CURRENT PRACTICE IN TREATMENT APPROACH FOR BULLOUS PEMPHIGOID: COMPARISON BETWEEN NATIONAL SURVEYS FROM THE NETHERLANDS AND THE UK

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Abstract

Treatment approaches for bullous pemphigoid (BP), the most common autoimmune skin blistering disease, are largely based on national and international guidelines. We conducted a national survey among dermatologists in The Netherlands to explore the current treatment of BP, and compared the results with those of a previously published survey from the UK. Almost all responders in The Netherlands (n=175) used very potent topical corticosteroids, both as monotherapy and as adjunctive therapy. In contrast to UK dermatologists, the majority recommended whole-body application rather than local application to lesions. Systemic antibiotics were used by >70% of responders. Half of the responders in The Netherlands considered systemic steroids the first-choice treatment, with the majority also using adjunctive therapy as a routine. Despite many similarities in treatment approach between the two countries, these surveys provide an important insight into the gap between actual and recommended practice at a country level in relation to the best external evidence.
LEARNING POINTS

• High-quality evidence about current practice and optimum treatment for BP is limited.
• Treatment of BP is usually based on topical and/or systemic corticosteroids, although systemic antibiotics and adjunctive immunosuppressants are also widely used.
• Dermatologists in the UK and The Netherlands show variations in practice with regard to whole-body application of very potent topical corticosteroids, but preferences for topical corticosteroids and anti-inflammatory systemic antibiotics are similar.
• Whole-body application of very potent topical corticosteroids is not always preferred, owing to differences in national guidelines, health service models and practical factors.
• Systemic anti-inflammatory antibiotics are used widely, and considered safe and effective in mild disease; results about their effectiveness in current practice are expected.
• More multicentre comparative studies are needed to validate outcomes of common practice for the treatment of BP.
Bullous pemphigoid (BP) is the most common autoimmune skin blistering disease worldwide, and mainly affects elderly patients. The incidence is estimated between 6.6 and 43 cases per million persons per year, with a substantially increasing incidence with age.1 Because of the high burden of the disease due to its severe itching/blistering and its increasing incidence, an effective treatment approach is needed.1,2 High-quality evidence regarding current treatment practice and optimum treatment approach for BP is limited. BP is usually treated with topical and systemic glucocorticosteroids.3 However, treatment with high-dose systemic corticosteroids in an elderly population is associated with serious adverse effects. According to recent surveys, systemic anti-inflammatory antibiotics, such as tetracyclines, are used widely for treatment of BP in Germany and the UK.4,5 Results of a current randomized controlled trial (RCT) comparing the effectiveness of tetracyclines versus systemic corticosteroids in the treatment of BP [the Bullous Pemphigoid Steroids and Tetracyclines (BLISTER) study] are expected soon.6 To gain further insight into the current practice for the treatment of BP we have carried out a nationwide online survey in The Netherlands and compared the results with those of an earlier survey in the UK.

REPORT

A nationwide online survey (Limesurvey.org, Hamburg, Germany) was conducted in The Netherlands among dermatologists and residents in dermatology who were members of The Netherlands Society of Dermatology and Venereology (NVDV) in spring 2014. We used a validated translation of the questionnaire previously used in a UK survey (The UK Association of Dermatologists Guideline Development Group 2012; see Supplementary material) with permission, in order to permit a direct comparison with the treatment approach of dermatologists in the UK.5

Fisher exact test was used to compare independent proportions, Mann Whitney U-test was used to compare mean ranks. For all tests, two-sided p-values of <0.05 were considered to indicate statistical significance.

Dermatologists (n=475) and residents in dermatology (n=200) in The Netherlands were contacted, of whom 175 (25.9%) responded. The majority of responders were dermatologists (n=145, 82.9%), and the remaining 30 responders (17.1%) were residents. Half of the responders reported <5 new patients with BP diagnosed per year, with another 36.0% reporting 5-10/year and 6.8% reporting >10/year.

