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Cost and quality-adjusted life year differences in the treatment of active ulcerative colitis using once-daily 4 g or twice-daily 2 g mesalazine dosing

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Abstract

Background: Improved compliance in active ulcerative colitis (UC) is likely to improve healthcare efficiency by reducing time spent in active mild to moderate UC state. To establish whether once daily (OD) mesalazine offers economic advantages over twice daily (BD) dosing in active UC, we evaluated the outcomes and costs of a recently published randomized study.
Methods: A cost-effectiveness model with four week Markov cycles was developed to reflect current treatment practices in the Netherlands with OD and BD mesalazine for active UC. The health service perspective of the Netherlands was reflected in the model and considered a 32 week time horizon with 4 weekly Markov cycles. Outcomes evaluated in the model were time spent in active and remission UC and the corresponding health-related quality of life associated with different clinical states. This was then used to derive quality adjusted life-years (QALYs) at each treatment stage.
Results: A greater proportion of subjects on 4 g OD achieved remission at weeks 4 and 8 compared with 2 g BD. After 32 weeks the average costs per patient with active UC were €3097 and €3548 for those treated with OD and BD mesalazine respectively, with an average saving of €451 per patient treated with OD mesalazine. The average costs per QALY for OD and BD mesalazine were €5433 and €6324 for OD and BD, respectively.

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Conclusions: Based on the results from a single randomized study, OD dosing resulted in a shorter time spent in active UC which resulted in lower healthcare costs.

1. Background

Increasing healthcare costs has increased the need for prescribers to optimize treatment outcomes across many different diseases within constrained budgets. The need for improved efficiency has placed increased emphasis on adopting cost saving interventions.[1] Taking into consideration the increasing prevalence of inflammatory bowel disease, the opportunity to optimize treatment with limited budgets would be welcomed considering the likely demand for treatment.[2]

Treatment compliance is important for maintaining and achieving clinical goals, with the added advantage of potentially saving costs.[3] Previous investigations have shown that compliance to ulcerative colitis (UC) maintenance therapy can reduce the frequency of UC flares, which translates into less need for more costly treatment interventions.[4,5] A retrospective study in the United States evaluated mesalazine medication possession and overall healthcare costs. It was shown that reduced medication possession resulted in elevated gastro-related inpatient care, with treatment persistent patients incurring reduced medical costs.[6]

UC is a chronic inflammatory disease of the colon that is characterized by periods of remission, with unpredictable episodes of relapse causing rectal bleeding, urgent diarrhea, abdominal discomfort and fatigue.[7] Following induction of remission, preventing recurrence of active UC offers benefits for patients and healthcare systems. Consequently, the choice of maintenance therapy is important as it offers opportunity to influence outcomes like patients' quality of life (QoL) and to save costs. Compliance to oral mesalazine treatment in clinical trials is often very high. However, outside of clinical trials, compliance in treatment will be lower resulting in higher relapse rates and longer time to remission in daily practice.[8] Dosing frequency is one mechanism by which physicians can improve patient compliance and outcomes.

Because dosing frequency is an important treatment consideration known to influence compliance and outcomes in treating active UC, we evaluate in this analysis the economic consequences of outcome differences observed in the MOTUS study comparing mesalazine 4 g once daily (OD) versus 2 g twice daily (BD) dosing in combination with 1 g mesalazine enema in patients with active UC.[9]

2. Methods

Previous studies have defined optimal treatment practices for management of active UC to be in combination treatment with oral and topical mesalazine.[10] Based on recently reported evidence, there are variations in outcomes between OD and BD dosing of the oral mesalazine within this regimen. We estimated the cost differences between OD and BD dosing arising from these variations.

2.1. Treatment practices in the Netherlands

The model was designed to take into consideration the current treatment practices for mild to moderate active UC treatment practices in the Netherlands according to national guidelines.[11] In clinical practice a step-up regimen for treatment of active UC is normally used, starting with an escalated treatment of combined oral and topical mesalazine therapy. In patients who do not respond to intensive mesalazine therapy corticosteroids, topically and/or orally are added. An 8-week course of 40 mg tapered prednisolone is mostly used. In selected cases non-response to oral corticosteroids results in admission for intravenous corticosteroids. Finally, escalation to Infliximab is initiated as a rescue therapy if combination of intensive mesalazine and corticosteroids fails to achieve remission. Infliximab is administered in an outpatient setting at weeks 0, 2, and 6 and then every 8 weeks.

2.2. Model description

The economic evaluation described here is based on the ability to achieve remission in mild-to-moderate active UC based on changes from baseline in the ulcerative colitis disease activity instrument (UCDAI). Because active UC significantly affects costs in the healthcare system and patient's QoL, a cost-utility analysis (CUA) was used to express the cost and QoL burden associated with active disease.

The clinical data on which the economic model is based was obtained from the multicenter, controlled, randomized, investigator-blinded study comparing OD with BD mesalazine for active mild-to-moderate UC.[9] The investigators reported a significant difference in the time to remission at 4 weeks with a trend towards improved clinical remission at 8 weeks. For the purposes of the model described here and aligned with treatment practices in the Netherlands, we used the Flourié et al. data reported treatment outcomes at 4 weeks.

A Markov model was constructed based on previously reported cost-effectiveness analyses of active UC to evaluate differences in costs and health outcomes in terms of quality-adjusted life year (QALY) over time.[12] The health service perspective was reflected in the model and considered 32-weeks of treatment with 4 weekly treatment cycles (Markov cycles). The model comprised of five health states: (1) mesalazine active UC (treated with OD or BD mesalazine); (2) mesalazine-refractory active UC (treated with prednisolone); (3) steroid-refractory active UC (treated with Infliximab); (4) continuous Infliximab active UC; and (5) remission. A description of the model is shown in the figure below (Fig. 1).