Towards evidence based medicine for paediatricians

Edited by Bob Phillips

In order to give the best care to patients and families, paediatricians need to integrate the highest quality scientific evidence with clinical expertise and the opinions of the family. Archimedes seeks to assist practising clinicians by providing “evidence based” answers to common questions which are not at the forefront of research but are at the core of practice. In doing this, we are adapting a format which has been successfully developed by Kevin Macaway-Jones and the group at the Emergency Medicine Journal—“BestBets.”

A word of warning. The topic summaries are not systematic reviews, through they are as exhaustive as a practising clinician can produce. They make no attempt to statistically aggregate the data, nor search the grey, unpublished literature. What Archimedes offers are practical, best evidence based answers to practical, clinical questions.

The format of Archimedes may be familiar. A description of the clinical setting is followed by a structured clinical question. (These aid in focusing the mind, assisting searching, and gaining answers.) A brief report of the search used follows—this has been performed in a hierarchical way, to search for the best quality evidence to answer the question. A table provides a summary of the evidence and key points of the critical appraisal. For further information on critical appraisal, and the measures of effect (such as number needed to treat, NNT) books by Sackett5 and Moyer6 may help. To pull the information together, a commentary is provided. But to make it all much more accessible, a box provides the clinical bottom lines.

Electronic-only topics that have been published on the BestBets site (www.bestbets.org) and may be of interest to paediatricians include:

- Does intranasal or oral sumatriptan effectively relieve migraine headaches in adolescents?
- Do we need to give steroids in children with Bell’s palsy?
- In the paediatric population, should minor mucosal tongue lacerations be sutured?
- Topical anaesthetic or lidocaine infiltration to allow closure of skin wounds in children?
- How useful is ultrasound in the diagnosis of testicular torsion?

Readers wishing to submit their own questions—with best evidence answers—are encouraged to review those already proposed at www.bestbets.org. If your question still hasn’t been answered, feel free to submit your summary according to the Instructions for Authors at www.archdischild.com. Three topics are covered in this issue of the journal.

- Is polyethylene glycol safe and effective for chronic constipation in children?
- Are antiemetics helpful in young children suffering from acute viral gastroenteritis?

Rule of three

There are many “rules of three” in medicine, but one in particular stands out in the practice of critical appraisal and evidence based medicine. It’s the rule first described by Handley and Lippmann-Hand in 1983, and applies to situations where a study has found no events, or alternatively, everyone has had an event (that is, 0% and 100% outcomes).

This rule of three describes the 95% confidence interval for such a situation. It is calculated by 3/n, where n is the number of subjects studied. (For accuracy, n should be greater than 30.) For example, if you have a trial where 120 children received a new antiemetic, and there were no obvious adverse events, the upper bound of the 95% confidence interval would be 3/120 = 2.5%. You could be fairly sure that no more than about 1 in 40 children would suffer a side effect from this study’s results.

It also works for the other end of the spectrum, where a new therapy (for instance a new antibiotic) has no therapeutic failures in treating impetigo in a trial of 90 children. If 45 received the new antibiotic, then the confidence interval calculated by our rule would be 3/45 = 6.6%; that is, the 95% confidence intervals would be between 93.4% and 100%.

Taking this simple rule to the reading of spectacular results gives the clinician a relatively powerful way of defining what we know instinctively to be true—no news doesn’t necessarily mean good news.

Reference


- Should aciclovir be prescribed for immunocompetent children presenting with chicken pox?

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References

4 http://celmjr2.ex.ac.uk/docs/levels.htm (accessed July 2002)
Is polyethylene glycol safe and effective for chronic constipation in children?

Report by R Arora, R Srinivasan, Llandough Hospital, Cardiff, UK; reemaraman@doctors.org.uk doi: 10.1136/adc.2005.072918

Chronic constipation is a frequently encountered problem in the paediatric wards and clinics. Your usual line of management has been to prescribe adequate doses of regular lactulose and use sodium picosulphate as a second line laxative or as add on treatment. Recently, you have become aware of a new drug—polyethylene glycol (PEG). As you have not prescribed this drug earlier, you want to appraise the evidence before using it in your clinical practice.

Structured clinical question

In children with chronic constipation [patients] is polyethylene glycol [intervention] better in improving stool frequency and consistency [outcome] while causing fewer side effects?

