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Drugs for treating giardiasis.

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Drugs for treating giardiasis

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ABSTRACT

Background

Giardiasis infection may be asymptomatic, or can cause diarrhoea (sometimes severe), weight loss, malabsorption, and, in children, failure to thrive. It is usually treated with metronidazole given three times daily for five to 10 days.

Objectives

To evaluate the relative effectiveness of alternative antibiotic regimens for treating adults or children with symptomatic giardiasis.

Search methods

We searched the Cochrane Infectious Disease Group Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 6 2012); MEDLINE, EMBASE, LILACS and the International Clinical Trials Registry Platform Search Portal (3 July 2012).

Selection criteria

We included randomized controlled trials (RCT) comparing metronidazole administered for five to 10 days with any of the following drugs: metronidazole (single dose), tinidazole, albendazole, mebendazole, and nitazoxanide. The primary outcomes were parasitological and clinical cure.

Data collection and analysis

Two authors independently assessed studies for inclusion, performed the risk of bias assessment, and extracted data. We summarized data using risk ratios and mean differences and we presented the results in forest plots and performed meta-analyses where possible. We assessed heterogeneity using the Chi² test, I² statistic and visual inspection; and we explored this by using subgroup analyses. We assessed the quality of evidence by using the GRADE approach.

Main results

We included 19 trials, involving 1817 participants, of which 1441 were children. Studies were generally small, with poor methods reporting. Most reported parasitological outcomes rather than clinical improvement.

Ten trials, from India, Mexico, Peru, Iran, Cuba, and Turkey, compared albendazole (400 mg once daily for five to 10 days) with metronidazole (250 mg to 500 mg three times daily for five to 10 days). This once-daily regimen of albendazole is probably equivalent

to metronidazole at achieving parasitological cure (RR 0.99, 95% CI 0.95 to 1.03; 932 participants, 10 trials; *moderate quality evidence*), and improving symptoms (RR 0.98, 95% confidence interval (CI) 0.93 to 1.04; 483 participants, five trials; *moderate quality evidence*), but the duration of follow-up was short (two to three weeks). Albendazole probably has fewer side effects than metronidazole (gastrointestinal side effects: RR 0.29, 95% CI 0.13 to 0.63; 717 participants, eight trials; *moderate quality evidence*; neurological side effects: RR 0.34, 95% CI 0.18 to 0.64; 453 participants, five trials; *low quality evidence*).

Five trials from Turkey, Spain and the UK compared mebendazole (200 mg three times daily for five to 10 days) with metronidazole (5 mg/kg (or 250 mg) three times daily for five to 10 days). These trials were small in size, and at high risk of bias. Consequently, reliable conclusions on the relative effectiveness cannot be made (*very low quality evidence*).

Five further trials, from Iran, Spain and Peru, have evaluated shortened regimens of tinidazole (single dose; 179 participants, three trials), metronidazole (single dose; 55 participants, one trial), and nitazoxanide (three days; 55 participants, one trial). Again, these trials were at high risk of bias and too small to reliably detect or exclude important differences (*very low quality evidence*).

Authors' conclusions

Albendazole may be of similar effectiveness to metronidazole, may have fewer side effects, and has the advantage of a simplified regimen. Large, high quality trials, assessing clinical outcomes (such as diarrhoea) will help assess further alternatives.

PLAIN LANGUAGE SUMMARY

Drugs for treating giardiasis

Giardiasis is an infection of the small intestine caused by a microscopic organism called *Giardia lamblia*. The infection is passed from person to person by ingesting faecally contaminated water or food. Symptoms frequently include diarrhoea, abdominal pain, flatulence, bloating, vomiting, and weight loss. In this review, we assess alternatives to the most commonly used treatment for giardiasis; metronidazole given orally for five or more days.

We identified 19 trials involving 1817 participants, of which 1441 were children. Most trials had a small number of participants and were at high risk of bias. Albendazole is probably of similar effectiveness to metronidazole, probably has fewer side effects, and has the advantage of a simplified regimen. Large, high quality trials, assessing clinical outcomes are required to assess further alternatives.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Albendazole (5+ days) compared to metronidazole (5+ days) for treating giardiasis						
Patient or population: People with giardiasis infection Settings: Endemic settings Intervention: Albendazole once daily for five or more days Comparison: Metronidazole three times daily for five or more days						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Metronidazole (three times daily for 5 to 10 days)	Albendazole (once daily for 5 to 10 days)				
Parasitological cure (Follow-up: 1 to 2 weeks)	91 per 100	90 per 100 (86 to 94)	RR 0.99 (0.95 to 1.03)	932 (10 studies)	⊕⊕⊕○ moderate ^{1,2,3}	
Clinical improvement (Follow-up: 2 to 3 weeks)	91 per 100	89 per 100 (85 to 95)	RR 0.98 (0.93 to 1.04)	483 (5 studies)	⊕⊕⊕○ moderate ^{1,2,3}	
Gastrointestinal side effects (Follow-up: 1 to 3 weeks)	29 per 100	8 per 100 (4 to 18)	RR 0.29 (0.13 to 0.63)	717 (8 studies)	⊕⊕⊕○ moderate ^{1,2}	
Neurological side effects (Follow-up: 1 to 3 weeks)	15 per 100	5 per 100 (3 to 10)	RR 0.34 (0.18 to 0.64)	453 (5 studies)	⊕⊕○○ low ^{1,2,4}	
*The basis for the assumed risk (eg the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: Confidence interval; RR: Risk Ratio						

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ These trials were conducted in adults and children in India, Mexico, Peru, Cuba, and Turkey. The dose of metronidazole was 250 mg to 500 mg three times daily for 5 to 10 days. The dose of albendazole was 400 mg once daily for five to 10 days.

² Downgraded by 1 for risk of bias as none of these trials adequately described allocation concealment or blinding.

³ The finding of no difference between treatments is consistent across trials, and the 95% CI excludes clinically important differences.

⁴ Downgraded by 1 for imprecision as the number of neurological side effects in these trials was very low.

BACKGROUND

Description of the condition

Giardia lamblia (also known as *Lambli* *intestinalis* and *Giardia duodenalis*) is an intestinal protozoan parasite that infects a wide range of host species, including humans and domestic mammals. The prevalence of *G. lamblia* infection varies in different parts of the world, but it is generally higher in developing countries where reported prevalences range from 3% to 38% (Cifuentes 2000; Cifuentes 2004; Park 2004; Celiksöz 2005; Al-Saeed 2006; Barnawi 2007; de Souza 2007). Seroprevalence studies suggest that in some settings between 23% and 40% of children are infected before six months of age (Miotti 1986; Abdel 1991). In developed countries, *G. lamblia* infects about 2% of adults and between 6% to 8% of children, and is responsible for frequent waterborne outbreaks of diarrhoea (Garner 2001; Laupland 2005; Yoder 2007). Hörman 2004 estimated the prevalence of *G. lamblia* infection, determined by stool examination, in the Nordic countries (Denmark, Finland, Norway, and Sweden) by combining data from 13 studies; the estimated prevalence in asymptomatic populations was 2.97% (95% confidence interval (CI) 2.64 to 3.31) and 5.81% (95% CI 5.34 to 6.30) in symptomatic populations.

G. lamblia is transmitted by the ingestion of cysts excreted in the faeces of infected persons or animals. Risk factors for infection include consuming untreated or inadequately treated water (Chute 1987; Pinheiro 2011), travelling to disease-endemic areas (Jelinek 2000; Ekdahl 2005; Freedman 2006), age between one and nine years (particularly in childcare settings), close or intimate contact with infected people (Yoder 2007), poor hygienic conditions (eg living in a household without a latrine or with a mud floor in the sleeping rooms) (Mahmud 1995), contact with infected animals (Yoder 2007), and oral-anal sexual contact (Yoder 2007). Cysts can survive for several months in cold water, but once they are ingested and reach the small intestine, they develop into the disease-causing form (trophozoite). A prospective study suggested that the time between infection and the appearance of *G. lamblia* cysts in the stool is 12 to 19 days (Jokipii 1985). However, symptoms may appear between one and 75 days after infection and usually at six to 15 days from the date of infection. Symptoms are usually gastrointestinal disturbances (Rendtorff 1954; Brodsky 1974; Fricker 2007).

Giardia trophozoites (disease-causing forms) damage the epithelial absorptive surface and upper intestine. This results in the malabsorption of glucose, sodium, and water, and reduces disaccharidase activity, which can lead to diarrhoea and malnutrition. The trophozoites do not invade the surrounding tissues or enter the blood stream, but the immune response results in an increased inflammation of the intestine (Garner 2001; Buret 2007). Generally, giardiasis is a self-limiting clinical illness. The spectrum of giardiasis disease varies from asymptomatic carriage to severe diarrhoea, weight loss, malabsorption, and failure of children to thrive. Acute

giardiasis is typically characterized by the sudden onset of acute, watery diarrhoea usually containing neither blood nor pus. Other symptoms may include abdominal cramps, malaise, nausea, vomiting, epigastric pain, bloating, weight loss, and weakness. Acute giardiasis generally resolves in one to four weeks, but may become chronic and persist for months, leading to malabsorption and malnutrition particularly in children (Yoder 2007). Chronic giardiasis may or may not have been preceded by an acute episode, and is typically characterized by intermittent or periodic episodes of diarrhoea, increased flatulence, epigastric pain, and weight loss (AAP 2006; Yoder 2007). The infection can be prolonged in people who are immunocompromised (Libanore 1991; Newman 2001). Malnutrition and intestinal parasitic infections are common among children in developing countries and have been associated with poor physical development and impaired resistance to infections (Goek 2003; Mukhopadhyay 2007).

Giardiasis is diagnosed by the identification of cysts or trophozoites in stool specimens, duodenal fluid, or small bowel biopsy. Repeated samplings may be necessary to find the parasite in symptomatic people. Different staining techniques of three separate stool specimens are frequently used to identify cysts; trophozoites are rarely identified in stools and are usually detected in duodenal biopsies (Mank 2001). Alternate methods used for detection of parasites include antigen detection tests by enzyme-linked immunosorbent assay (ELISA) and immunofluorescence. These tests have a sensitivity of 88% to 98% and a specificity of 87% to 100% (Schunk 2001; Garcia 2006; Weitzel 2006). About 85% to 90% of cases are detected when three separate stool samples are examined (Hiatt 1995). Stool microscopy is relatively inexpensive and commonly used. However if a single stool exam is performed, *G. lamblia* cysts may be missed resulting in under-diagnosis of cases. Duodenal aspirate biopsy (needle aspiration) is more invasive and requires an endoscopy. In direct comparison studies to stool microscopy, this method may have a lower diagnostic yield (Havenik 2007). Notably, the copro-antigen assays are less time-consuming, easier to perform, and more sensitive and specific (over 90%) than stool specimen examination (Schunk 2001; Garcia 2006; Weitzel 2006).

Description of the intervention

Many different treatments for giardiasis have been described, especially members of the 5-nitroimidazole family (metronidazole, secnidazole, ornidazole, and tinidazole) and the benzimidazole family (including albendazole and mebendazole)

An earlier Cochrane Review found that treatment options included nitroimidazoles derivatives, particularly a single dose of tinidazole and metronidazole treatment longer than three days (Zaat 1998); however, the included trials were of poor methodological quality. A recent non-Cochrane review reported that albendazole, when given as a single dose of 400 mg/day for five days, was comparable to that of metronidazole, with fewer side effects

(Solaymani-Mohammadi 2010). Other reports of decreased susceptibility to metronidazole and poor compliance to metronidazole treatment have raised concerns and have led to the search for other treatments that are in use, such as tinidazole, nitazoxanide, albendazole, and mebendazole (Argüello-García 2004; Escobedo 2007; Solaymani-Mohammadi 2010).

How the intervention might work

The mode of action of the 5-nitroimidazoles is mediated by free nitro radicals, which are formed during the metabolic reduction of the drug and cause cytotoxicity (Argüello-García 2004). Treatment with metronidazole usually ranges from five to seven days (Solaymani-Mohammadi 2010). The benzimidazoles are broad-spectrum drugs that have been used for many years in the treatment of helminthiasis in animals and humans. Their primary mode of action against helminths is via inhibition of tubulin, which causes trophozoite detachment and distortion of morphology and general structure (Morgan 1993).

Why it is important to do this review

This Cochrane Review supersedes the original Cochrane Review on drugs for giardiasis (Zaat 1998). This update focuses on addressing the effects of treatments for symptomatic giardiasis in adults and children.

OBJECTIVES

To evaluate the relative effectiveness of alternative antibiotics for treating adults and children with symptomatic giardiasis.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (quasi-randomized controlled trials were excluded).

Types of participants

Adults and children with clinically diagnosed symptomatic giardiasis (gastrointestinal symptoms plus positive laboratory results).

Trials were eligible if they included participants with *G. lamblia* and other intestinal parasitic infections; or if they enrolled symptomatic and asymptomatic participants, and information regarding symptomatic participants could be extracted, or if at least 75% of participants were symptomatic.

Diagnosis of symptomatic giardiasis may have involved the examination of stool specimens or detection of *Giardia* copro-antigen in faeces, using direct fluorescent antibody (DFA), ELISA, or other methods.

Types of interventions

Intervention

Any of the following drugs used for treating giardiasis: metronidazole (single dose), tinidazole, albendazole, mebendazole, or nitazoxanide.

Control

Metronidazole for treating giardiasis, usually for five to 10 days.

Types of outcome measures

Primary outcomes

- Parasitological cure (as defined by trialists).
- Parasitological and clinical cure (as defined by trialists).

Parasitological cure refers to no G. lamblia trophozoites or cysts found in post-treatment in faecal specimens, or no detection of G. lamblia antigen in stool specimens using diverse methods.

Clinical cure refers to clinical improvements of symptoms such as abdominal pain and cramps, diarrhoea, weight loss, and malnutrition as diagnosed by the trialist.

