

HEALTH ECONOMIC IMPACT OF MACROGOL 3350 PLUS ELECTROLYTES (MOVICOL®/MOVICOL PAEDIATRIC PLAIN®) COMPARED TO ENEMAS AND SUPPOSITORIES AND MANUAL EVACUATION IN TREATING PAEDIATRIC FAECAL IMPACTION IN THE UK

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INTRODUCTION

- The current management of constipation in children is largely based on good clinical practice rather than evidence based on controlled clinical trials.
- The relatively recent availability of paediatric formulations of macrogol 3350 plus electrolytes (macrogol 3350; Movicol®; Movicol Paediatric Plain®) has been shown to be effective in both paediatric faecal impaction in an inpatient setting and subsequent maintenance therapy [1-3].
- This present study assessed the clinical and economic impact of using macrogol 3350 in an outpatient setting compared to enemas and suppositories and manual evacuation in treating paediatric faecal impaction, based on actual clinical practice in England and Wales.

METHODOLOGY

Study Design

- This was a retrospective review of the case notes of a cohort of children with faecal impaction who initially received either macrogol 3350 or enemas and suppositories or manual evacuation for disimpaction at five centres in England and Wales.

Patient Selection

- Patients were eligible for inclusion into the study if they were 2-11 years of age and suffering from constipation judged severe enough to require disimpaction and initially disimpacted between 1st January 2001 and 31st January 2006.
- Patients were excluded if they had any condition contraindicating the use of macrogol 3350, enemas and suppositories.
- Eligible patients were identified from patients' medical case notes and prescribing databases.
- All eligible patients for whom records were available were included in the study.

Decision Modelling

- A decision model was constructed using the clinical outcomes and resource use values extracted from patients' case notes.

- The model depicts the treatment paths and associated resource use attributable to managing children during the disimpaction phase and for a period of 12 weeks following initial disimpaction and considers the decision by a clinician to initially disimpact a child with macrogol 3350 (in an outpatient setting), enemas and suppositories or manual evacuation.
- Within the model, a variety of laxatives are used during the 12 week period post-disimpaction and patients can re-impaction during this period.
- By assigning unit costs [4-6] at 2005/06 prices to the resource utilisation estimates within the model, the healthcare costs for disimpaction and 12 weeks following disimpaction were estimated.
- None of the children were impacted at 12 weeks following initial disimpaction. Hence, a cost-minimisation analysis was performed. Such an analysis identifies the treatment strategy that achieves the same outcome for least cost.

Sensitivity Analyses

- Probabilistic sensitivity analyses were undertaken using Monte Carlo simulations (1,000 iterations of the model) by simultaneously varying the probabilities and resource use values within the model.
- In addition, deterministic sensitivity analyses were performed to identify how the healthcare costs associated with each treatment pathway would change by varying different parameters in the model.

Ethical Approval

- Local Research Ethics Committee approval was obtained for Birmingham Children's Hospital NHS Trust, Chelsea & Westminster Hospital and Singleton Hospital.
- Ethics approval was not required by Queen Elizabeth Hospital and St Richard's Hospital as their respective Local Research Ethics Committee considered the study to be an audit. However, in both cases a letter of approval was obtained from the hospital's audit Governance Committee.

RESULTS

Patient Characteristics

- 224 patients were included in the study of whom 112 were initially disimpacted with macrogol 3350, 101 with enemas and suppositories and 11 who underwent a manual evacuation.
- The mean age of patients initially disimpacted with macrogol 3350 was 6.5 years (95% CI: 4.8; 8.3) compared with 5.4 years (95% CI: 3.7; 7.2) for those initially disimpacted with enemas and suppositories and 4.3 years (95% CI: 2.0; 6.9) for those who underwent a manual evacuation.
- Forty six percent of patients initially disimpacted with macrogol 3350 were female compared with 47% of those initially disimpacted with enemas and suppositories and 27% of those who underwent a manual evacuation. The remainder were male.

Clinical Outcomes

- Ninety-seven percent of macrogol 3350-treated children were successfully disimpacted within 5 days, compared to 73% of those treated with enemas and suppositories and 89% of those who underwent a manual evacuation (Table 1). A mean 29 sachets (95% CI: 13; 44) of macrogol 3350 and 36 sachets (95% CI: 11; 60) of the paediatric plain formulation were required for successful disimpaction within 5 days.
- A mean 2 enemas (95% CI: 1; 3) were required for successful disimpaction within 5 days together with 1 (95% CI: 1; 2) suppository.

