Clinical Evidence Summary: Do dietary interventions, such as probiotics, improve pain in children with recurrent abdominal pain (RAP)?

Tamsin Newlove-Delgado¹, PhD (corresponding author) Rebecca A Abbott², PhD

Alice E Martin³, PhD

 University of Exeter Medical School, College House, Heavitree Road, Exeter, UK Email: t.newlove-delgado@exeter.ac.uk
 University of Exeter Medical School, NIHR CLAHRC South West Peninsula (PenCLAHRC), Exeter, UK
 Bristol Royal Hospital for Children, Bristol, UK

Word count: 737 Date of revision: 11.9.18

Acknowledgements

The work of the evidence synthesis team is funded by the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care South West Peninsula (PenCLAHRC). The funder had no role in any of the following: the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. The authors warmly thank all those who contributed to the 2017 Cochrane review (Alison Bethel, Jo Thompson-Coon and Stuart Logan), as well as acknowledging the work of the authors of the original 2009 review.

Clinical question: Do dietary interventions, such as probiotics, improve pain in children with recurrent abdominal pain (RAP)?

Clinical application: Compared to placebo, children treated with probiotic preparations were more likely to experience improvement in pain in the short term (odds ratio of 1.63, 95% confidence interval 1.07-2.47); suggesting that clinicians could consider probiotics as part of a holistic management strategy in RAP.

Introduction

RAP is a significant problem in paediatric practice, and is associated with emotional disorders, school absence and hospital admissions^{1,2}. It is estimated to affect up to 25% of school age children at some point^{1,3}. RAP refers to a group of functional gastrointestinal disorders that have an unclear aetiology which are diagnosed according to Rome Foundation criteria⁴. We use RAP as an umbrella term to refer to the Rome III category of childhood abdominal pain-related functional gastrointestinal disorders, which are: functional dyspepsia, irritable bowel syndrome, abdominal migraine, functional abdominal pain, and functional abdominal pain syndrome. Different treatment approaches have been taken for RAP, which can be grouped as pharmacological, dietary, or psychosocial. Our Cochrane systematic review⁵ (updating a 2009 review⁶) focused on any intervention with dietary changes intended to improve the symptoms of RAP. We used standard Cochrane methods including the GRADE approach to assess the overall quality of the body of evidence for each specific outcome.

Summary of Findings

We found 19 eligible studies, 15 of which were not included in the previous review. Fourteen trials recruited children with a diagnosis under the umbrella of RAP or functional gastrointestinal disorders; five recruited children with irritable bowel syndrome. Thirteen trials used differing probiotic-based interventions (the most commonly used strain being Lactobacillus rhamnosus GG in five trials). Four trials examined fibre interventions. We found only two studies of different exclusion/restriction diets.

At 0-3 months post intervention children treated with probiotics were more likely to experience improvement in pain than those given placebo, based on moderate quality evidence (OR 1.63, 95% confidence interval 1.07 to 2.47, 7 studies, 772 children). The number needed to treat for an additional beneficial outcome was 8. Children treated with probiotics also reported a greater reduction in pain frequency (standardised mean difference (SMD) -0.55, 95% CI -0.98 to -0.12; 6 trials; 523 children) and intensity at the same time point (SMD -0.50, 95% CI -0.85 to -0.15; 7 trials; 575 children). However, we judged the evidence for these outcomes to be of low quality. Only two studies reported outcomes 3-6 months post-intervention, finding that those treated with probiotics were more likely to experience an improvement in pain (OR 1.94, 95% CI 1.10 to 3.43; 2 studies; 224 children, moderate quality evidence). Please see our Cochrane systematic review⁵ for full details of all meta-analyses performed.

Children treated with fibre-based interventions were no more likely to experience an improvement in pain at 0 to 3 months postintervention than children given placebo (OR 1.83, 95% CI 0.92 to 3.65; 2 studies; 136 children), based on low quality evidence.

