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Commentary

Commentary on 'Lactulose versus polyethylene glycol for chronic constipation'

This is a commentary on a Cochrane review, published in this issue of EBCH, first published as: Lee-Robichaud H, Thomas K, Morgan J, Nelson RL. Lactulose versus polyethylene glycol for chronic constipation. *Cochrane Database of Systematic Reviews* 2010, Issue 7. Art. No.: CD007570. DOI: 10.1002/14 651 858.CD007570.pub2.

Further information for this Cochrane review is available in this issue of EBCH in the accompanying Summary article.

In their meta-analyses of all ten controlled trials comparing the efficacy of polyethylene glycol (PEG), a macrogol, to lactulose, a non absorbable sugar, in the treatment of constipation, Lee-Robichaud *et al*. (1) came to the conclusion that overall, PEG scores better for stool frequency, form of stool, relief of abdominal pain and the need for additional products. According to the analysis, relief of abdominal pain may not be different between lactulose and PEG in children (1).

Both lactulose and PEG are osmotic laxatives: non-absorbable agents increasing the amount of water in the bowel. Lactulose is fermented in the colon, stimulates the growth of bifidobacteria and lactobacilli, and results in acid stool and gas production. Therefore, we would expect a better overall pain relief with PEG. Of all outcomes, pain relief is likely to be the most important one for the patient. The fact that pain relief in children is not different for lactulose or PEG may be related to withholding behaviour in children as a mechanism of constipation while it is most likely irrelevant in adults (2, 3). Because of the difference between adults and children in certain mechanisms causing constipation, it may be more relevant to evaluate data by age group. This was not done in this Cochrane analysis.

Although constipation is known to be a frequent condition, the true incidence is not well known since the reported range is very large, from 2% to 35% (1). Well conducted studies evaluate the efficacy of an intervention in populations with clear-cut inclusion criteria, mostly the Rome II or Rome III criteria. However, in daily life, not all patients needing intervention fulfill these criteria. Also, many studies are performed in tertiary care centres or at least in centres with a special interest in constipation. Because these centres are known for their knowledge and expertise in this field, there might be a selection bias in their patient population. In other words: as these results are from highly selected homogenous study groups, it is questionable as to whether the results can be applied to a broader population of people who need intervention but do not fulfil the strict criteria of specialized centres. Although constipation is mainly a problem for primary health care, data from first line health care are missing.

Among all medications available to treat constipation, macrogols occupy a central place. This group of medication is the best one studied in constipation, and because of its efficacy and safety, the use of alternatives has decreased. This Cochrane review provides stronger evidence for actual clinical practice.

The efficacy of PEG seems satisfactory as long as it is administered on a regular basis, but it is unclear from the literature how many patients will relapse after stopping its regular administration. Very few or no data are available regarding long term outcomes.

Beyond the scope of this review, the existence and use of macrogols with and without electrolytes merits a separate evaluation and discussion as f.ex. macrogols with electrolytes may be less desirable in geriatric patients.

Several alternatives are in use to treat constipation in childhood despite the scarce clinical evidence. 'Specially designed' infant formulas are developed for constipation in infants as PEG is not registered for use under the age of 12 months. However, the evidence of efficacy of these formulas is very limited (4, 5).

The impact of dietary habits, like fluid and/or fibre intake, on constipation is poorly studied. In constipated children, a decreased fibre and fluid intake is often noticed and dietary measures are often recommended. Despite those general rules, there is a lack of studies and there is no real evidence for their benefit. A study with a fluid fibre mixture and lactulose gives comparable results in the treatment of childhood constipation (6) and another one showed no efficacy of increased fluid intake in children with constipation (7). It might be that an increased fibre and fluid intake

is ineffective in treatment of constipation, but they might have a role in prevention or recurrence of the problem. Although the following statement was not studied, and thus needs to be validated, it can be hypothesized that an increased intake of fibre and water may be ineffective in treatment, but effective in prevention.

Data about the influence of increased physical activity on childhood constipation is also lacking. In theory, behavioural changes are the cornerstone of constipation treatment and macrogols should only be used temporarily, nevertheless biofeedback training has no additional benefit in children with encopresis (8) and a Cochrane analysis concluded that behavioural and cognitive interventions with or without other treatments for the management of constipation and fecal incontinence in children was of no benefit (9).

The role of gastrointestinal flora is another topic of interest. Infant formula supplemented with pre and/or probiotics induces bifidobacteria and/or lactobacilli rich gastrointestinal flora. Especially with prebiotics, manipulation of the gastrointestinal flora in infants has been suggested to prevent constipation, although published data are limited. Most literature on treatment of constipation with probiotics is negative (10, 11). A recent paper concluded that administration of Lactobacillus reuteri was effective in the treatment of constipation in infants (12).

In conclusion: PEG is an effective and safe treatment for constipation, and can now be considered the 'standard approach'. More data are needed on efficacy and safety according to age (especially in very young and old patients). Data from primary health care are also a priority for future research. Optimal dosage and duration of treatment should be further evaluated As well as the role of behavioural and dietary approaches to better understand the long term outcome and prevention of relapse.

Declarations of Interest

YVDP is consultant for United Pharmaceuticals and Biocodex; member of advisory boards for Abbott, Danone, Mead Johnson, Shire (Movetis), Nestle Nutrition, Norgine.

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