and, in some cases, burning. There is evidence that combing benzoyl peroxide with clindamycin may be more effective (Table 1). A recent systematic assessment of evidence on management of acne confirms that benzyl peroxide should be considered as first line treatment in mild acne [3]. This assessment provides GRADE tables for the studies and has compared benzyl peroxide with other treatments. The evidence tables can be accessed from http://www.clinicalevidence.bmj.com/x/systematic-review/1714/overview.html. The evidence
assessment tables on benzoyl peroxide can be accessed at http://www.clinicalevidence.bmj.com/x/systematic-review/1714/intervention/sr-1714-i2.html The analyses also found that topical antibiotics or topical retinoids are indicated as treatments for mild acne that does not respond to benzoyl peroxide. Within the antibiotic class, there is more evidence of benefit with topical clindamycin or erythromycin than with erythromycin plus zinc or tetracycline.

Other recent publications also recommend benzyl peroxide for the treatment of acne as compared to other treatment modalities for acne [4]. Topical antibiotics and retinoids are recommended as alternatives.

Table 1 From Review Haider and Shaw 2004 [2]

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of patients</th>
<th>Treatment length (wks)</th>
<th>Severity</th>
<th>Arms of study</th>
<th>Reduction of lesions %--inflammatory</th>
<th>Reduction of lesions %--non-inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lookingbill et al 1997 JAAD</td>
<td>334</td>
<td>11</td>
<td>Mild – moderate</td>
<td>Clindamycin1% + Benzoyl Peroxide 5% gel</td>
<td>61</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>1997 37:590-595</td>
<td></td>
<td></td>
<td>Clindamycin1%gel</td>
<td>35</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Benzoyl peroxide5%gel</td>
<td>39</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vehicle</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

Benzoyl peroxide is available in different concentrations from 2.5-10% but there is no firm evidence linking concentration with clinical efficacy [5] although there is a higher risk of skin irritation with high strength concentrations eg 10%. The principle adverse reaction associated with the application of benzoyl peroxide containing medications is skin inflammation such as erythema and scaling and irritant contact dermatitis which is seldom severe. The adverse events are also assessed in the evidence tables mentioned above and can be accessed using the same links.

The age range of those tested in clinical trials has generally been over 14 years. However a recent review of paediatric use in younger children assessed the clinical trial safety data and efficacy and concluded that benzoyl peroxide could be safely used in younger children [6]. This included the rare condition, infantile acne, although authors stipulated that caution should be exercised in view of the irritancy seen in some patients.

There is also no evidence that there is any difference in skin irritancy potential in populations from different and multiple ethnic backgrounds [8]

Regulatory status
It is an OTC medication in most countries. A review by the Federal Drug Administration in 2011 [7] of the safety of the use of benzoyl peroxide containing medications stated the following.

..to include benzoyl peroxide as a generally recognized as safe and effective (GRASE) active ingredient in over-the-counter (OTC) topical acne drug products. In addition, this final rule includes new warnings and directions required for OTC acne drug products containing benzoyl peroxide.

- Do not use benzoyl peroxide on very sensitive skin.
- Keep benzoyl peroxide products away from the eyes, lips, and mouth.
- Benzoyl peroxide may bleach hair or dye fabric.

References


7. Federal Drug Administration , HHS. Classification of benzoyl peroxide as safe and effective and revision of labeling to drug facts format; topical acne drug products for over-the-counter human use; final rule. Fed Regist. 2010;75:9767-77