Secondary (measures of clinical improvement)

- Number of participants with cessation of abdominal pain, vomiting, or diarrhoea at specific times of follow up.
- Reduction in symptoms of diarrhoea.
- Relapse (as defined by trial authors).
- Weight gain.
- Dehydration.
- Any other functional indicators such as quality of life, time off work.
- Time to recovery (to clinical improvement).

Adverse events

- Serious adverse events (those leading to hospitalizations and/or death).
- Other adverse events (gastrointestinal, allergic/cutaneous, fever, neurological, hematological, hepatic, among others).
- Non-compliance to treatment.

Search methods for identification of studies

We attempted to identify all relevant trials regardless of language or publication status (published, unpublished, in press, and in progress).

Electronic searches

We searched the following databases using the search terms detailed in [Appendix 1](#): Cochrane Infectious Disease Group Specialized Register; Cochrane Central Register of Controlled Trials (CENTRAL), published in *The Cochrane Library* (Issue 6 2012); MEDLINE (1966 to July 2012); EMBASE (1980 to July 2012); and LILACS (1982 to July 2012). We also searched the International Clinical Trials Registry Platform Search Portal (ICTRP) using 'Giardia*' as the search term (July 2012).

Searching other resources

To help identify unpublished and ongoing trials, we contacted individual researchers working in the field and organizations, including the World Health Organization.

We also checked the reference lists of all studies identified by the above methods.

Data collection and analysis

Selection of studies

Two authors (CG, LR) assessed the article titles and abstracts identified from the literature searches for eligibility. If eligibility was unclear, we obtained the full text for assessment. We (CG, LR) decided individually which trials met the inclusion criteria and then we compared decisions to reach a consensus. In cases of disagreement, a third author (LU) was invited to comment. We recorded excluded studies and the reasons for exclusion. In certain cases, we contacted the authors of studies to obtain more information about the trials.

Data extraction and management

One author (CG or LR) extracted data using a pre-designed data extraction form, and a second author (LU or CC) independently cross-checked the data. We extracted data for all outcomes for all relevant drugs, paying particular attention to the dosage and periodicity of treatment. We extracted the number of participants randomized and the number of participants for which outcomes were measured for all outcomes in all treatment arms. For dichotomous data, we extracted the number of events and the number of participants in each treatment arm. For continuous data, we extracted the arithmetic means and standard deviations for each treatment group together with the number of participants in each group. We resolved disagreements by consensus.

Assessment of risk of bias in included studies

Two review authors (CG, LR, LU, or CC) independently assessed the risk of bias of each trial using The Cochrane Collaboration's risk of bias tool ([Higgins 2008](#)) and a pre-designed assessment form. We followed the guidance to make judgements on the risk of bias in six domains, focusing on the 'parasitological cure' outcome measure: sequence generation; allocation concealment; blinding of participants, personnel, and outcome assessors; incomplete outcome data; selective outcome reporting; and other sources of bias (eg trial stopped early, no sample size calculation). We categorized these judgements as 'yes' (low risk of bias), 'no' (high risk of bias), or 'unclear'. Where our judgement was unclear we attempted to contact the trial authors for clarification. We summarized the information into a risk of bias summary figure and risk of bias graph.

Measures of treatment effect

We expressed the results for dichotomous data using risk ratios and 95% CIs.

We expressed results for continuous outcomes using the mean difference and 95% CIs when the data were summarized by arithmetic means and standard deviations.

Dealing with missing data

We performed a complete case analysis, which included only patients with reported outcomes.

Assessment of heterogeneity

We inspected visually the forest plots to detect overlapping CIs. We tested for heterogeneity using a standard χ^2 test with significance being set at $P < 0.1$. We used the I^2 test to estimate the total variation across trials due to heterogeneity rather than chance ([Deeks 2008](#)).

Assessment of reporting biases

We planned to assess publication bias with a visual inspection of a funnel plot if nine or more trials were meta-analysed.

Data synthesis

We analysed data using [Review Manager 5](#) and stratified the analyses according to treatments and comparators.

A fixed-effect or random-effects model was used according to the heterogeneity assessment. If statistical heterogeneity was detected ($\chi^2 P < 0.1$), we used the random-effects model for the pooled analysis.

Assessment of evidence quality

We assessed the quality of evidence using the GRADE methodology (Balshem 2011). The GRADE system considers quality to be a judgment of the extent to which we can be confident that the estimates of effect are correct. The level of quality is judged on a four-point scale. Evidence from randomized controlled studies is initially graded as high and downgraded by one, two or three levels after full consideration of any limitations in the design of the studies, the directness (or applicability) of the evidence, the consistency and precision of the results, and the possibility of publication bias.

The estimates of effect, and the GRADE assessments of our confidence in these estimates are displayed in 'summary of findings tables' for the main comparisons. Where we have downgraded the evidence our reasons for doing so are displayed in the footnotes. When making conclusions about the relative effects of the interventions, we have used language which reflects the GRADE assessments and our confidence in the estimates, ie if the evidence was high quality we would say "albendazole is equivalent to..."; moderate quality "albendazole is probably equivalent..."; low quality ("albendazole may be equivalent to..."); and where the evidence is of very low quality we have not drawn conclusions.

Subgroup analysis and investigation of heterogeneity

Where appropriate, we attempted to investigate the following sources of heterogeneity using subgroup analyses: disease severity groups (ie hospitalized patients); participant age (children (aged less 18 years) versus adults (aged 18 or more years); pregnancy (yes

or no); co-infection (yes or no); HIV/AIDS (positive/negative); cancer (yes or no); type of diagnostic methods (stool microscopy, copro-antigen detection, duodenal fluid, or small bowel biopsy); country classification (low income, lower middle income, upper middle income, and high income (World Bank 2009)).

Sensitivity analysis

If we identified significant heterogeneity in the trials' risk of bias, we performed a sensitivity analysis against risk of bias (low, unclear, or high risk of bias) when possible.

RESULTS

Description of studies

Results of the search

We identified 1213 references using our search strategy (see Figure 1). After we removed duplicates, we had 1072 references remaining. We screened all 1072 references by abstract and identified 40 potential studies for inclusion. We assessed the full text articles of these 40 studies and we identified 19 studies which met the inclusion criteria, one of which had two publications (Misra 1995 IND).

Figure 1. Study flow diagram.

Included studies

We identified 19 studies that met the inclusion criteria and included 1817 participants, of which 1441 were children. One study had two publications ([Misra 1995 IND](#)). The oldest trial was conducted in 1972 ([Bhandari 1972 IND](#)) and the most recent in 2012 ([Cañete 2012 CUB](#)). However, most trials were conducted during the 1990s.

Trial setting

Four studies were conducted in Turkey ([Kalayci 1995 TUR](#); [Bulut 1996 TUR](#); [Karabay 2004 TUR](#); [Yereli 2004 TUR](#)), four in India ([Bhandari 1972 IND](#); [Hall 1993 IND](#); [Dutta 1994 IND](#); [Misra 1995 IND](#)), three in Spain ([Gascon 1989 ESP](#); [Perez-Choliz 1989 ESP](#); [Gascón 1990 ESP](#)) and two in Peru ([Chan Del Pino 1999 PER](#); [Ortiz 2001 PER](#)), Mexico ([Romero-Cabello 1995 MEX](#); [Rodríguez 1996 MEX](#)) and Iran ([Alizadeh 2006 IRN](#); [Fallah 2007 IRN](#)); one study was conducted in the United Kingdom ([Al-Waili 1992 GBR](#)) and Cuba ([Cañete 2012 CUB](#)).

Participants

Fourteen studies were conducted exclusively in children (aged above three years); three were exclusively conducted in adults ([Gascon 1989 ESP](#); [Karabay 2004 TUR](#); [Cañete 2012 CUB](#)), two in both children and adults ([Gascón 1990 ESP](#); [Alizadeh 2006 IRN](#)), and one did not report the proportion of included children ([Alizadeh 2006 IRN](#)).

The inclusion criteria of all studies included the presence of cysts or trophozoites, or both, in the faeces on stool examination. All studies included symptomatic participants and eight trials reported

improvement of symptoms as an outcome ([Perez-Choliz 1989 ESP](#); [Dutta 1994 IND](#); [Romero-Cabello 1995 MEX](#); [Chan Del Pino 1999 PER](#); [Ortiz 2001 PER](#); [Yereli 2004 TUR](#); [Fallah 2007 IRN](#); [Cañete 2012 CUB](#)).

Interventions

Five groups of RCTs were described comparing alternative drug regimens with metronidazole given three times daily for five to 10 days:

- Albendazole ([Hall 1993 IND](#); [Dutta 1994 IND](#); [Misra 1995 IND](#); [Romero-Cabello 1995 MEX](#); [Rodríguez 1996 MEX](#); [Chan Del Pino 1999 PER](#); [Karabay 2004 TUR](#); [Yereli 2004 TUR](#); [Alizadeh 2006 IRN](#); [Cañete 2012 CUB](#))
- Mebendazole ([Gascon 1989 ESP](#); [Gascón 1990 ESP](#); [Al-Waili 1992 GBR](#); [Kalayci 1995 TUR](#); [Bulut 1996 TUR](#))
- Tinidazole ([Perez-Choliz 1989 ESP](#); [Chan Del Pino 1999 PER](#); [Fallah 2007 IRN](#))
- Metronidazole; single dose ([Bhandari 1972 IND](#))
- Nitazoxanide ([Ortiz 2001 PER](#))

A full description of these studies is available in the “[Characteristics of included studies](#)” section.

Excluded studies

Twenty studies were excluded. The reasons for exclusion are reported in the “[Characteristics of excluded studies](#)” table.

Risk of bias in included studies

The risk of bias assessments are summarised in [Figure 2](#) and [Figure 3](#) and detailed in the “[Characteristics of included studies](#)” table.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias): Stools examination	Blinding of outcome assessment (detection bias): Other outcomes	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Alizadeh 2006 IRN	?	+	+	?	+	?	+
Al-Waili 1992 GBR	?	?	+	+	+	?	+
Bhandari 1972 IND	?	?	?	-	+	?	?
Bulut 1996 TUR	?	?	+	-	?	?	?
Cañete 2012 CUB	+	?	+	?	+	+	+
Chan Del Pino 1999 PER	+	-	-	-	+	+	-
Dutta 1994 IND	?	?	?	-	+	?	+
Fallah 2007 IRN	?	-	-	-	+	?	?
Gascon 1989 ESP	?	?	?	?	?	-	?
Gascón 1990 ESP	?	?	?	?	?	-	?
Hall 1993 IND	+	+	+	-	+	-	?
Kalayci 1995 TUR	?	?	+	?	+	+	+
Karabay 2004 TUR	?	-	-	-	+	?	+
Misra 1995 IND	?	-	-	-	+	?	-
Ortiz 2001 PER	+	?	+	?	+	+	+
Perez-Choliz 1989 ESP	?	?	?	?	-	?	?
Rodríguez 1996 MEX	?	?	?	?	+	?	-
Romero-Cabello 1995 MEX	?	?	-	-	+	+	+
Yereli 2004 TUR	?	?	?	-	+	-	+

Allocation

Only four trials reported the method of random sequence generation, and were judged to be at low risk for this domain (Hall 1993 IND; Chan Del Pino 1999 PER; Ortiz 2001 PER; Cañete 2012 CUB). No information was presented for the remaining trials, although all were described as 'randomized'.

Only one trial adequately described allocation concealment to be at considered at low risk of bias (Alizadeh 2006 IRN).

Blinding

Only one trial adequately blinded participants and personnel to be considered at low risk of bias (Al-Waili 1992 GBR).

In seven trials (Al-Waili 1992 GBR; Hall 1993 IND; Kalayci 1995 TUR; Bulut 1996 TUR; Ortiz 2001 PER; Alizadeh 2006 IRN; Cañete 2012 CUB) the people who performed the stool examinations were blinded. However, the evaluators of other outcomes were only blinded in one (Al-Waili 1992 GBR).

Incomplete outcome data

Fifteen trials were judged to be at low risk for this domain, one was deemed to be high risk (Perez-Choliz 1989 ESP) and three had unclear risk of bias (Gascon 1989 ESP; Gascón 1990 ESP; Bulut 1996 TUR).

Selective reporting

Four trials showed some evidence of selective outcome reporting (Kalayci 1995 TUR; Romero-Cabello 1995 MEX; Chan Del Pino 1999 PER; Ortiz 2001 PER).

Other potential sources of bias

Seven studies were judged as having unclear risk of bias due to the lack of baseline data to assess the risk of confounding (Bhandari 1972 IND; Gascon 1989 ESP; Perez-Choliz 1989 ESP; Gascón 1990 ESP; Hall 1993 IND; Bulut 1996 TUR; Fallah 2007 IRN) while three other trials studies were considered as having high risk of bias due to baseline differences between groups (Misra 1995 IND; Rodríguez 1996 MEX; Chan Del Pino 1999 PER).

Effects of interventions

See: [Summary of findings for the main comparison](#); [Summary of findings 2](#); [Summary of findings 3](#)

Albendazole (once daily) versus metronidazole (three times daily)

Dosing: Albendazole was given as 400 mg once daily for five days. For metronidazole, the usual dosage was 5 mg/kg (250 mg or 500 mg in adults) three times daily for five to 10 days.

Four studies were from India, two from Turkey, two from Mexico, one from Peru, and one from Cuba. In addition, six of the included trials were conducted exclusively in children (see [Characteristics of included studies](#)).

No significant difference was found between treatments when assessing the rate of parasitological cure after one to three weeks of treatment (932 participants, 10 trials, [Analysis 1.1](#)). Although moderate heterogeneity was detected ($I^2 = 30\%$), this relates to one small study which found a statistically significant benefit with metronidazole (Chan Del Pino 1999 PER). One trial (Misra 1995 IND) found less time was needed to achieve parasitological cure in children treated with albendazole (Mean difference: -19.00, 95% CI -34.72 to -3.28; 57 participants, one trial, [Analysis 1.2](#)).

No significant differences were found in the rate of clinical improvement between treatments (483 participants, five trials, [Analysis 1.3](#)) and in the time needed for symptomatic improvement (97 participants, two trials, [Analysis 1.4](#)).