The majority of responders used topical steroids as sole treatment for localized BP (98.9%) and as adjunctive treatment for widespread BP (88.0%). Nearly 68% of responders also used topical steroids alone for widespread BP. Very potent topical steroids were favoured by the majority of responders (89.3%). More than half of the responders (52.4%) recommended applying topical steroids over the whole body including the healthy skin but sparing the face, as described by Joly et al.7 The majority (58.2%) of survey responders discontinued the use of topical steroids after remission of BP (Fig. 1).

Anti-inflammatory antibiotics were used to treat BP by the majority of the responders (72.8%). The preferred drugs were doxycycline (41.0%), tetracycline (16.0%) and minocycline (12.0%) (Fig. 2). Almost 60% of the responders who prescribed anti-inflammatory antibiotics considered these medications to be ‘sometimes effective’, whereas 17.1% found them ‘often
effective’ and 23.4% did not find them at all effective in treatment of BP. The majority of responders did not observe any adverse effects. The most commonly reported adverse effects were gastrointestinal complaints (n=19), hyperpigmentation (n=5), vertigo (n=5), photosensitivity (n=3), abnormal liver function (n=2) and Candida infection (n=1).

Half of the responders (50.6%) used systemic corticosteroids as first choice in treatment of BP. The majority (57.7%) used an adjunctive therapy routinely with systemic corticosteroids, mostly azathioprine as an immunosuppressive adjunctive therapy (by 44%).

Compared with dermatologists in the UK, dermatologists and residents in dermatology in The Netherlands recommended whole-body application of topical steroids more often (14.4% and 52.4%, respectively) (Fig. 1). Furthermore, dermatologists in the UK reported a different treatment strategy, as they were more likely to continue with the application of topical steroids after remission in order to control flares (66.2% vs. 41.8%, respectively). Preferences for topical steroids, anti-inflammatory antibiotics and preferred antibiotic were remarkably similar (Table 1).

There appears to be variation in the mode of use of topical steroids. However, the treatment approach of the UK dermatologists who were surveyed in 2012 concurs with the

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**Fig. 1** Preferences in the use of topical corticosteroids in treatment for BP compared between Dutch dermatologists and residents in dermatology (n=175) and British dermatologists (n=375, data shared with permission, Taghipour et al.).
recommendation of the British Association of Dermatologists (BAD) guideline for the management of BP, whereas dermatologists in The Netherlands appear to follow the treatment strategy advised by The Netherlands Center for Blistering Diseases. The BAD guideline does not recommend whole-body application in severe disease because of practical considerations, possible systemic absorption and adverse effects. By contrast, the recommended treatment strategy in The Netherlands is whole-body application of very potent topical steroids in mild, moderate and severe disease.

A national survey performed in Germany in 2007, showed that only a minority (27%) of dermatologists working in (university) hospitals used topical steroids exclusively for treatment of BP. The difference in the recommendation of whole-body application of topical steroids may be explained by differences in national guidelines and health service models, such as the availability of caregivers to apply the topical treatment or the initiation of treatment during inpatient stays in Germany; in The Netherlands, patients with BP are usually treated as outpatients. Although the evidence from RCTs for whole-body application of topical corticosteroids dates from 2002 and 2009, it appears that the widespread adoption of such a treatment strategy is dependent on its reinforcement by national expert recommendations, e.g. the first German guideline for the treatment of bullous pemphigoid was published in 2014.

Fig. 2 Preferences in anti-inflammatory systemic antibiotics for treatment of BP among Dutch dermatologists and residents in dermatology (n=175, survey question 7).
Despite several similarities in the current practice in treatment approach for BP, more multicentre comparative studies are needed to evaluate outcomes of common practice for the treatment of BP. In addition, further research is needed to determine the optimum starting dose of systemic corticosteroids, to compare effectiveness of adjunctive immunosuppressants, and to assess whether the continued use of topical corticosteroids or tetracyclines should be recommended to prevent relapses. Our study suggests that the results of a clinical trial in BP, such as the BLISTER study, influences the treatment approach only when guidelines or national experts recommend it. Surveys such as the one presented could be used to evaluate whether a new guideline or results from clinical trials are being followed.

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