

therefore hypothesized that topical application of dapsone may be effective in acne vulgaris. Two randomized control trials of the 5% gel formulation were carried out that demonstrated statistically significant clinical improvement in inflammation and lesion counts over 12 weeks. The product was subsequently licensed by the FDA for treatment of acne vulgaris in the United States (Draeos *et al.*, 2007). Subsequent studies appeared to demonstrate that, although minimal systemic absorption does occur, the development of the common side effects of dapsone—namely, methemoglobinemia and hemolysis—did not occur (Roberts *et al.*, 2005; Thiboutot *et al.*, 2007). Subsequent to these reports, a case of methemoglobinemia after the use of topical dapsone was published (Swartzentruber *et al.*, 2015). The role of dapsone and other agents in the treatment of severe acne has recently been reviewed (Aslam *et al.*, 2015).

After the demonstration of its efficacy in immune thrombocytopenia (ITP), dapsone has been recommended as second-line therapy, with response rates of up to 63% reported (Provan *et al.*, 2010; Rodrigo and Gooneratne, 2013). Various mechanisms for its mode of action in patients with this disorder have been proposed, and doses have varied between 50 mg and 300 mg daily (Hill, 2015). A recent report suggested the response rate is considerably lower, and further studies are warranted in ITP (Oo and Hill, 2015)

Dapsone has been found to have anticonvulsant activity in animals, and an open-label trial in patients with drug-resistant complex partial seizures demonstrated a significant reduction in seizure activity in 16 of 22 subjects enrolled (Lopez-Gomez *et al.*, 2011). A potential explanation for this observation was proposed by Kast *et al.* (2012)—namely, that seizures are often associated with elevated levels of IL-8, and that because dapsone inhibits IL-8 release and function, the seizure threshold is raised, especially when associated with glioblastomas (Kast *et al.*, 2012).

Dapsone has been found to have an effect superior to placebo and similar to hydroxychloroquine in rheumatoid arthritis. It is considered an effective second-line agent for the treatment of the disease, but not a disease-modifying agent (Chang *et al.*, 1996).

The understanding of the pathogenesis of asthma has evolved to focus on an underlying disorder causing airway inflammation. Dapsone has been demonstrated to inhibit a number of parameters of neutrophil activity in airways (Kanoh *et al.*, 2011) and has been proposed as a steroid sparing agent in severe steroid-dependent asthma. An open-label historical controlled trial was carried out in 10 patients who had severe chronic steroid-dependent asthma. Seven of the 10 patients were able to have their steroids ceased with no sign of worsening disease (Berlow *et al.*, 1991). A structured Cochrane review in 2002 reported no further evidence about dapsone's use in asthma (Dewy *et al.*, 2002).

A number of case reports have strongly suggested that dapsone is effective in reducing the aphthous ulceration in patients with Behçet's disease (Ghate and Jorizzo, 1999; Wolf *et al.*, 2000). Larger trials have yet to be reported.

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