There were significantly fewer gastrointestinal mild adverse events in the albendazole group (RR 0.29, 95% CI 0.13 to 0.63; 717 participants, eight trials, [Analysis 1.5](#)). There were also significantly lower rates of neurological adverse events (RR 0.34, 95% CI 0.18 to 0.64; 453 participants, five trials, [Analysis 1.6](#)) and metallic taste (RR 0.03, 95% CI 0.01 to 0.13; 327 participants, three trials, [Analysis 1.7](#)). Other adverse events were uncommon and no significant differences were observed between groups ([Analysis 1.8](#); [Analysis 1.9](#); [Analysis 1.10](#); [Analysis 1.11](#)).

One RCT assessed non-compliance to treatment (Karabay 2004 TUR); no significant difference was reported between groups (57 participants, one trial, [Analysis 1.12](#)). No serious adverse events were reported in either group.

Mebendazole (three times daily) versus metronidazole (three times daily)

Dosing: The usual dosage of mebendazole was 200 mg three times daily for five to 10 days. For metronidazole, the usual dosage was 5 mg/kg (or 250 mg) three times daily for five to 10 days.

We found two trials from Spain, two from Turkey and one from the United Kingdom.

When pooling all studies, no significant difference was found between mebendazole and metronidazole in the rate of parasitological cure at one or two weeks (142 participants, five trials, [Analysis 2.1](#)). Furthermore, no significant difference was found in the subgroup of children (100 participants, three trials, [Analysis 2.1](#)). Two

studies recruiting mainly adults ([Gascon 1989 ESP](#); [Gascón 1990 ESP](#)) found a significantly higher parasitological cure rate with metronidazole (RR 0.15, 95% CI 0.05 to 0.44; 42 participants, two trials, [Analysis 2.1](#)). However these studies were small and underpowered to reliably detect or exclude an effect. None of the studies reported clinical recovery.

No significant differences in the rate of mild adverse events was found between groups ([Analysis 2.2](#); [Analysis 2.3](#); [Analysis 2.4](#)). No severe adverse events were reported.

Tinidazole (single dose) versus metronidazole (three times daily)

Dosing: Tinidazole was given at 50 mg/kg as a single dose, (maximum dose 1.5 to 2 g). The dose of metronidazole was more variable; 15 to 25 mg/kg/day three times daily for seven to 10 days, and [Perez-Choliz 1989 ESP](#) repeated the course three times one week apart.

Two small studies from Iran and Spain found that tinidazole significantly increased parasitological cure compared to metronidazole, while one study from Peru found no difference with a 100% cure rate in both arms. Overall, there was no significant difference detected between groups (179 participants, three trials, [Analysis 3.1](#)).

No significant difference was found in the rate of clinical improvement (179 participants, three trials, [Analysis 3.2](#)).

The number of adverse events reported was not significantly dif-

ferent between the two treatment arms ([Analysis 3.3](#); [Analysis 3.4](#); [Analysis 3.5](#); [Analysis 3.6](#)), and there were no serious adverse events reported from any of the three trials.

Metronidazole (single dose) versus metronidazole (three times daily)

Dosing: The dosage of metronidazole was 35 mg/kg single dose, repeated at two weeks, versus metronidazole 20 mg/kg/day three times daily for 5 days, repeated at two weeks.

In this one small trial in Indian children, both treatment regimens achieved a 100% parasitological cure rate when assessed at two weeks (54 participants, one trial, [Analysis 4.1](#)).

Side-effects were rare during the two weeks follow-up with no differences between the groups (54 participants, one trial, [Analysis 4.2](#)). There were no serious adverse events reported.

Nitazoxanide (twice daily) versus metronidazole (twice daily)

Dosing: Nitazoxanide was given for three days (100 to 200 mg twice daily) and metronidazole for 5 days (125 to 250 mg twice daily).

In one trial conducted in Peru, no significant differences were found in the rates of parasitological cure (110 participants, one trial, [Analysis 5.1](#)), improvement of diarrhoea (110 participants, one trial, [Analysis 5.2](#)) or mild adverse events ([Analysis 5.3](#); [Analysis 5.4](#); [Analysis 5.5](#); [Analysis 5.6](#)).

ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Mebendazole (5+ days) compared to metronidazole (5+ days) for treating giardiasis						
Patient or population: People with giardiasis infection Settings: Endemic settings Intervention: Mebendazole once daily for five or more days Comparison: Metronidazole three times daily for five or more days						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Metronidazole (three times daily for 5 to 10 days)	Mebendazole (three times daily for 5 to 10 days)				
Parasitological cure (Follow-up: 1 to 2 weeks)	90 per 100	52 per 100 (29 to 95)	RR 0.58 (0.32 to 1.06)	142 (5 studies)	⊕○○○ very low ^{1,2,3}	
Clinical improvement	-	-	-	(0 studies)	-	Not reported
Side effects: nausea/vomiting	8 per 100	3 per 100 (0 to 15)	RR 0.32 (0.05 to 1.9)	100 (3 studies)	⊕○○○ very low ^{1,2,3}	
Side effects: headache	8 per 100	2 per 100 (0 to 17)	RR 0.24 (0.03 to 2.06)	74 (2 studies)	⊕○○○ very low ^{1,2,3}	
Serious adverse events	-	-	-	142 (5 studies)	-	Not reported
<p>*The basis for the assumed risk (eg the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).</p> <p>CI: Confidence interval; RR: Risk Ratio</p>						

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹These trials were conducted in adults and children from Spain, Turkey, and the UK. The usual dose of mebendazole was 200 mg three times daily for five to 10 days, and metronidazole 5 mg/kg (or 250 mg) three times daily for five to 10 days.

² Downgraded by 1 for risk of bias. None of these trials adequately described allocation concealment or blinding.

³ Downgraded by 2 for imprecision. The trials were very small and underpowered to detect differences. The 95% CI is wide and includes no difference between treatments.

Tinidazole (single dose) compared to metronidazole (5+ days) for treating giardiasis						
Patient or population: People with giardiasis infection Settings: Endemic settings Intervention: Tinidazole single dose Comparison: Metronidazole three times daily for five or more days						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Metronidazole (three times daily for 5 to 10 days)	Tinidazole (single dose)				
Parasitological cure (Follow-up: 3 to 4 weeks)	73 per 100	89 per 100 (63 to 100)	RR 1.23 (0.87 to 1.73)	179 (3 studies)	⊕○○○ very low ^{1,2,3}	
Clinical improvement (Follow-up: 3 to 4 weeks)	76 per 100	87 per 100 (76 to 100)	RR 1.15 (1 to 1.32)	179 (3 studies)	⊕○○○ very low ^{1,2,3}	
Gastrointestinal side effects (Follow-up: 3 to 4 weeks)	8 per 100	5 per 100 (2 to 13)	RR 0.58 (0.21 to 1.62)	179 (3 studies)	⊕○○○ very low ^{1,2,3}	
Neurological side effects (Follow-up: 3 to 4 weeks)	4 per 100	5 per 100 (1 to 22)	RR 1.3 (0.29 to 5.92)	138 (2 studies)	⊕○○○ very low ^{1,2,3}	
Serious adverse events	-	-	-	179 (3 studies)	-	Not reported

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹These trials were conducted in Iran, Spain and Peru. The usual dose of tinidazole was 50mg/kg as a single dose, and metronidazole 5 mg/kg (or 250 mg) three times daily for five to 10 days.

² Downgraded by 1 for risk of bias. None of these trials adequately described allocation concealment or blinding.

³ Downgraded by 2 for imprecision. The trials were very small and underpowered to detect differences. The 95% CI is wide and includes no difference between treatments.

DISCUSSION

Summary of main results

This review of interventions for treating giardiasis found 19 RCTs incorporating 1817 participants, of which 1441 were children. Once-daily albendazole is probably equivalent to metronidazole given three times daily at achieving parasitological cure (*moderate quality evidence*), and improving symptoms (*moderate quality evidence*), but the duration of follow-up was short (two to three weeks). Albendazole probably also has fewer gastrointestinal and neurological side effects (*moderate quality evidence*). Mebendazole has been evaluated in five studies but these are poorly conducted and too small to make reliable conclusions on the relative effectiveness (*very low quality evidence*). Five further trials have evaluated shortened regimens of tinidazole, metronidazole, and nitazoxanide, but again these were at high risk of bias and too small to reliably detect or exclude important differences (*very low quality evidence*).

Overall completeness and applicability of evidence

The studies included in this review are from a variety of clinical settings across many different countries. Although the major findings can probably be generalized to elsewhere, several important limitations of these data should be noted; only one trial included HIV positive participants (Gascon 1989 ESP), only one included malnourished children (Chan Del Pino 1999 PER), and none of the trials included pregnant women. Further trials in these groups may be helpful.

Quality of the evidence

The quality of evidence was assessed using the GRADE methodology and is displayed in the three summary of findings tables: [Summary of findings for the main comparison](#); [Summary of findings 2](#); [Summary of findings 3](#).

The evidence that albendazole is equivalent to metronidazole for treating giardiasis is considered to be of moderate quality. This implies that we can have reasonable confidence in the estimates but that further research may change the result. This evidence was downgraded due to concerns about the high risk of bias of all the trials comparing these two drugs. However, despite this risk, there was a consistent finding of no statistical or clinically important difference between the drugs across eight trials.

The evidence comparing all other regimens with metronidazole is considered to be of very low quality due to both the high risk of bias of the included trials, and the trials being too small, and significantly underpowered, to reliably detect or exclude a difference. Reliable conclusions on the relative efficacy of tinidazole,

nitazoxanide, or single dose metronidazole can therefore not be made.

Potential biases in the review process

We have attempted to avoid publication bias by searching for both published and unpublished studies. However, we did not identify any and we are not aware of any that exist.

Most of the trials included in this review are at unclear or high risk for selection bias or reporting bias as a result of inadequate randomization or blinding. Inclusion of these trials in meta-analyses can produce biased or misleading conclusions. However, we have used the GRADE approach to assessing quality of evidence to allow us to express our decreased confidence in the results of our meta-analysis as a consequence of these faults. Many of the trials are also at unclear or high risk for selective outcome reporting as important outcomes, such as clinical improvement and adverse events, were frequently not reported.

Agreements and disagreements with other studies or reviews

Solaymani-Mohammadi and colleagues published a similar systematic review of albendazole versus metronidazole for treating giardiasis in 2010, and concluded that 'the effectiveness of albendazole...was comparable to that of metronidazole', and 'patients treated with albendazole tended to have fewer side effects compared with those who took metronidazole's (Solaymani-Mohammadi 2010). Our review includes one additional study for this comparison, and confirms this conclusion.

AUTHORS' CONCLUSIONS

Implications for practice

Albendazole given once daily is probably as effective as metronidazole given three times daily for treating giardiasis in both children and adults, but with the advantages of a simplified regimen and fewer side effects.

Implications for research

This systematic review has identified the need for well-designed, adequately powered RCTs to assess the benefits and harms of treatments for symptomatic giardiasis. Many questions remain open and some important considerations for future research are as follows.

1. Clinical outcomes and compliance need to be better addressed and considered for study sample size calculations.

2. Studies are needed to determine the effects in specific populations such as pregnant women, people infected with human immunodeficiency virus, and malnourished children.

3. Studies should follow the CONSORT guidelines for randomized trials (Schulz 2010): <http://www.consort-statement.org/>).

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REFERENCES

References to studies included in this review

Alizadeh 2006 IRN {published data only}

Alizadeh A, Ranjbar M, Kashani KM, Taheri MM, Bodaghi M. Albendazole versus metronidazole in the treatment of patients with giardiasis in the Islamic Republic of Iran. *Eastern Mediterranean Health Journal* 2006 Sep;**12**(5): 548–54.

Al-Waili 1992 GBR {published data only}

Al-Waili NS, Hasan UN. Mebendazole in giardial infection: a comparative study with metronidazole. *Journal of Infectious Diseases* 1992;**165**(6):170–1.

Bhandari 1972 IND {published data only}

Bhandari B, Upadhyay R. Standard and single dosage regimens of “Flagyl” (metronidazole) in giardiasis in children. *Indian Pediatrics* 1972;**9**(12):800–4.

Bulut 1996 TUR {published data only}

Bulut BU, Gülnar SB, Aysev D. Alternative treatment protocols in giardiasis: a pilot study. *Scandinavian Journal of Infectious Diseases* 1996;**28**(5):493–5.

Cañete 2012 CUB {published data only}

Cañete R, Rodríguez P, Mesa L, Brito K, Prior A, Guilhem D, et al. Albendazole versus metronidazole in the treatment of adult giardiasis: a randomized, double-blind, clinical trial. *CMRO: Current Medical Research & Opinion* 2012;**28**(1):149–54.

Chan Del Pino 1999 PER {published data only}

Chan Del Pino M, Cueva Cornejo L, Troyes Rivera L. Comparative study of albendazole versus nitrofurans and nitroimidazoles in the treatment of giardiasis in children. *Revista de Gastroenterología del Peru* 1999;**19**(2):95–108.

Dutta 1994 IND {published data only}

Dutta AK, Phadke MA, Bagade AC, Joshi V, Gazder A, Biswas TK, et al. A randomised multicentre study to compare the safety and efficacy of albendazole and metronidazole in the treatment of giardiasis in children. *Indian Journal of Pediatrics* 1994;**61**(6):689–93.

Fallah 2007 IRN {published data only}

Fallah M, Rabiee S, Moshtaghi AA. Comparison between efficacy of a single dose of tinidazole with a 7-day standard

dose course of metronidazole in giardiasis. *Pakistan Journal of Medical Sciences* 2007;**23**(1):43–6.

Gascon 1989 ESP {published data only}

Gascon J, Moreno A, Valls ME, Miró JM, Corachán M. Failure of mebendazole treatment in *Giardia lamblia* infection. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1989;**83**(5):647.

Gascón 1990 ESP {published data only}

Gascón J, Abós R, Valls ME, Corachán M. Mebendazole and metronidazole in giardial infections. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1990;**84**(5): 694.

