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3g mesalazine granules are superior to 9mg budesonide for achieving remission in active ulcerative colitis: A double-blind, double-dummy, randomized trial.

Gross V, Bunganic I, Belousova EA, Mikhailova TL, Kupcinskas L, Kiudelis G, Tulassay Z, Gabalec L, Dorofeyev AE, Derova J, Dilger K, Greinwald R, Mueller R; The International BUC-57 Study Group

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Clinical trials with the objective of direct comparison of two or more different therapeutics for the treatment of IBD are rare. Often medication is used without knowing the exact mode of action or one drug is preferred without having evidence for better efficacy. Although budesonide and mesalazine are both often used in the treatment of ulcerative colitis, only three small studies have compared these medications when administered orally. Usually budesonide is administered rectally in distal colitis with very good success, while mesalazine can be delivered orally or rectally.

This paper by Gross et al. provides a direct comparison of orally administered budesonide 9mg once daily (OD) and mesalazine 3g OD in mild-to-moderate ulcerative colitis with the aim of demonstrating non-inferiority of budesonide for inducing clinical remission. 288 patients completed the study. Physician's Global Assessment and laboratory tests were performed. At baseline and week 8, endoscopy was performed and biopsies were taken to determine endoscopic and histological indices.

Key findings

Mesalazine granules 3g OD are superior to oral pH-modified release budesonide capsules 9mg OD for achieving clinical remission in mild-tomoderate active ulcerative colitis.

However, both treatments were effective in induction of remission (39.5% in the budesonide group vs. 54.8% in the mesalazine group). The between-group difference exceeded the prespecified non-inferiority margin of 15% by 0.3% (p=0.52) and therefore the primary objective of this study was not met. Mesalazine was superior in terms of remission rate (59.7% vs. 43.8%), reduction of CAI scores and reduction of endoscopic scores (81.9% vs. 68.9%) and these differences held true in all explored subgroups (based on localisation of disease, disease severity and CRP levels). The number of adverse events was similar in both treatment groups.

Since rectal budesonide has been shown to be equivalent to rectal mesalazine, the authors discuss possible reasons for the inferiority of orally administered budesonide compared with mesalazine. One potential reason for the divergence in efficacy relates to galenic formulation: budesonide is equipped with an enteric coating but not with a matrix polymer, unlike mesalazine.

Differences between budesonide and mesalazine in terms of reduction in the number of bloody stools and median time to first resolution of symptoms were minor. Therefore, budesonide could be an interesting alternative to mesalazine in non-responders or in cases of intolerance.

Why is this paper interesting to physicians?

Even though statistically mesalazine is superior to budesonide in inducing remission in ulcerative colitis, budesonide could be an interesting option for patients, especially those refractory to mesalazine. Importantly, galenics and disease extent and localisation should always be considered when choosing medication and the mode of application.