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[Intervention Review]

# Pharmacological interventions for recurrent abdominal pain in childhood

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## ABSTRACT

### Background

Between 4% and 25% of school-aged children at some stage complain of recurrent abdominal pain (RAP) of sufficient severity to interfere with their daily lives. When no clear organic cause is found, the children are managed with reassurance and simple measures; a large range of pharmacological interventions have been recommended for use in these children.

### Objectives

To determine the effectiveness of pharmacological interventions for RAP in children of school age.

### Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), Ovid MEDLINE, Embase, and eight other electronic databases up to June 2016. We also searched two trials registers and contacted researchers of published studies.

### Selection criteria

Randomised controlled trials involving children aged five to 18 years old with RAP or an abdominal pain-related functional gastrointestinal disorder, as defined by the Rome III criteria ([Rasquin 2006](#)). The interventions were any pharmacological intervention compared to placebo, no treatment, waiting list, or standard care. The primary outcome measures were pain intensity, pain duration or pain frequency, and improvement in pain. The secondary outcome measures were school performance, social or psychological functioning, and quality of daily life.

### Data collection and analysis

Two review authors independently screened titles, abstracts, and potentially relevant full-text reports for eligible studies. Two review authors extracted data and performed a 'Risk of bias' assessment. We used the GRADE approach to rate the overall quality of the evidence. We deemed a meta-analysis to be not appropriate as the studies were significantly heterogeneous. We have consequently provided a narrative summary of the results.

### Main results

This review included 16 studies with a total of 1024 participants aged between five and 18 years, all of whom were recruited from paediatric outpatient clinics. Studies were conducted in seven countries: seven in the USA, four in Iran, and one each in the UK, Switzerland, Turkey, Sri

Lanka, and India. Follow-up ranged from two weeks to four months. The studies examined the following interventions to treat RAP: tricyclic antidepressants, antibiotics, 5-HT4 receptor agonists, antispasmodics, antihistamines, H2 receptor antagonists, serotonin antagonists, selective serotonin re-uptake inhibitors, a dopamine receptor antagonist, and a hormone. Although some single studies reported that treatments were effective, all of these studies were either small or had key methodological weaknesses with a substantial risk of bias. None of these 'positive' results have been reproduced in subsequent studies. We judged the evidence of effectiveness to be of low quality. No adverse effects were reported in these studies.

### Authors' conclusions

There is currently no convincing evidence to support the use of drugs to treat RAP in children. Well-conducted clinical trials are needed to evaluate any possible benefits and risks of pharmacological interventions. In practice, if a clinician chooses to use a drug as a 'therapeutic trial', they and the patient need to be aware that RAP is a fluctuating condition and any 'response' may reflect the natural history of the condition or a placebo effect, rather than drug efficacy.

## PLAIN LANGUAGE SUMMARY

### Drug treatment of recurrent abdominal pain in children

#### Review question

Do medications improve the pain or other symptoms experienced by children with recurrent abdominal pain (RAP)?

#### Background

Recurrent abdominal pain in childhood is a term used to describe unexplained episodes of tummy pain for which no cause can be found. The pain is often accompanied by other symptoms, such as diarrhoea or facial pallor. Some researchers have therefore classified different syndromes of unexplained pain according to these other associated symptoms. Recurrent abdominal pain is common in children. It is likely that the underlying cause or trigger differs among children.

#### Study characteristics

We searched the scientific literature worldwide up to June 2016 for research studies of drug treatments for children with RAP. We found 16 studies that met our criteria, examining antidepressants, antibiotics, antihistamines, antispasmodics, a dopamine receptor antagonist, and a hormone treatment. Fourteen studies compared drug treatments to a placebo, and two to usual medical care. The trials were carried out in seven countries: seven in the USA, four in Iran, one in the UK, one in Switzerland, one in Turkey, one in Sri Lanka, and one in India. The studies included a total of 1024 children aged between five and 18 years. All children were recruited from outpatient clinics. Follow-up lasted between two weeks and four months.

#### Key results

This review suggests there is no evidence for the use of medications to improve symptoms or the child's quality of life. Consequently, if medications are prescribed, this should be done within a well-conducted clinical trial. If a medication is prescribed to a child with RAP, it must be remembered that RAP varies with time, and therefore any improvement or worsening may be due to the natural history of the condition rather than a medication response.

#### Quality of evidence

Many of the studies had some weaknesses in their design and how they were reported, therefore the overall quality of the evidence for medications in RAP is low. The studies with better methods included few children and have not been reproduced by other researchers since.