Hall 1993 IND {published data only}

Hall A, Nahar Q. Albendazole as a treatment for infections with *Giardia duodenalis* in children in Bangladesh. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1993;**87**(1):84–6.

Kalayci 1995 TUR {published data only}

Kalayci AG, Cetinkaya F, Gunaydm M, Gurses N. Comparison of mebendazole with metronidazole and furazolidone in the treatment of giardiasis in children. *Annals of Saudi Medicine* 1995;**15**(6):655–6.

Karabay 2004 TUR {published data only}

Karabay O, Tamer A, Gunduz H, Kayas D, Arinc H, Celebi H. Albendazole versus metronidazole treatment of adult giardiasis: an open randomized clinical study. *World Journal of Gastroenterology* 2004;**10**(8):1215–7.

Misra 1995 IND {published data only}

Misra PK, Kumar A, Agarwal V, Jagota SC. A comparative clinical trial of albendazole versus metronidazole in children with giardiasis. *Indian Pediatrics* 1995 Mar;**32**(3):291–4. Corrected and republished in: *Indian Pediatrics*. 1995 Jul; **32**(7):779–82.

* Misra PK, Kumar A, Agarwal V, Jagota SC. A comparative clinical trial of albendazole versus metronidazole in children with giardiasis. *Indian Pediatrics* 1995;**32**(7):779–82. Corrected and republished from: *Indian Pediatrics*. 1995; **32**(3):291–4.

Ortiz 2001 PER {published data only}

Ortiz JJ, Ayoub A, Gargala G, Chegne NL, Favennec L. Randomized clinical study of nitazoxanide compared to metronidazole in the treatment of symptomatic giardiasis in children from Northern Peru. *Alimentary Pharmacology and Therapeutics* 2001;**15**(9):1409–15.

Perez-Choliz 1989 ESP {published data only}

Perez-Choliz V, Clavel A, Olivan G, Castillo FJ, Bueno G, Tosao A, et al. Treatment of giardiasis: a comparative study in paediatrics, between multiple-dose of metronidazole and single-dose of tinidazole [Tratamiento de la giardiasis: estudio comparativo en pediatría, entre metronidazol en dosis múltiple y tinidazol en dosis única]. *Archivos de Pediatría* 1989;**40**(3):245–9.

Rodríguez 1996 MEX {published data only}

Rodríguez R, Aburto M, Sánchez MI. Effectiveness of albendazole in the treatment of giardiasis in children [Eficacia del albendazol en el tratamiento de giardiasis en niños]. *Boletín Médico del Hospital Infantil de México* 1996;**53**(4):173–7.

Romero-Cabello 1995 MEX {published data only}

Romero-Cabello R, Robert L, Muñoz-García R, Tanaka J. Randomized study comparing the safety and efficacy of albendazole and metronidazole in the treatment of giardiasis in children [Estudio aleatorio para comparar seguridad y eficacia de Albendazol y Metronidazol en el tratamiento de la giardiasis en niños]. *Revista Latinoamericana de Microbiología* 1995;**37**(4):315–23.

Yereli 2004 TUR {published data only}

Yereli K, Balcioglu IC, Ertan P, Limoncu E, Onag A. Albendazole as an alternative therapeutic agent for childhood giardiasis in Turkey. *Clinical Microbiology and Infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases* 2004;**10**(6): 527–9.

References to studies excluded from this review

Bakshi 1978 {published data only}

Bakshi JS, Ghiara JM, Nanivadekar AS. How does tinidazole compare with metronidazole? A summary report of Indian trials in amoebiasis and giardiasis. *Drugs* 1978;**15**(Suppl 1): 33–42.

Baqai 2001 {published data only}

Baqai R, Zuberi SJ, Qureshi H, Ahmed W, Hafiz S. Efficacy of albendazole in giardiasis. *Eastern Mediterranean Health Journal* 2001;**7**(4/5):787–90.

Bassily 1987 {published data only}

Bassily S, Farid Z, el-Masry NA, Mikhail EM. Treatment of intestinal *E. histolytica* and *G. lamblia* with metronidazole, tinidazole and ornidazole: a comparative study. *American Journal of Tropical Medicine and Hygiene* 1987;**90**(1):9–12.

Besirbellioglu 2006 {published data only}

Besirbellioglu BA, Ulcay A, Can M, Erdem H, Tanyuksel M, Avci IY, et al. *Saccharomyces boulardii* and infection due to *Giardia lamblia*. *Scandinavian Journal of Infectious Diseases* 2006;**38**(6–7):479–81.

Botero 1974 {published data only}

Botero D. Experiences with a new nitroimidazole derivative versus metronidazole in the treatment of intestinal amoebiasis and giardiasis. Third International Congress of Parasitology, Munich. August 25–31, 1974.

Gazder 1978 {published data only}

* Gazder AJ, Banerjee M. Single dose therapy of giardiasis with tinidazole and metronidazole. *Drugs* 1978;**15**(Suppl 1):30–2.

Gazder AJ, Banerjee M. Single dose treatment of giardiasis in children. A comparison of tinidazole and metronidazole. *Indian Pediatrics* 1977;**14**(9):715–7.

Gazder AJ, Banerjee M. Single-dose treatment of giardiasis in children: a comparison of tinidazole and metronidazole. *Current Medical Research and Opinion* 1977;**5**(2):164–8.

Grant 2001 {published data only}

Grant J, Mahanty S, Khadir A, MacLean JD, Kokoskin E, Yeager B, et al. Wheat germ supplement reduces cyst and trophozoite passage in people with giardiasis. *American Journal of Tropical Medicine and Hygiene* 2001;**65**(6): 705–10.

Guerrero 2000 {published data only}

Guerrero R, Paipilla S, Amaya A, Duque S, Arevalo A, Nicholls S, et al. A controlled trial for three drugs in the treatment of giardiasis. *Journal of Pediatric Gastroenterology and Nutrition* 2000;**31**(2):S84.

Jokipii 1978 {published data only}

Jokipii L, Jokipii AM. Comparison of four dosage schedules in the treatment of giardiasis with metronidazole. *Infection* 1978;**6**(2):92–4.

Jokipii 1979 {published data only}

Jokipii L, Jokipii AM. Single-dose metronidazole and tinidazole as therapy for giardiasis: success rates, side effects, and drug absorption and elimination. *Journal of Infectious Diseases* 1979;**140**(6):984–8.

Krishnamurthy 1978 {published data only}

Krishnamurthy KA, Saradhambal V. Single dose therapy of giardiasis: a comparative study of tinidazole and metronidazole in pediatric patients. *Indian Pediatrics* 1978;**15**(1):51–6.

Kyrönseppä 1981 {published data only}

Kyrönseppä H, Pettersson T. Treatment of giardiasis: relative efficacy of metronidazole as compared with tinidazole. *Scandinavian Journal of Infectious Diseases* 1981;**13**(4): 311–2.

Leary 1974 {published data only}

Leary PM, Jones C, Douglas F. Metronidazole suspension in the out-patient treatment of giardiasis. *Journal of Tropical Pediatrics and Environmental Child Health* 1974;**20**:198–200.

Levi 1977 {published data only}

Levi GC, de Avila CA, Amato Neto V. Efficacy of various drugs for treatment of giardiasis. A comparative study. *American Journal of Tropical Medicine and Hygiene* 1977;**26**(3):564–5.

Morrone 2004 {published data only}

Morrone FB, Carneiro JA, dos Reis C, Cardozo CM, Ubal C, de Carli GA. Study of enteroparasites infection frequency and chemotherapeutic agents used in pediatric patients in a community living in Porto Alegre, RS, Brazil. *Revista do Instituto de Medicina Tropical de São Paulo* 2004;**46**(2): 77–80.

Nigam 1991 {published data only}

Nigam P, Kapoor KK, Kumar A, Sarkari NB, Gupta AK. Clinical profile of giardiasis and comparison of its therapeutic response to metronidazole and tinidazole. *Journal of Association of Physicians of India* 1991;**39**(8): 613–5.

Sabchareon 1980 {published data only}

Sabchareon A, Chongsuphaisiddhi T, Attanath P. Treatment of giardiasis in children with quinacrine, metronidazole, tinidazole and ornidazole. *Southeast Asian Journal of Tropical Medicine and Public Health* 1980;**11**(2): 280–4.

Sadjjadi 2001 {published data only}

Sadjjadi SM, Alborzi AW, Mostovfi H. Comparative clinical trial of mebendazole and metronidazole in giardiasis of children. *Journal of Tropical Pediatrics* 2001;**47**(3):176–8.

Speelman 1985 {published data only}

Speelman P. Single-dose tinidazole for the treatment of giardiasis. *Antimicrobial Agents and Chemotherapy* 1985;**27**(2):227–9.

Suntornpoch 1981 {published data only}

Suntornpoch V, Chavalittamrong B. Treatment of giardiasis in children with tinidazole, ornidazole and metronidazole. *Southeast Asian Journal of Tropical Medicine and Public Health* 1981;**12**(2):231–5.

Additional references**AAP 2006**

American Academy of Pediatrics. *Red book: Report of the Committee on Infectious Diseases*. 27th Edition. Illinois: Academy of Pediatrics, 2006.

Abdel 1991

Abdel Fattah SM, Maklad KA, Gadallah MA. Age-related rate of seropositivity of antibody to *Giardia lamblia* in different age groups in Cairo. *Journal of the Egyptian Society of Parasitology* 1991;**21**(3):707–13.

Al-Saeed 2006

Al-Saeed AT, Issa SH. Frequency of *Giardia lamblia* among children in Dohuk, northern Iraq. *Eastern Mediterranean Health Journal* 2006;**12**(5):555–61.

Argüello-García 2004

Argüello-García R, Cruz-Soto M, Romero-Montoya L, Ortega-Pierres G. Variability and variation in drug susceptibility among *Giardia duodenalis* isolates and clones exposed to 5-nitroimidazoles and benzimidazoles in vitro. *Journal of Antimicrobial Chemotherapy* 2004;**54**(4):711–21.

Balshem 2011

Balshem H, Helfand M, Schunemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the

quality of evidence. *Journal of Clinical Epidemiology* 2011;**64**(4):401–6.

Barnawi 2007

Barnawi AB, Tonkal AM, Fouad MA, Al-Braiken FA. Detection of *Entamoeba histolytica* in stool specimens by using enzyme-linked immunosorbent assay in the population of Jeddah City, Saudi Arabia. *Journal of the Egyptian Society of Parasitology* 2007;**37**(1):143–50.

Brodsky 1974

Brodsky RE, Spencer HC, Schultz MG. Giardiasis in American travelers to the Soviet Union. *Journal of Infectious Diseases* 1974;**130**(3):319–23.

Buret 2007

Buret A. Mechanisms of epithelial dysfunction in giardiasis. *Gut* 2007;**56**(3):316–7.

Celiköz 2005

Celiköz A, Aciöz M, Degerli S, Cinar Z, Elaldi N, Erandaç M. Effects of giardiasis on school success, weight and height indices of primary school children in Turkey. *Pediatrics International* 2005;**47**(5):567–71.

Chute 1987

Chute CG, Smith RP, Baron JA. Risk factors for endemic giardiasis. *American Journal of Public Health* 1987;**77**(5): 585–7.

Cifuentes 2000

Cifuentes E, Gomez M, Blumenthal U, Tellez-Rojo MM, Romieu I, Ruiz-Palacios G, et al. Risk factors for *Giardia intestinalis* infection in agricultural villages practicing wastewater irrigation in Mexico. *American Journal of Tropical Medicine and Hygiene* 2000;**62**(3):388–92.

Cifuentes 2004

Cifuentes E, Suárez L, Espinosa M, Juárez-Figueroa L, Martínez-Palomo A. Risk of *Giardia intestinalis* infection in children from an artificially recharged groundwater area in Mexico City. *American Journal of Tropical Medicine and Hygiene* 2004;**71**(1):65–70.

de Souza 2007

de Souza EA, da Silva-Nunes M, Malafronte Rdos S, Muniz PT, Cardoso MA, Ferreira MU. Prevalence and spatial distribution of intestinal parasitic infections in a rural Amazonian settlement, Acre State, Brazil. *Cadernos de Saúde Pública* 2007;**23**(2):427–34.

Deeks 2008

Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors), *Cochrane Handbook of Systematic Reviews of Intervention*. Version 5.0.0 (updated February 2008). The Cochrane Collaboration 2008. Available from www.cochrane-handbook.org.

Ekdahl 2005

Ekdahl K, Andersson Y. Imported giardiasis: impact of international travel, immigration, and adoption. *American Journal of Tropical Medicine and Hygiene* 2005;**72**(6): 825–30.

Escobedo 2007

Escobedo AA, Cimerman S. Giardiasis: a pharmacotherapy review. *Expert Opinion on Pharmacotherapy* 2007;**8**(12): 1885–902.

Freedman 2006

Freedman DO, Weld LH, Kozarsky PE, Fisk T, Robins R, von Sonnenburg F, et al. Spectrum of disease and relation to place of exposure among ill returned travelers. *New England Journal of Medicine* 2006;**354**(2):119–30.

Fricker 2007

Fricker CR, Medema GD, Smith HV. Protozoan parasites (*Cryptosporidium*, *Giardia*, *Cyclospora*). *Guidelines for drinking-water quality*. Second Edition. Geneva: World Health Organization, 1993:70–118.

Garcia 2006

Garcia LS, Garcia JP. Detection of *Giardia lamblia* antigens in human fecal specimens by a solid-phase qualitative immunochromatographic assay. *Journal of Clinical Microbiology* 2006;**44**(12):4587–8.

Garner 2001

Garner TB, Hill DR. Treatment of giardiasis. *Clinical Microbiology Reviews* 2001;**14**(1):114–28.

Goek 2003

Goek LK. Update on the prevalence of malnutrition among children in Asia. *Nepal Medical College Journal* 2003;**5**(2): 113–22.