Treatment	Macrogol 3350	Enemas and suppositories	Manual evacuation	p
Macrogol 3350 alone	53% (14; 93)	14% (0; 32)	36% (15; 53)	<0.001
Macrogol 3350 & combinations	27% (0; 83)	23% (0; 46)	0% (0; 53)	<0.001
Lactulose alone	7% (0; 20)	4% (0; 10)	0% (0; 19)	<0.001
Lactulose & senna	20% (0; 44)	16% (0; 35)	11% (0; 33)	<0.001
Lactulose & picosulphate	0% (0; 0)	12% (0; 27)	0% (0; 53)	<0.001
Lactulose & other combinations	16% (0; 41)	0% (0; 21)	31% (15; 53)	<0.001
Picosulphate & combinations	3% (0; 8)	0% (0; 1)	3% (0; 13)	<0.001
Other laxatives	2% (0; 5)	4% (0; 7)	0% (0; 19)	<0.001
Nothing	0% (0; 21)	1% (0; 3)	0% (0; 19)	<0.001

Table 2: Management strategies post-disimpaction (95% confidence limits in parentheses)

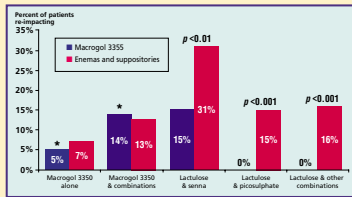


Figure 1: Relative risk of re-impacting on different laxative combinations (p<0.02).

Resource Use

- There were no significant differences between treatments in terms of outpatient visits (Table 3). However, patients initially disimpacted with macrogol 3350 had significantly fewer hospital admissions than those disimpacted with the other interventions and occupied fewer bed days.

Resource	Macrogol 3350	Enemas and Suppositories	Manual evacuation	p
Physician outpatient visits	2.8 (2.1; 3.4)	2.2 (1.7; 2.8)	2.7 (1.4; 4.0)	ns
Nurse outpatient visits	0.9 (0; 1.2)	0.2 (0; 0.3)	0.4 (0; 1.4)	ns
Hospital admissions	0.1 (0; 0.3)	1.4 (1.2; 1.9)	1.3 (0.8; 1.9)	<0.001
Occupied bed days	0.1 (0; 0.2)	1.3 (1.0; 1.5)	4.0 (1.7; 7.9)	0.05
Number of occupied bed days per admission	1.0	1.0	4.0	ns

Table 3: Healthcare resource use over the period of disimpaction and subsequent maintenance (95% confidence limits in parentheses).

Cost of Healthcare Resource Use

- The total NHS cost of disimpaction and subsequent maintenance of children initially treated with macrogol 3350 was estimated to be £694 (95% CI: £496; £892) per patient. This compared with £2,759 (95% CI: £1,266; £4,252) and £2,333 (95% CI: £1,609; £3,058) for those who initially received enemas and suppositories or underwent a manual evacuation, respectively (Figure 2).
- Irrespective of treatment for initial disimpaction, the cost of subsequent management was broadly similar (Figure 3).

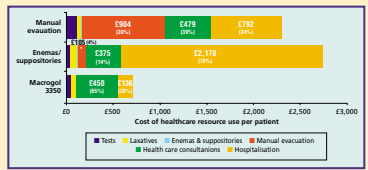


Figure 2: Cost of healthcare resource use per patient over the period of disimpaction and subsequent maintenance.

- The cost of initial disimpaction with macrogol 3350 was substantially cheaper than that with enemas and suppositories and manual evacuation. This is because (1) the cost of hospitalisation (£1,954) accounted for 91% of the cost of initial disimpaction with enemas and suppositories and (2) the cost of a manual evacuation (£904) and excess bed days (£788) collectively accounted for 86% of the cost of a child undergoing a manual evacuation.

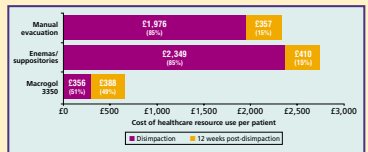


Figure 3: Cost of disimpaction and subsequent maintenance.