Discussion

The review provides low to moderate quality evidence that probiotics may be effective in the shorter term in improving pain in children with RAP. There was no convincing evidence suggesting that fibre supplements or other diets (e.g. low FODMAP - fermentable oligosaccharides, disaccharides, monosaccharides and polyols) are effective in RAP. Our updated search in November 2017 found two additional trials of probiotics; adding these studies did not alter these findings⁷.

Limitations

The chief limitations include the quality of evidence available, which was low to moderate, and the variation in the definition and scales used to assess pain outcomes. It was not possible to judge the extent of clinical significance of improvement. Post-hoc subgroup analyses of outcomes according to probiotic strain showed there is currently insufficient evidence to guide clinical practice relating to choice of strain, as dosages and regimes were different⁷. Only two included studies measured outcomes at 12 weeks or more.

Areas in Need of Future Study

Future trials should assess outcomes over the longer term and use validated and consistent outcome scales, agreed by research leaders in this area. Few studies reported on school absence, social or psychological functioning, and quality of life, which are highly significant outcomes for families. Future research should also examine the optimal strain and dosage for probiotic interventions, and consider effectiveness in different settings. It has been suggested that distinct subtypes of

RAP could guide treatment choice⁴; this needs further investigation to allow tailored management. Finally, further high-quality RCTs are needed to examine the

Evidence Profile

- 19 included studies, all randomised controlled trials
- Study years: 1985-2014; original literature search June 2016
- 1453 participants
- Girls outnumbered boys in most included trials
- Data on ethnic origin was not reported by most trials
- Mean age in individual trials between 6.3 and 13.1 years; age range 4-18 years
- Most common settings: paediatric gastroenterology clinics
- Countries: 8 countries (Italy, Iran, USA, Canada, Poland, Germany, Israel and India)
- Comparison: Dietary intervention (including probiotic-based interventions, fibre-based interventions, and exclusion/restriction diets) against a placebo comparison. One study used standard diet as the comparator.
- Primary outcomes:
 - Pain improvement (usually defined as a percentage or number of points improved from baseline, or being pain-free),
 - Pain severity or intensity
 - Pain frequency
- Secondary outcomes included school performance, social or psychological functioning, and quality of daily life
- This was an update of the original 2009 review⁶

References

- Youssef NN, Atienza K, Langseder AL, Strauss RS. Chronic abdominal pain and depressive symptoms: analysis of the national longitudinal study of adolescent health. Clinical Gastroenterology and Hepatology 2008;6(3):329–32
- Paul SP, Candy DC. Clinical update: recurrent abdominal pain in children. Community Practice 2013;86(11):48–51
- Korterink JJ, Diederen K, Benninga MA, Tabbers MM. Epidemiology of pediatric functional abdominal pain disorders: a meta-analysis. PLoS One 2015;10
- Drossman DA, Chang L, Chey WD, Kellow J, Tack
 J, Whitehead WE. Rome IV Functional Gastrointestinal
 Disorders: Disorders of Gut-Brain Interaction. Raleigh (NC): Rome
 Foundation, 2016.
- Newlove-Delgado TV, Martin AE, Abbott RA, Bethel A, Thompson-Coon J, Whear R, Logan S. Dietary interventions for recurrent abdominal pain in childhood. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD010972.
- Huertas-Ceballos A, Logan S, Bennett C, Macarthur C.
 Dietary interventions for recurrent abdominal pain (RAP) and irritable bowel syndrome (IBS) in childhood. Cochrane Database of Systematic Reviews 2009, Issue 1
- Abbott RA, Newlove-Delgado TV*, Martin AE, Bethel A, Thompson-Coon J, Whear R, Logan S. (2018) Recurrent abdominal pain in children: summary evidence from three systematic reviews of treatment effectiveness. Journal of

Pediatric Gastroenterology & Nutrition-Europe DOI:

10.1097/MPG.000000000001922