Havenik 2007

Hanevik K, Hausken T, Morken MH, Strand EA, Mørch K, Coll P, et al. Persisting symptoms and duodenal inflammation related to *Giardia duodenalis* infection. *Journal of Infection* 2007;**55**(6):524–30.

Hiatt 1995

Hiatt RA, Markell EK, Ng E. How many stool examinations are necessary to detect pathogenic intestinal protozoa?. *American Journal of Tropical Medicine and Hygiene* 1995;**53**(1):36–9.

Higgins 2008

Higgins JPT, Altman DG (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors), *Cochrane Handbook of Systematic Reviews of Intervention*. Version 5.0.0 (updated February 2008). The Cochrane Collaboration 2008. Available from www.cochrane-handbook.org.

Hörman 2004

Hörman A, Korpela H, Sutinen J, Wedel H, Hänninen ML. Meta-analysis in assessment of the prevalence and annual incidence of *Giardia* spp. and *Cryptosporidium* spp. infections in humans in the Nordic countries. *International Journal for Parasitology* 2004;**34**(12):1337–46.

Jelinek 2000

Jelinek T, Löscher T. Epidemiology of giardiasis in German travelers. *Journal of Travel Medicine* 2000;**7**(2):70–3.

Jokipii 1985

Jokipii AM, Hemila M, Jokipii L. Prospective study of acquisition of *Cryptosporidium*, *Giardia lamblia*, and gastrointestinal illness. *Lancet* 1985;**2**(8453):487–9.

Laupland 2005

Laupland KB, Church DL. Population-based laboratory surveillance for *Giardia* sp. and *Cryptosporidium* sp. infections in a large Canadian health region. *BMC Infectious Diseases* 2005;**16**(5):72.

Lefebvre 2008

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.0 (updated February 2008). The Cochrane Collaboration 2008. Available from www.cochrane-handbook.org.

Libanore 1991

Libanore M, Bicocchi R, Rossi MR, Montanari P, Sighinolfi L, Macario F, et al. Incidence of giardiasis in adults patients with acute enteritis. *Minerva Medica* 1991;**82**(6):375–80.

Mahmud 1995

Mahmud MA, Chappell C, Hossain MM, Habib M, Dupont HL. Risk factors for development of first symptomatic *Giardia* infection among infants of a birth cohort in rural Egypt. *American Journal of Tropical Medicine and Hygiene* 1995;**53**(1):84–8.

Mank 2001

Mank TG, Zaat JO. Diagnostic advantages and therapeutic options for giardiasis. *Expert Opinion on Investigational Drugs* 2001;**10**(8):1513–9.

Miotti 1986

Miotti PG, Gilman RH, Santosham M, Ryder RW, Yolken RH. Age related rate of seropositivity and antibody to *Giardia lamblia* in four diverse populations. *Journal of Clinical Microbiology* 1986;**24**(6):972–5.

Morgan 1993

Morgan UM, Reynoldson JA, Thompson RC. Activities of several benzimidazoles and tubulin inhibitors against *Giardia* spp. in vitro. *Antimicrobial Agents and Chemotherapy* 1993;**37**(2):328–31.

Mukhopadhyay 2007

Mukhopadhyay C, Wilson G, Pradhan D, Shivananda PG. Intestinal protozoal infestation profile in persistent diarrhea in children below age 5 years in western Nepal. *Southeast Asian Journal of Tropical Medicine and Public Health* 2007;**38**(1):13–9.

Newman 2001

Newman RD, Moore SR, Lima AA, Nataro JP, Guerrant RL, Sears CL. A longitudinal study of *Giardia lamblia* infection in north-east Brazilian children. *Tropical Medicine and International Health* 2001;**6**(8):624–34.

Park 2004

Park SK, Kim DH, Deung YK, Kim HJ, Yang EJ, Lim SJ, et al. Status of intestinal parasite infections among children

- in Bat Dambang, Cambodia. *Korean Journal of Parasitology* 2004;**42**(4):201–3.
- Pinheiro 2011**
Pinheiro Ide O, de Castro MF, Mitterofhe A, Pires FA, Abramo C, Ribeiro LC, et al. Prevalence and risk factors for giardiasis and soil-transmitted helminthiasis in three municipalities of Southeastern Minas Gerais State, Brazil: risk factors for giardiasis and soil-transmitted helminthiasis. *Parasitology Research* 2011;**108**(5):1123–30.
- Rendtorff 1954**
Rendtorff RC. The experimental transmission of human intestinal protozoan parasitesII. *Giardia lamblia* cysts given in capsules. *American Journal of Hygiene* 1954;**59**(2): 209–20.
- Review Manager 5 [Computer program]**
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.0. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008.
- Schulz 2010**
Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel-group randomized trials. *British Medical Journal* 2010;**340**:c332.
- Schunk 2001**
Schunk M, Jelinek T, Wetzel K, Nothdurft HD. Detection of *Giardia lamblia* and *Entamoeba histolytica* in stool samples by two enzyme immunoassays. *European Journal of Clinical Microbiology and Infectious Diseases* 2001;**20**(6):389–91.
- Solaymani-Mohammadi 2010**
Solaymani-Mohammadi S, Genkinger JM, Loffredo CA, Singer SM. A meta-analysis of the effectiveness of albendazole compared with metronidazole as treatments for infections with *Giardia duodenalis*. *PLoS Neglected Tropical Diseases* 2010;**4**(5):e682.
- Weitzel 2006**
Weitzel T, Dittrich S, Möhl I, Adusu E, Jelinek T. Evaluation of seven commercial antigen detection tests for *Giardia* and *Cryptosporidium* in stool samples. *Clinical Microbiology and Infection* 2006;**12**(7):656–9.
- World Bank 2009**
World Bank. Country classification. www.worldbank.org/data/countryclass/countryclass.html (accessed 16 February 2009).
- Yoder 2007**
Yoder JS, Beach MJ, Centers for Disease Control and Prevention (CDC). Giardiasis surveillance - United States, 2003–2005. *MMWR Surveillance summaries* 2007;**56**(7): 11–8.
- Zaat 1998**
Zaat JOM, Mank ThG, Assendelft WJJ. Drugs for treating giardiasis. *Cochrane Database of Systematic Reviews* 1998, Issue 3. DOI: 10.1002/14651858.CD000217
- * Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Al-Waili 1992 GBR

Methods	United Kingdom. No power calculation made. Intention to treat analysis. Duration: 21 days	
Participants	44 children (28 males); age: three to 13 years. Symptoms: anorexia, altered bowel habits, abdominal cramps, flatulence Asymptomatic: 0%. Microscopic stools examination: cysts in all cases and trophozoites in only two cases. Technique: not mentioned Exclusion criteria: not mentioned.	
Interventions	Rx 1. Mebendazole: 200 mg three times daily, 5 days (oral). Rx 2: Metronidazole: 200 mg three times daily, 5 days (oral)	
Outcomes	Parasitological cure: fecal specimens were examined on days 7 and 14 after treatment. Technique: not mentioned Any side effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"... were randomly to receive either mebendazole or metronidazole.."
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Stools examination	Low risk	"The examinations were done blindly.."
Blinding of outcome assessment (detection bias) Other outcomes	Low risk	".... and the investigators were unaware of the nature of the drugs used.."
Incomplete outcome data (attrition bias) All outcomes	Low risk	No withdrawals or loss to follow up.
Selective reporting (reporting bias)	Unclear risk	No mention of a systematic strategy for collecting side effects
Other bias	Low risk	No comments.

Methods	Iran. Intention to treat analysis. Duration: 10 days.	
Participants	120 participants (61 males); age: two to 53 years, mean 22.3 ± 11 years Symptoms: were not specified. Asymptomatic: 0%. Inclusion criteria: acute symptoms of giardiasis and a positive stool examination report for trophozoites of the pathogen Microscopic stools examination: cysts in all cases and trophozoites in only two cases. Technique: not mentioned Exclusion criteria: not mentioned.	
Interventions	Rx 1. Albendazole: 400 mg single dose for 5 days (oral). Rx 2. Metronidazole: 250 mg three times daily for 5 days (oral)	
Outcomes	“A week after starting the treatment, stool examination to detect trophozoites of <i>G. lamblia</i> was performed three times in three consecutive days for all the patients”. Technique: not mentioned Parasitological cure: negative stool examination for trophozoites and cysts Any side effects.	
Notes	Sample size calculation: “(alpha level of 0.05 and beta level of 0.2), the sample size needed was calculated to be 120 documented cases of the disease”	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“before starting the study one number was assigned for each case. All the numbers were assigned in two groups at random...”
Allocation concealment (selection bias)	Low risk	“and a physician was assigned to give the needed numbers to the clinics”
Blinding of outcome assessment (detection bias) Stools examination	Low risk	“one parasitologist who was blinded to the treatment received was responsible for detecting the trophozoites in the samples before and after treatment”
Blinding of outcome assessment (detection bias) Other outcomes	Unclear risk	Not mentioned.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 120 paediatric patients were included in the statistical analysis
Selective reporting (reporting bias)	Unclear risk	One of the expected outcomes is symptomatic improvement, but it was not reported

Other bias	Low risk	No comments.
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Bhandari 1972 IND

Methods	India. No power calculation made. Intention to treat analysis. Duration: 21 weeks
Participants	54 participants (41 males), from 18 months to 12 years old; There is not any specification about symptoms. However, improvement on clinical symptoms was reported as outcome Inclusion criteria: positive stools reports on two successive days Exclusion criteria: not mentioned.
Interventions	Rx 1. Metronidazole: 35 mg/K single dose, repeated at two weeks (oral) Rx 2. Metronidazole: 20 mg/K/d three times daily for 5 days, repeated at two weeks (oral) Metronidazole was administrated mixed with honey, after meals
Outcomes	Clinical assessment and stools were repeated on days four, eight, 12 and 16 post-treatment. Any side effect volunteered by the patient was noted Parasitological cure: stool negative for <i>G. lamblia</i> . The study does not specify the technique of stool examination Cure: stool negative for <i>G. lamblia</i> , and complete relief of symptoms or marked clinical improvement
Notes	Any patient with treatment failure was given a third regimen of therapy, which was not specified. None of the patients received treatment before nine weeks

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Treatment schedules in a random manner".
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Stools examination	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Other outcomes	High risk	Not mentioned. Probably not, this study compares therapy with metronidazole, 5 days versus 1 day. There is no mention about placebo plus metronidazole in the second group
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data.

Bhandari 1972 IND (Continued)

Selective reporting (reporting bias)	Unclear risk	No mention of a systematic strategy for collecting side effects
Other bias	Unclear risk	Characteristics of included patients were not described in a comparative manner

Bulut 1996 TUR

Methods	Turkey. No power calculation made. Per protocol analysis. Duration: 14 days	
Participants	Information only on 48 participants (30 males); age: six to 12 years Symptoms: two children had diarrhoea. "Nonspecific gastrointestinal symptoms, such as abdominal pain, nausea, and viscid stool, were found in the remaining 46" Microscopic stools examination: "standard methods" in fresh stool samples. Technique: not mentioned Exclusion criteria: not mentioned.	
Interventions	Rx 1. Mebendazole 100 mg three times daily for one day. Rx 2: Mebendazole 100 mg three times daily for seven days. Rx 3: Metronidazole 15mg/kg single dose for seven days. Rx 4: Ornidazole 40 mg/day single dose.	
Outcomes	Parasitological cure: absence of cystic or trophozoite forms of <i>G. lamblia</i> in the stools (three tests) at two weeks. Technique: not mentioned Adverse effects.	
Notes		

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization without more information.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) Stools examination	Low risk	"fresh stool samples were examined microscopically for parasites by an examiner blinded"
Blinding of outcome assessment (detection bias) Other outcomes	High risk	"open label".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Stool test were not done in 12 children. However authors reported that symptoms disappeared. No specific information was

Bulut 1996 TUR (Continued)

		provided
Selective reporting (reporting bias)	Unclear risk	Symptoms outcomes are mentioned but not reported.
Other bias	Unclear risk	No information concerning baseline characteristics for each groups

Cañete 2012 CUB

Methods	Cuba. Duration: seven days.
Participants	150 participants (73 male); age: 18 to 38 years, mean 30 years Symptoms: were not specified. Asymptomatic: 0%. Inclusion criteria: adults (older than 18 years) with acute symptoms of giardiasis (with or without diarrhoea) and a positive stool examination report. No pregnant women were included Microscopic stools examination: cysts or trophozoites. Technique: "microscopic examination of fecal samples, as wet mounts and/or after Ritchie concentration" Exclusion criteria: (1) history of sensitivity to benzimidazole compounds or, (2) antiparasitic drugs in the preceding four weeks or, (3) diseases other than giardiasis or, (4) attending other clinical trial
Interventions	Rx 1. Albendazole: 400 mg single dose for five days (oral). Rx 2. Metronidazole: 250 mg three times daily for 5 five days (oral)
Outcomes	Stool samples from all cases were examined on the 3rd, 5th and 7th days following completion of treatment Adverse events: any reported.
Notes	Sample size calculation: "statistical power 80%, confidence level 95%, cure rate of alternative drug of 70% and 90% of efficacy for the drug applied to the control group ..."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"A random-number table was used to allocate each of these 150 adults ..."
Allocation concealment (selection bias)	Unclear risk	"a random table was developed to (blindly) identify with a number the drug to be administered to each participant, only disclosed at the end of the study"
Blinding of outcome assessment (detection bias) Stools examination	Low risk	"Neither investigators nor patients had information on the drug used throughout the study"

Blinding of outcome assessment (detection bias) Other outcomes	Unclear risk	“Neither investigators nor patients had information on the drug used throughout the study”. The frequency of administration of both drugs was different
Incomplete outcome data (attrition bias) All outcomes	Low risk	“All patients who began treatment completed the study period and were included in the statistical analysis”
Selective reporting (reporting bias)	Low risk	Apparently, all relevant outcomes were reported. Protocol was not available
Other bias	Low risk	No comments.