Sensitivity Analyses

- Sensitivity analyses demonstrated that the decision model was relatively robust to plausible changes in model inputs and thus our findings are potentially reproducible in other UK hospitals that did not participate in this study.

Budget Impact

- Based on the Hospital Episode Statistics [7], it was estimated that each year in England 5,020 children aged 2-11 years undergo faecal disimpaction with either macrogol 3350, enemas and suppositories or manual evacuation of which:
 - 2,510 children are initially treated with macrogol 3350.
 - 2,250 children are initially treated with enemas & suppositories.
 - 250 children are initially treated with a manual evacuation.
- By extrapolating the estimates from England to the whole UK, 6,280 children aged 2-11 years were estimated to undergo faecal disimpaction with one of these three treatments costing the NHS £10.6 million for disimpaction and subsequent maintenance and accounting for 5,426 hospital admissions.
- Disimpacting all 6,280 children with macrogol 3350 was estimated to reduce the annual NHS cost by £6 million (59%) from £10.6 million to £4.4 million and reduce the number of hospital to admissions by 5,426 (92%) from 5,884 to 458 admissions, thereby releasing healthcare resources for alternative use within the system.

DISCUSSION

- Disimpaction with macrogol 3350 was found to be more effective among paediatric outpatients than among inpatients (97% disimpacted within 5 days in actual clinical practice compared to 92% within 7 days in a clinical trial setting [2]). The disimpaction rate among children treated with enemas and suppositories was found to be comparable to that observed in clinical trials (73% in five days versus 79% within 8 days [8]). The re-impaction rate following management with lactulose and senna has been reported to be 23% in clinical trials [2], whereas in our study we found that 15% and 31% of patients initially disimpacted with macrogol 3350 and enemas & suppositories respectively re-impacted while being managed on lactulose & senna.
- The naturalistic approach of this study has its limitations. Patients were not randomised to treatment, patients in each treatment group were not specifically matched and sample sizes varied between centres. Nevertheless, all patients required disimpaction, there were no differences in patients' age and gender between centres and treatment groups and all eligible patients at each centre were included in the analysis. Hence, this study represents a census of use of macrogol 3350, enemas and suppositories and manual evacuation for faecal disimpaction in children at these five centres. Moreover, the clinical effectiveness of the various interventions for disimpaction was comparable to that observed in clinical trials and was concordant between the five centres.
- This study covered a period of disimpaction between January 2001 and 2006, but macrogol 3350 was not licensed for paediatric use until September 2003. Hence, all the patients disimpacted before September 2003 received either enemas and suppositories or a manual evacuation, except at one centre which used macrogol 3350 for faecal disimpaction off-label. If treatment for disimpaction was selected on the basis of symptom severity, one would expect this to result in a higher proportion of patients requiring manual evacuation. Consequently, we consider that disease severity was the same for all treatment groups and that patients' treatment for disimpaction at any one centre was based on the preferred strategy at that centre and not on the severity of patients' symptoms.
- The treatments during the week before disimpaction are unlikely to be an important confounder since all the patients were faecally impacted at baseline. Moreover, regression analysis found no correlation between treatment during the week before disimpaction and any of the outcomes.
- Patients may have consumed healthcare resources in the community which may not have been captured in their hospital records. The incidence of re-impaction may have been under-recorded if patients re-impacted whilst being managed by their GP and not subsequently

referred back to their hospital physician. However, in most instances a re-impacted child would be sent back to his or her hospital consultant. It was assumed that patients continued with their management strategy for 12 weeks post-disimpaction, however some children may discontinue treatment, but this was not recorded in their hospital records.

- Notwithstanding these limitations, there was considerable concordance between the centres, suggesting that the outcomes and level of healthcare resource use observed in this analysis would be indicative of other centres across the UK.

Conclusion

Within the limitations of our model, use of macrogol 3350 affords the NHS a clinically effective and cost-effective treatment for the disimpaction of children suffering from faecal impaction compared to enemas and suppositories or a manual evacuation and has the potential to release healthcare resources for alternative use within the system.

ACKNOWLEDGEMENTS

This study was sponsored financially by Norgine Ltd, Harefield, UK, manufacturers of Movicol (macrogol 3350 plus electrolytes). However, the authors have no other conflicts of interest that are directly relevant to this study.

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