Chan Del Pino 1999 PER

Methods	Peru. No power calculation was done. Per protocol analysis. Duration: 3 weeks
Participants	<p>79 participants. The mean age was 7.83 ± 2.66 years. The mean weight was 24.06 ± 7.48 kg. 38% were preschool children. 67% were malnourished first degree. Clinical manifestations were abdominal pain (89.87%), diarrhoea (81.01%), hyporexia (70.88%), and abdominal distension (59.49%).</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Children infected with <i>G. lamblia</i> only. Confirmed by parasitological stool examinations. • Children, both sexes, aged three to 15 years of age. • Consent of parents or guardians of children. <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Children with malnutrition grade II or III. • Children who have received anti-giardial drugs in the past two months. • Children with acute febrile illness.
Interventions	<p>Rx 1. Tinidazole: 50 mg/kg/day, single dose (oral).</p> <p>Rx 2. Metronidazole: 15 mg/kg/day, three times daily for 10 days (oral)</p> <p>Rx 3. Albendazole: 400 mg/day for five days (oral).</p> <p>Rx 4. Furazolidone: 5mg/kg/day, every six hours, for 10 days</p> <p>Rx 5. Secnidazole: 30 mg/kg/day, single dose (oral).</p>
Outcomes	<p>Clinical signs and symptoms (cured, improvement, not cured, relapse)</p> <p>Parasitological (disappearance of cysts or trophozoites, reinfection, infection by other parasites). Coproparasitology examination: direct microscopy, using the technique of Willis. The samples were collected during the first seven days, and days 14 and 21</p> <p>Global efficacy (excellent: parasitological cured at 3 days; Good: parasitological cured between three and seven days; moderate: parasitological cured after seven days; bad: parasite presence)</p> <p>Tolerance (excellent: no adverse events; good: one mild adverse event with no discontinuation; etc)</p>
Notes	

Chan Del Pino 1999 PER (Continued)

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table.
Allocation concealment (selection bias)	High risk	First, children were randomized to 5 groups and drug subsequently randomized to these groups. 16 children were subsequently excluded after being randomized
Blinding of outcome assessment (detection bias) Stools examination	High risk	"We performed a prospective, longitudinal, comparative, open and randomised study . . ."
Blinding of outcome assessment (detection bias) Other outcomes	High risk	"We performed a prospective, longitudinal, comparative, open and randomised study . . ."
Incomplete outcome data (attrition bias) All outcomes	Low risk	No significant differences in loss to follow up.
Selective reporting (reporting bias)	Low risk	The study report include expected outcomes, including those that were pre-specified
Other bias	High risk	Raw water intake was higher in the groups of children assigned to albendazole and secnidazole

Dutta 1994 IND

Methods	India (multicentre study). No power calculation made. Intention to treat analysis. Duration: 21 days
Participants	150 hospitalised participants (79 males), from two to 10 years old. Diarrhea, abdominal pain and anorexia were the main presenting symptoms Inclusion criteria: children (two to 10 years) with proven giardia infection (trophozoites and/or cyst of <i>G lamblia</i> in stool specimens). Exclusion criteria: "... acute febrile conditions, chronic diarrhoea, severe malnutrition or receiving long term therapy". Treatment of <i>Giardia</i> or intestinal helminthic infection in the previous seven days
Interventions	Rx 1. Albendazole: 400 mg/d, single dose, for five days (oral suspension) Rx 2. Metronidazole: 7.5mg/kg three times daily (22.5 mg/kg/day) for five days (oral suspension)

Dutta 1994 IND (Continued)

Outcomes	Clinical assessment and stools were repeated on days one to seven, 14 and 21 post-treatment. Stool samples were examined microscopically (direct smear and formal ether concentration tests) Hematological and biochemical parameters on the 7th and 14th day after treatment Reported side-effects.
Notes	This study has a similar methodology to the Misra 1995 IND study, but different patients (different hospitals).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated.
Allocation concealment (selection bias)	Unclear risk	"eligible children were randomised according to pre-determined lists at each site"
Blinding of outcome assessment (detection bias) Stools examination	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Other outcomes	High risk	"Patient's response to therapy and severity of side-effects were recorded by a co-investigator who was unaware of the treatment given to the patient". However, patients were probably aware about treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data.
Selective reporting (reporting bias)	Unclear risk	No mention of a systematic strategy for collecting side effects
Other bias	Low risk	No comments.

Fallah 2007 IRN

Methods	Iran. No power calculation made. Intention to treat analysis. Duration: three weeks
Participants	106 participants (69 males). Children, 75% of them were less than 12 years old "... from public and private health centres ...". There is no any specification about symptoms Inclusion criteria: <i>Giardia intestinalis</i> -positive children. Exclusion criteria: not mentioned.

Interventions	Rx 1. Tinidazole: 50 mg/kg, maximum 2 g, once a day, single dose (tablets) Rx 2. Metronidazole: 15 mg/kg/day, three times daily for seven days (suspension)	
Outcomes	Clinical and parasitological follow-up was carried out before, and at 7, 14, 21 days after treatment Parasitological cure was documented when there were three consecutive negative stool examination for <i>G. intestinalis</i> at 1-3 weeks after therapy termination. Stool examination was done by formalin ether concentration technique Duration of symptoms of patients.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“were randomly allocated to two groups”.
Allocation concealment (selection bias)	High risk	“a randomised, open-label, clinical trial”.
Blinding of outcome assessment (detection bias) Stools examination	High risk	“a randomised, open-label, clinical trial”.
Blinding of outcome assessment (detection bias) Other outcomes	High risk	“a randomised, open-label, clinical trial”.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data.
Selective reporting (reporting bias)	Unclear risk	“Clinical and parasitological follow-up was carried out ...”. However, in the outcomes there is no mention about any clinical improvement
Other bias	Unclear risk	No baseline comparison.

Gascon 1989 ESP

Methods	Spain. No power calculation made. Intention to treat analysis. Duration: 30 days
Participants	23 adults; 17 male; Age was not specified. All symptomatic (information provided by author) Microscopic stools examination: "harbouring <i>G. lamblia</i> ". Technique: not mentioned. Exclusion criteria: not mentioned.

Gascon 1989 ESP (Continued)

Interventions	Rx 1. Mebendazole 200 mg three times daily for one day. Rx 2: Metronidazole 250 mg every 8 h for seven days.	
Outcomes	Parasitological cure: faecal specimens were examined on days three and seven after treatment, and finally one month later. Technique: not mentioned	
Notes	11 patients included from a travellers' clinic. The infections were acquired in Africa (4) , Asia (3), Latin America (4) 4 patients were from an acquired immune deficiency syndrome (AIDS) clinic	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"They were all given a random number".
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Stools examination	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Other outcomes	Unclear risk	Not mentioned.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The authors do not specifically mention that there were no losses to follow-up
Selective reporting (reporting bias)	High risk	Symptoms outcomes are mentioned but not reported.
Other bias	Unclear risk	No information concerning baseline characteristics for each groups

Gascón 1990 ESP

Methods	Spain. No power calculation made. Intention to treat analysis. Duration: 30 days	
Participants	19 participants (10 M); mean age: 29 ± 12 years; 16 adults. All symptomatic (information provided by author) Microscopic stools examination: "excreting cysts of <i>G. lamblia</i> in their stools". Technique: not mentioned. Exclusion criteria: not mentioned.	

Gascón 1990 ESP (Continued)

Interventions	Rx 1. Mebendazole 200 mg three times daily for five days. Rx 2: Metronidazole 250 mg every 8 h for seven days.	
Outcomes	Parasitological cure: faecal specimens were examined on days three, seven, and 30 after treatment. Technique: not mentioned No mention of adverse events.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"They, were all given a random number..."
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Stools examination	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Other outcomes	Unclear risk	Not mentioned.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The authors do not specifically mention that there were no losses to follow-up
Selective reporting (reporting bias)	High risk	No mention of symptoms or adverse events.
Other bias	Unclear risk	No information concerning baseline characteristics for each groups

Hall 1993 IND

Methods	India. No power calculation made. Per protocol analysis. Duration: 15 days	
Participants	Children between 5 and 10 years old. Confirmed presence of <i>Giardia</i> cysts or trophozoites in faeces. 426 children (222 in the first phase, and 204 in the second phase) There is not any specification about symptoms. Exclusion criteria: not mentioned.	
Interventions	Phase 1: Rx 1. Albendazole: 600 mg single dose (chewable tablets). Rx 2. Albendazole: 400 mg single dose, for three days (chewable tablets) Rx 3. Metronidazole: 125 mg three times daily (375 mg/d) for five days (oral)	

	Phase 2: Rx 4. Albendazole: 800 mg single dose (chewable tablets). Rx 5. Albendazole: 400 mg single dose, for five days (chewable tablets) Rx 6. Metronidazole: 125 mg three times daily (375 mg/d) for five days (oral)
Outcomes	Direct microscopy of faeces in saline. Three stools samples collected from each child over a period of 10 days after treatment Cure: Stool negative for <i>G. lamblia</i> . Adverse events.
Notes	This study took into account as the unit of analysis "infections" (one child could participate more than once). However, also considered as the unit of analysis "children in their first (and / or unique) infection". For this systematic review, we consider data from the first Infection of children Similarly, for this systematic review, we consider treatments Rx 5 and Rx 6. Since this scheme albendazole is used more frequently, and it was the best response rate in this study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"A list of the numbers 1, 2 and 3 was randomly generated by a computer program"
Allocation concealment (selection bias)	Low risk	"... sealed in serially numbered envelopes by someone not concerned with treatment. The envelopes were opened in the field by the project physician, case by case, ..."
Blinding of outcome assessment (detection bias) Stools examination	Low risk	"... each of the 3 stool samples collected after treatment was identified only by a unique serial number when examined microscopically, ..."
Blinding of outcome assessment (detection bias) Other outcomes	High risk	"Because of the very different drug regimens being used in the investigation, a double-blind study was considered impracticable."
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data.
Selective reporting (reporting bias)	High risk	The outcomes of adverse events were incompletely reported. Adverse events were not specified for each treatment group
Other bias	Unclear risk	No baseline comparison.

Kalayci 1995 TUR

Methods	Turkey. No power calculation made. Intention to treat analysis. Duration: 10 days	
Participants	45 children; ages 34 months to 16 years. All symptomatic. Symptoms: abdominal cramps (82%), vomiting (27%), greasy stools (24%), flatulence (18%), weight loss (18%), and anorexia (67%). The children had these complaints for 45 to 120 days (mean 86 days) Microscopic stools examination: “.. within one hour after being passed for both cysts and trophozoites of <i>G. lamblia</i> ”. <i>G. lamblia</i> cysts were seen in all cases and trophozoites in 14 cases. Technique: not mentioned Exclusion criteria: children with a history of any treatment for giardiasis	
Interventions	Rx 1. Mebendazole 200 three times daily for 10 days (oral). Rx 2. Metronidazole 5mg/kg three times daily for 10 days. Rx 3. Furazolidone 2mg/kg four times daily for 10 days.	
Outcomes	Clinical monitoring and three fecal specimens were re-examined (technique not mentioned.) for 7 to 10 days after treatment Side-effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“.. and chosen randomly to receive..”
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Stools examination	Low risk	“.. by investigators who were unaware of the drugs used or the results of the treatment”
Blinding of outcome assessment (detection bias) Other outcomes	Unclear risk	Not mentioned.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no losses to follow-up.
Selective reporting (reporting bias)	Low risk	All outcomes were included in the analyses.
Other bias	Low risk	No comments.

Karabay 2004 TUR

Methods	Turkey. No power calculation made. Per protocol analysis. Duration: 15 days
Participants	Adults with diarrhoea at the outpatient clinic of the Department of Infectious Diseases of Social Security Hospital in Turkey: 67 patients (29 male) Inclusion criteria: adults with diarrhoea (more than four times of unformed stools per day) and <i>G intestinalis</i> cyst or trophozoites (direct faecal microscopic examination) Exclusion criteria: antiparasitic drugs during the 10 days prior to beginning the study; fever, pregnant women, mothers who were breast feeding, known hypersensitivity to either treatments, patients for whom any of the treatments used in the study were contraindicated
Interventions	Rx 1. Albendazole: 400 mg/day single dose, for five days (oral) Rx 2. Metronidazole: 500 mg three times daily (1500 mg/d), for five days (oral)
Outcomes	Clinical response and parasitological response with 2 stool samples between days 7 and 15 after initiation of treatment (direct faecal microscopic examination) Noncompliance: failure to attend the controls, or inappropriate use of medications (dose, duration) After starting treatment, healing of symptoms in hours. Side effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization without more information.
Allocation concealment (selection bias)	High risk	"An open randomised clinical study".
Blinding of outcome assessment (detection bias) Stools examination	High risk	"An open randomised clinical study".
Blinding of outcome assessment (detection bias) Other outcomes	High risk	"An open randomised clinical study".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data balanced in numbers across intervention groups (with similar reasons)
Selective reporting (reporting bias)	Unclear risk	In the methods section, the authors do not describe all outcomes that subsequently reported in results section
Other bias	Low risk	No comments.

Misra 1995 IND

Methods	India. No power calculation made. Per protocol analysis. Duration: 21 days
Participants	64 hospitalised participants (38 males), from twp to 10 years old; Diarrhea, abdominal pain, anorexia, nausea, and vomiting were the more frequent symptoms Inclusion criteria: Children (twp to 12 years) with proven <i>Giardia</i> infection (trophozoites and/or cyst of <i>G lamblia</i> in stool specimens). Exclusion criteria: "... acute febrile conditions, chronic diarrhoea, severe malnutrition or receiving long term therapy". Treatment of <i>Giardia</i> or intestinal helminthic infection in the previous seven days
Interventions	Rx 1. Albendazole: 400 mg/d, single dose, for five days (oral suspension) Rx 2. Metronidazole: 7.5mg/kg three times daily (22.5 mg/kg/day), for five days (oral suspension)
Outcomes	Clinical assessment and stools were repeated on days one to seven, 14 and 21 post-treatment. Stool samples were examined microscopically (direct smear and formal ether concentration tests) Hematological and biochemical parameters on the 7th and 14th day after treatment Reported side-effects.
Notes	More severe presenting symptoms (abdominal pain, vomiting and watery stools) in children in the group treated with metronidazole This study has a similar methodology to the Dutta 1994 IND study, but different patients (different hospitals).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"An open randomised parallel..."
Allocation concealment (selection bias)	High risk	"An open ..."
Blinding of outcome assessment (detection bias) Stools examination	High risk	"An open ..."
Blinding of outcome assessment (detection bias) Other outcomes	High risk	"An open ..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	The losses were distributed similarly in both groups. "All these children had responded to the therapy and parents did not want the children to be hospitalised any further"

Selective reporting (reporting bias)	Unclear risk	No results were reported hematological and biochemical variables. The report mentions that there were no significant differences in these variables
Other bias	High risk	More severe presenting symptoms (abdominal pain, vomiting and watery stools) in children in the group treated with metronidazole

Ortiz 2001 PER

Methods	Peru. Intention to treat and per protocol analysis. Duration: 14 days
Participants	110 (54 males); ages two to 11 years, mean of age 5.67 (± 2.56). All symptomatic Symptoms: duration of diarrhoea: 2 to 154 days. Pain, distension, and/or tenderness in 32.7%. Diarrhea was defined as more than three unformed stools per day or unformed stools without increased stool frequency for more than four weeks Enzyme immunoassay (Triage Parasite Panel, Biosite Diagnostic, San Diego, California) for <i>G. lamblia</i> , <i>Entamoeba histolytica</i> or <i>Cryptosporidium parvum</i> . Positive results for <i>G. lamblia</i> were confirmed using a direct examination and a Ritchie concentration technique Exclusion criteria: children with positive enzyme immunoassay of faecal samples for <i>E. histolytica</i> or <i>C. parvum</i> ; children using any drug with antiprotozoal activity within two weeks of enrolment; children known to have or suspected of having AIDS were excluded from the study; patients with positive coprocultures for bacterial causes of diarrhoea were excluded from the analysis of clinical response
Interventions	Rx 1. Nitazoxanide: 5 mL (ages 2 to 3 years) or 10 mL (ages four to 11 years) of nitazoxanide (100 mg per 5 mL) strawberry-flavoured oral suspension, BID for three days Rx 2: Metronidazole: 5 mL of 125 mg per 5 mL (ages two to five years) or 250 mg per 5 mL (ages six to 11 years) of metronidazole suspension BID for five days
Outcomes	Clinical response (at the day 7 follow-up): "well" (no symptoms, no watery stools and no more than two soft stools, and has no hematochezia within the past 24 h or no symptoms and no unformed stools within the past 48 h); or "continuing illness" (any number of watery stools, more than two soft stools per 24 h, or hematochezia or enteric symptoms plus the passage of any number of soft or watery stools during the past 48 h); or "clinical treatment failure" (clinical deterioration or worsening of symptoms after at least 24 h of treatment resulting in the patients being removed from the study) Parasitological response: "eradicated" (no cysts observed in either post-treatment stool sample); or "persistence" (cysts observed in either or both post-treatment stool samples). Two stool samples were collected on consecutive days between day 7 and 10, following the initiation of treatment for evaluation of parasitological response. Stool samples collected at follow-up were examined for <i>G. lamblia</i> using a direct examination and a Ritchie concentration technique

Ortiz 2001 PER (Continued)

Notes	Sample size calculation: For the two treatment groups (n 55) (80% of power; 20% in risk differences)	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“Computer-generated randomisation list”.
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Stools examination	Low risk	“parasitologist conducting the stool examinations was blinded to the patients treatment group assignment”
Blinding of outcome assessment (detection bias) Other outcomes	Unclear risk	Not mentioned.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow up were reported.
Selective reporting (reporting bias)	Low risk	All outcomes were included in the analyses.
Other bias	Low risk	No comments.

Perez-Choliz 1989 ESP

Methods	Spain. No power calculation made. Per protocol analysis. Duration: 1 month
Participants	52 children (30 male) with parasitological diagnosis of giardiasis (paediatric outpatient). The mean age was 7.62 ± 3.23 (1.4 to 14.1 years) There is not any specification about baseline symptoms, they were presumably 100% symptomatic Exclusion criteria: Not mentioned.
Interventions	Rx 1. Tinidazole: 50 mg/kg, maximum 1.5g, single dose (oral). During or after a main meal Rx 2. Metronidazole: 20-25 mg/kg/d, max 0.5 g per day (oral). Three cycles of eight days with seven days between them
Outcomes	Examination of four stool samples, one month after treatment ends. The study does not specify the technique of stool examination Parasitological cure: stool negative for <i>G. lamblia</i> . Symptoms collected in unsystematically through medical charts Side effects: questioning the patient and family, especially: headache, allergic reactions or any gastrointestinal symptoms

Notes	The study provides no explanation for the loss to follow up.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"The allocation was set so random and alternating with tinidazole and metronidazole"
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Stools examination	Unclear risk	"Randomized, double blind trial". Not specified. Both treatments are different in terms of duration of therapy
Blinding of outcome assessment (detection bias) Other outcomes	Unclear risk	"Randomized, double blind trial". Not specified. Both treatments are different in terms of duration of therapy
Incomplete outcome data (attrition bias) All outcomes	High risk	Two losses to follow up in tinidazole group, and nine in the metronidazole group
Selective reporting (reporting bias)	Unclear risk	Symptoms collected in unsystematically through medical charts
Other bias	Unclear risk	No baseline comparison.

Rodríguez 1996 MEX

Methods	Mexico. No power calculation made. Intention to treat analysis. Duration: three weeks
Participants	<p>49 participants (25 males). Ages 3 to 12 years.</p> <p>The main clinical manifestations were abdominal pain (65%), diarrhoea (35%), and hyporexia (49%). 8% of children were asymptomatic.</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Children between three and 12 years old • Children infected with <i>G. lamblia</i>. Confirmed by parasitological stool examinations (Faust's technique). • Consent of parents or guardians of children. <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Children who have received anti-giardial drugs in the past three months.
Interventions	<p>Rx 1. Albendazole: 200 mg three times daily for 5 days (oral)</p> <p>Rx 2. Metronidazole: 30 mg/kg/day, three times daily, for 5 days (oral)</p>

Rodríguez 1996 MEX (Continued)

Outcomes	Parasitological (disappearance of cysts or trophozoites). Coproparasitology examination: direct microscopy, using the technique of Faust. The samples were collected on days 14 and 21, and he/she was considered cured if both samples were negative Reported side-effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“Two groups were formed randomly”.
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Stools examination	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Other outcomes	Unclear risk	Not mentioned.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no losses to follow-up.
Selective reporting (reporting bias)	Unclear risk	No mention of a systematic strategy for collecting side effects
Other bias	High risk	There are differences in baseline characteristics of both groups. For example, preschool children were 51% in the albendazole group and 40% for metronidazole arm. Similarly, 74% of the children complained of abdominal pain in the albendazole group and 54% did so in the metronidazole group

Romero-Cabello 1995 MEX

Methods	Mexico. No power calculation made. Intention to treat analysis. Duration: 21 days
Participants	100 participants (49 males), from four to 11 years old (median: eight years old); symptoms (93%): 42% abdominal pain, 39% hyporexia, 8% diarrhoea, 2% nausea, and 2% debility Inclusion criteria: children infected with <i>G. lamblia</i> . Stool samples were examined microscopically.

Romero-Cabello 1995 MEX (Continued)

	Exclusion criteria: any drug with antiprotozoal activity in the last two months; or another class of treatment in children with denutrition II or III grade	
Interventions	Rx 1. Albendazole: 400 mg/day single dose, for five days (oral) Rx 2. Metronidazole: 7.5 mg/kg three times daily, for five days (oral)	
Outcomes	Parasitological cure: absence of the cystic or trophozoite form of <i>G. lamblia</i> in the stools. Stools were repeated on days one to seven, 14, and 21 after beginning the treatment. Direct microscopy (three successive days) Clinical response at one to seven days after beginning of treatment. Time to recovery Side-effects: on days one to seven, 14, and 21. Cell blood count and blood chemistry after treatment.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated.
Allocation concealment (selection bias)	Unclear risk	“using an aleatory code A and B”.
Blinding of outcome assessment (detection bias) Stools examination	High risk	“Open label”.
Blinding of outcome assessment (detection bias) Other outcomes	High risk	“Open label”.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No reported losses to follow up.
Selective reporting (reporting bias)	Low risk	Apparently, all outcomes were reported.
Other bias	Low risk	No comments.

Yereli 2004 TUR

Methods	Turkey. No power calculation made. Intention to treat analysis. Duration: 21 days (14 days after completing treatment)
Participants	107 children, from three to 15 years old; Symptoms (gastrointestinal complaints, diarrhoea, weight loss, anorexia, and fatigue) and <i>G. lamblia</i> cysts and or trophozoites in stools. Stool samples were assessed for giardiasis by the saline-Lugol, formalin ethyl acetate

	concentration, and trichrome staining methods Exclusion criteria: not mentioned.	
Interventions	Rx 1. Albendazole: 10 mg/kg/day, single dose, for five days (tablets) Rx 2. Metronidazole: 20 mg/kg/day, three times daily, for seven days (tablet or liquid)	
Outcomes	Stool samples from all cases were examined on the 7th, 10th and 14th days following completion of treatment Clinical symptoms: the method was not specified. Side-effects: the method was not specified.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“was divided into two random groups”.
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Stools examination	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) Other outcomes	High risk	No masking of drugs.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No withdrawals or loss to follow up.
Selective reporting (reporting bias)	High risk	Symptoms were not adequately reported.
Other bias	Low risk	No comments.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Bakshi 1978	It is not a randomized clinical trial. Meta-analysis of clinical trials in India
Baqai 2001	No randomization.
Bassily 1987	It is not a randomized clinical trial.

(Continued)

Besirbellioglu 2006	This study included two groups treated with metronidazole plus <i>Saccharomyces boulardii</i> .
Botero 1974	The study was presented in a congress. No data available.
Gazder 1978	This study compared single dose of metronidazole against single dose of tinidazole
Grant 2001	This study included two groups treated with metronidazole plus wheat germ, or placebo
Guerrero 2000	Authors were contacted. The study was presented in a congress, data were not provided
Jokipii 1978	It is not a randomized clinical trial.
Jokipii 1979	It is not a randomized clinical trial.
Krishnamurthy 1978	This study compared single dose of metronidazole against single dose of tinidazole
Kyrönseppä 1981	This study compared treatment with single dose tinidazole, against treatment with metronidazole for two days
Leary 1974	This study compared treatment with metronidazole for one day, against treatment with metronidazole for two days
Levi 1977	It is not a randomized clinical trial.
Morrone 2004	It is not a randomized clinical trial.
Nigam 1991	This study compared single dose of metronidazole against single dose of tinidazole
Sabchareon 1980	It is not a randomized clinical trial.
Sadjjadi 2001	Asymptomatic children.
Speelman 1985	This study compared single dose tinidazole against single dose metronidazole, and another arm with metronidazole for three days
Suntornpoch 1981	It is not a randomized clinical trial.

DATA AND ANALYSES

Comparison 1. Albendazole (once daily) versus metronidazole (three times daily)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parasitological cure (at 1 to 3 weeks)	10	932	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.95, 1.03]
2 Time to achieve parasitological cure (hours)	1	57	Mean Difference (IV, Fixed, 95% CI)	-19.0 [-34.72, -3.28]
3 Clinical improvement (at 2 to 3 weeks)	5	483	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.93, 1.04]
4 Time of symptomatic improvement (hours)	2	97	Mean Difference (IV, Fixed, 95% CI)	-5.69 [-22.10, 10.73]
5 Other adverse events (gastrointestinal at 1 to 3 weeks)	8	717	Risk Ratio (M-H, Random, 95% CI)	0.29 [0.13, 0.63]
6 Other adverse events (neurological at 1 to 3 weeks)	5	453	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.18, 0.64]
7 Other adverse events (metallic taste at 3 weeks)	3	327	Risk Ratio (M-H, Fixed, 95% CI)	0.03 [0.01, 0.13]
8 Other adverse events (allergic/cutaneous at 3 weeks)	2	154	Risk Ratio (M-H, Fixed, 95% CI)	0.2 [0.01, 4.08]
9 Other adverse events (fever at 3 weeks)	1	34	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.23, 4.27]
10 Other adverse events (transient elevation of liver enzymes at 3 weeks)	1	150	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.06, 15.69]
11 Other adverse (transient neutropenia at 3 weeks)	1	150	Risk Ratio (M-H, Fixed, 95% CI)	5.0 [0.24, 102.42]
12 Non-compliance to treatment (at 2 weeks)	1	57	Risk Ratio (M-H, Fixed, 95% CI)	0.74 [0.27, 2.06]

Comparison 2. Mebendazole (three times daily) versus metronidazole (three times daily)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parasitological cure (at 1 to 2 weeks)	5	142	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.32, 1.06]
1.1 Children	3	100	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.62, 1.17]
1.2 Children and adults	2	42	Risk Ratio (M-H, Random, 95% CI)	0.15 [0.05, 0.44]
2 Other adverse events (nausea/vomiting at 1 to 2 weeks)	3	100	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.05, 1.90]

3 Other adverse events (headache at 1 to 2 weeks)	2	74	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.03, 2.06]
4 Other adverse events (urticaria at 1 to 2 weeks)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 3. Tinidazole (single dose) versus metronidazole (three times daily)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parasitological cure (at 3 weeks to 1 month)	3	179	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.87, 1.73]
2 Clinical improvement (at 3 weeks to 1 month)	3	179	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [1.06, 1.36]
3 Other adverse events (gastrointestinal at 3 weeks to 1 month)	3	179	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.21, 1.62]
4 Other adverse events (neurological at 3 weeks to 1 month)	2	138	Risk Ratio (M-H, Fixed, 95% CI)	1.30 [0.29, 5.92]
5 Other adverse events (allergic/cutaneous at 3 weeks to 1 month)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6 Other adverse events (fever at 3 weeks to 1 month)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
7 Serious adverse events (at 3 weeks to 1 month)	3	179	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 4. Metronidazole (single dose) versus metronidazole (three times daily)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parasitological cure (at 2 weeks)	1	54	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.93, 1.08]
2 Other adverse events (gastrointestinal at 2 weeks)	1	54	Risk Ratio (M-H, Fixed, 95% CI)	2.70 [0.26, 27.96]
3 Serious adverse events (at 2 weeks)	1	54	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 5. Nitazoxanide (twice daily) versus metronidazole (twice daily)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parasitological cure (at 1 week)	1	110	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.76, 1.20]
2 Reduction in symptoms of diarrhea (at 1 week)	1	110	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.90, 1.27]
3 Other adverse events (at 1 week)	1	110	Risk Ratio (M-H, Fixed, 95% CI)	1.1 [0.51, 2.38]
4 Other adverse events (abdominal pain at 1 week)	1	110	Risk Ratio (M-H, Fixed, 95% CI)	1.67 [0.65, 4.27]
5 Other adverse events (nausea/vomiting at 1 week)	1	110	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 8.01]
6 Other adverse events (headache at 1 week)	1	110	Risk Ratio (M-H, Fixed, 95% CI)	0.14 [0.01, 2.70]

Analysis 1.1. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 1 Parasitological cure (at 1 to 3 weeks).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 1 Parasitological cure (at 1 to 3 weeks)

Analysis 1.2. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 2 Time to achieve parasitological cure (hours).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 2 Time to achieve parasitological cure (hours)

Analysis 1.3. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 3 Clinical improvement (at 2 to 3 weeks).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 3 Clinical improvement (at 2 to 3 weeks)

Analysis 1.4. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 4 Time of symptomatic improvement (hours).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 4 Time of symptomatic improvement (hours)

Analysis 1.5. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 5 Other adverse events (gastrointestinal at 1 to 3 weeks).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 5 Other adverse events (gastrointestinal at 1 to 3 weeks)

Analysis 1.6. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 6 Other adverse events (neurological at 1 to 3 weeks).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 6 Other adverse events (neurological at 1 to 3 weeks)

Analysis 1.7. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 7 Other adverse events (metallic taste at 3 weeks).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 7 Other adverse events (metallic taste at 3 weeks)

Analysis 1.8. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 8 Other adverse events (allergic/cutaneous at 3 weeks).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 8 Other adverse events (allergic/cutaneous at 3 weeks)

Analysis 1.9. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 9 Other adverse events (fever at 3 weeks).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 9 Other adverse events (fever at 3 weeks)

Analysis 1.10. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 10 Other adverse events (transient elevation of liver enzymes at 3 weeks).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 10 Other adverse events (transient elevation of liver enzymes at 3 weeks)

Analysis 1.11. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 11 Other adverse (transient neutropenia at 3 weeks).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 11 Other adverse (transient neutropenia at 3 weeks)

Analysis 1.12. Comparison 1 Albendazole (once daily) versus metronidazole (three times daily), Outcome 12 Non-compliance to treatment (at 2 weeks).

Review: Drugs for treating giardiasis

Comparison: 1 Albendazole (once daily) versus metronidazole (three times daily)

Outcome: 12 Non-compliance to treatment (at 2 weeks)

Analysis 2.1. Comparison 2 Mebendazole (three times daily) versus metronidazole (three times daily), Outcome 1 Parasitological cure (at 1 to 2 weeks).

Review: Drugs for treating giardiasis

Comparison: 2 Mebendazole (three times daily) versus metronidazole (three times daily)

Outcome: 1 Parasitological cure (at 1 to 2 weeks)

Analysis 2.2. Comparison 2 Mebendazole (three times daily) versus metronidazole (three times daily), Outcome 2 Other adverse events (nausea/vomiting at 1 to 2 weeks).

Review: Drugs for treating giardiasis

Comparison: 2 Mebendazole (three times daily) versus metronidazole (three times daily)

Outcome: 2 Other adverse events (nausea/vomiting at 1 to 2 weeks)

Analysis 2.3. Comparison 2 Mebendazole (three times daily) versus metronidazole (three times daily), Outcome 3 Other adverse events (headache at 1 to 2 weeks).

Review: Drugs for treating giardiasis

Comparison: 2 Mebendazole (three times daily) versus metronidazole (three times daily)

Outcome: 3 Other adverse events (headache at 1 to 2 weeks)

Analysis 2.4. Comparison 2 Mebendazole (three times daily) versus metronidazole (three times daily), Outcome 4 Other adverse events (urticaria at 1 to 2 weeks).

Review: Drugs for treating giardiasis

Comparison: 2 Mebendazole (three times daily) versus metronidazole (three times daily)

Outcome: 4 Other adverse events (urticaria at 1 to 2 weeks)

Analysis 3.1. Comparison 3 Tinidazole (single dose) versus metronidazole (three times daily), Outcome 1 Parasitological cure (at 3 weeks to 1 month).

Review: Drugs for treating giardiasis

Comparison: 3 Tinidazole (single dose) versus metronidazole (three times daily)

Outcome: 1 Parasitological cure (at 3 weeks to 1 month)

Analysis 3.2. Comparison 3 Tinidazole (single dose) versus metronidazole (three times daily), Outcome 2 Clinical improvement (at 3 weeks to 1 month).

Review: Drugs for treating giardiasis

Comparison: 3 Tinidazole (single dose) versus metronidazole (three times daily)

Outcome: 2 Clinical improvement (at 3 weeks to 1 month)

Analysis 3.3. Comparison 3 Tinidazole (single dose) versus metronidazole (three times daily), Outcome 3 Other adverse events (gastrointestinal at 3 weeks to 1 month).

Review: Drugs for treating giardiasis

Comparison: 3 Tinidazole (single dose) versus metronidazole (three times daily)

Outcome: 3 Other adverse events (gastrointestinal at 3 weeks to 1 month)

Analysis 3.4. Comparison 3 Tinidazole (single dose) versus metronidazole (three times daily), Outcome 4 Other adverse events (neurological at 3 weeks to 1 month).

Review: Drugs for treating giardiasis

Comparison: 3 Tinidazole (single dose) versus metronidazole (three times daily)

Outcome: 4 Other adverse events (neurological at 3 weeks to 1 month)

Analysis 3.5. Comparison 3 Tinidazole (single dose) versus metronidazole (three times daily), Outcome 5 Other adverse events (allergic/cutaneous at 3 weeks to 1 month).

Review: Drugs for treating giardiasis

Comparison: 3 Tinidazole (single dose) versus metronidazole (three times daily)

Outcome: 5 Other adverse events (allergic/cutaneous at 3 weeks to 1 month)

Analysis 3.6. Comparison 3 Tinidazole (single dose) versus metronidazole (three times daily), Outcome 6 Other adverse events (fever at 3 weeks to 1 month).

Review: Drugs for treating giardiasis

Comparison: 3 Tinidazole (single dose) versus metronidazole (three times daily)

Outcome: 6 Other adverse events (fever at 3 weeks to 1 month)

Analysis 3.7. Comparison 3 Tinidazole (single dose) versus metronidazole (three times daily), Outcome 7 Serious adverse events (at 3 weeks to 1 month).

Review: Drugs for treating giardiasis

Comparison: 3 Tinidazole (single dose) versus metronidazole (three times daily)

Outcome: 7 Serious adverse events (at 3 weeks to 1 month)

Analysis 4.1. Comparison 4 Metronidazole (single dose) versus metronidazole (three times daily), Outcome 1 Parasitological cure (at 2 weeks).

Review: Drugs for treating giardiasis

Comparison: 4 Metronidazole (single dose) versus metronidazole (three times daily)

Outcome: 1 Parasitological cure (at 2 weeks)

Analysis 4.2. Comparison 4 Metronidazole (single dose) versus metronidazole (three times daily), Outcome 2 Other adverse events (gastrointestinal at 2 weeks).

Review: Drugs for treating giardiasis

Comparison: 4 Metronidazole (single dose) versus metronidazole (three times daily)

Outcome: 2 Other adverse events (gastrointestinal at 2 weeks)

Analysis 4.3. Comparison 4 Metronidazole (single dose) versus metronidazole (three times daily), Outcome 3 Serious adverse events (at 2 weeks).

Review: Drugs for treating giardiasis

Comparison: 4 Metronidazole (single dose) versus metronidazole (three times daily)

Outcome: 3 Serious adverse events (at 2 weeks)

Analysis 5.1. Comparison 5 Nitazoxanide (twice daily) versus metronidazole (twice daily), Outcome 1 Parasitological cure (at 1 week).

Review: Drugs for treating giardiasis

Comparison: 5 Nitazoxanide (twice daily) versus metronidazole (twice daily)

Outcome: 1 Parasitological cure (at 1 week)

Analysis 5.2. Comparison 5 Nitazoxanide (twice daily) versus metronidazole (twice daily), Outcome 2 Reduction in symptoms of diarrhea (at 1 week).

Review: Drugs for treating giardiasis

Comparison: 5 Nitazoxanide (twice daily) versus metronidazole (twice daily)

Outcome: 2 Reduction in symptoms of diarrhea (at 1 week)

Analysis 5.3. Comparison 5 Nitazoxanide (twice daily) versus metronidazole (twice daily), Outcome 3 Other adverse events (at 1 week).

Review: Drugs for treating giardiasis

Comparison: 5 Nitazoxanide (twice daily) versus metronidazole (twice daily)

Outcome: 3 Other adverse events (at 1 week)

Analysis 5.4. Comparison 5 Nitazoxanide (twice daily) versus metronidazole (twice daily), Outcome 4 Other adverse events (abdominal pain at 1 week).

Review: Drugs for treating giardiasis

Comparison: 5 Nitazoxanide (twice daily) versus metronidazole (twice daily)

Outcome: 4 Other adverse events (abdominal pain at 1 week)

Analysis 5.5. Comparison 5 Nitazoxanide (twice daily) versus metronidazole (twice daily), Outcome 5 Other adverse events (nausea/vomiting at 1 week).

Review: Drugs for treating giardiasis

Comparison: 5 Nitazoxanide (twice daily) versus metronidazole (twice daily)

Outcome: 5 Other adverse events (nausea/vomiting at 1 week)

Analysis 5.6. Comparison 5 Nitazoxanide (twice daily) versus metronidazole (twice daily), Outcome 6 Other adverse events (headache at 1 week).

Review: Drugs for treating giardiasis

Comparison: 5 Nitazoxanide (twice daily) versus metronidazole (twice daily)

Outcome: 6 Other adverse events (headache at 1 week)

APPENDICES

Appendix I. Search methods: detailed search strategies

Search set	CIDG SR ^a	CENTRAL	MEDLINE ^b	EMBASE ^b	LILACS ^b
1	Giardia lamblia	GIARDIA LAMBLIA	GIARDIA LAMBLIA	GIARDIA-LAMBLIA	GIARDIA LAMBLIA
2	giardiasis	GIARDIASIS	GIARDIASIS	GIARDIASIS	GIARDIASIS
3	1 or 2	1 OR 2	1 OR 2	1 OR 2	1 OR 2
4	-	-	CARBAMATES	CARBAMIC-ACID DERIVATIVE	CARBAMATES
5	-	-	BENZIMIDAZOLES	BENZIMIDAZOLE- DERIVATIVE	BENZIMIDAZOLES
6	-	-	NITROIMIDA- ZOLES	NITROIMIDA- ZOLE-DERIVATIVE	NITROIMIDA- ZOLES

(Continued)

7	-	-	IMIDAZOLES	IMIDAZOLE-DERIVATIVE	IMIDAZOLES
8	-	-	ANTITRI-CHOMONAL AGENTS	ANTITRI-CHOMONAL AGENT	ANTITRI-CHOMONAL AGENTS
9	-	-	albendazole	albendazole	albendazole
10	-	-	metronidazole	metronidazole	metronidazole
11	-	-	mebendazole	mebendazole	mebendazole
12	-	-	tinidazole	tinidazole	tinidazole
13	-	-	nitazoxanide	nitazoxanide	nitazoxanide
14	-	-	4-13/OR	4-13/OR	4-13/OR
15	-	-	3 AND 14	3 AND 14	3 AND 14
16	-	-	Limit 15 to humans	Limit 15 to humans	-

^aCochrane Infectious Diseases Group Specialized Register.

^bSearch terms used in combination with the search strategy for retrieving trials developed by The Cochrane Collaboration ([Lefebvre 2008](#)); upper case: MeSH or EMTREE heading; lower case: free text term.

CONTRIBUTIONS OF AUTHORS

Carlos Granados conceived the review question, developed and coordinated the protocol and the review, completed the first draft of the review, assessed the studies, extracted and analysed data, approved the final version prior to submission, and is guarantor for the review.

Ludovic Reveiz developed the protocol and the review, completed the first draft of the review, assessed the studies, extracted and analysed data, and approved the final version prior to submission. He performed part of the writing/editing of the review. He contributed to this systematic review in a personal capacity and during his spare time. Most of the work was performed before joining the Pan American Health Organization. The Pan American Health Organization does not assume responsibility for the statements contained therein.

Claudia Criollo developed the protocol and the review, completed the first draft of the review, assessed the studies, extracted data, and approved the final version prior to submission.

Luis Uribe developed the protocol and the review, completed the first draft of the review, assessed the studies, extracted data, and approved the final version prior to submission.

DECLARATIONS OF INTEREST

None known.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have modified the 'comparison' as a result of suggestions from the editorial base of the Cochrane Infectious Diseases Group. We only included studies assessing the standard treatment (metronidazole for five or more days) against a number of frequently used drugs.

Luis Gabriel Cuervo was an author of the protocol.

INDEX TERMS

Medical Subject Headings (MeSH)

Albendazole [therapeutic use]; Antiparasitic Agents [*therapeutic use]; Giardiasis [*drug therapy]; Mebendazole [therapeutic use]; Metronidazole [therapeutic use]; Randomized Controlled Trials as Topic; Thiazoles [therapeutic use]; Tinidazole [therapeutic use]

MeSH check words

Adult; Child; Humans