Search strategy and outcome

Primary sources

Medline via Pubmed: Search was done using headings “Child”[MeSH] AND “Polyethylene Glycols”[MeSH] AND (“Constipation”[MeSH] OR “Fecal Impaction”[MeSH]). Twenty articles were found of which eight were relevant. To find articles that had been published but were still waiting to be indexed, another search was carried out with the terms “polyethylene glycol AND constipation AND child”*. Two further relevant articles were found.

Proceedings of major meetings: The abstract of one relevant unpublished article was also included which was presented at the 2nd World Congress of Pediatric Gastroenterology, Hepatology and Nutrition in Paris in 2004 after contacting the author and obtaining additional information.

Secondary sources

Cochrane database, BestBets: No papers found.

Summary

See table 1.

Commentary

Chronic constipation in children is a common gastrointestinal disorder encountered in general paediatric clinics and forms a substantial part of the paediatric gastroenterologist’s workload. The majority of constipated children have functional constipation and despite laxative use, success is modest. Management options include a combination of healthy eating aimed at increasing fibre and fluid intake, regular toileting, reinforcement with appropriate rewards, and laxative therapy. Combining laxative use with behavioural therapy has been shown to be better than laxative use alone. A high level of motivation and perseverance are necessary for these measures to be successful, and hence a continued search for a better laxative in terms of efficacy, safety, and compliance continues.

High dose PEG with electrolytes has been available for intestinal lavage preceding radiological and surgical procedures in children for some time. The electrolytes are added to prevent their loss through the faeces due to the large volume of the lavage, but this gives the lavage solution an unpleasant salty taste. A low dose version, such as PEG 3350, is available with electrolytes (in the UK and Netherlands) or without electrolytes (in the USA); it has been in commercial use only in the last few years and is used in much smaller volumes. It has been classed as an iso-osmotic laxative and acts by opposing absorption of water from faecal material in the large bowel and thus retaining water in the faeces, which is different from the laxatives such as lactulose which draw fluid from the body into the bowel lumen due to its high osmotic load. PEG is physiologically inert and is not absorbed or metabolised in the gut, giving it an unlimited “ceiling of action”.

From the available evidence it is clear that PEG is effective for both disimpaction and maintenance in children of all age groups with chronic constipation. The compliance with PEG treatment is high. In the controlled studies, PEG has been shown to be more effective than a placebo and lactulose, and at least as effective as milk of magnesia, with a much higher compliance than any of the others. It seems safe with or without added electrolytes. Only one of the above studies actually assessed the serum electrolyte levels post-treatment; abnormal levels were not found. Literature search did not reveal any case reports of adverse effects to the use of low dose PEG 3350 with or without electrolytes.

There are still some unresolved questions such as the issue of adding electrolytes, the most effective molecular weight of PEG (PEG 3350 v PEG 4000), and the safety profile of the drug in all age groups. The drug appears promising, and though its use at present is mainly in those with inadequate response to other laxatives, it is increasingly being used as first line treatment.

CLINICAL BOTTOM LINE

- Low dose PEG is effective, both in the short and long term management of constipation in children.
- Low dose PEG with or without added electrolytes is safe in the treatment of chronic constipation in children.
- More studies are needed to determine the most safe and effective form of PEG in children.

REFERENCES

Table 1 Polyethylene glycol in constipation

<table>
<thead>
<tr>
<th>Citation, country</th>
<th>Study group</th>
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</tr>
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<tbody>
<tr>
<td>Voskuijl et al (2004), Netherlands</td>
<td>100 children (6 months–15 years) with constipation treated with PEG 3350 or lactulose for 8 weeks. They were then asked to continue in an open-label assessment for an additional 18 weeks. 91 completed the study</td>
<td>Multicentre, double blind RCT (level 1b)</td>
<td>Clinical efficacy at 8 weeks</td>
<td>Significant increase in the mean defaecation frequency/week and a significant decrease in the mean encopresis frequency/week were found in both groups. 56% (95% CI 39–70) in PEG group were successfully treated compared to 29% (95% CI 16–44) in lactulose group</td>
<td>Used PEG 3350 (with electrolytes) in lower doses than used in other studies</td>
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<tr>
<td>Loening-Baucke (2004), USA</td>
<td>51 children aged 2–11 years (mean 5 y) entered a double blind treatment phase and were randomised to receive either PEG 3350 or matching placebo for 1st 2 weeks. After a 2 week washout period cross-over to receive alternative treatment was done for another 2 weeks</td>
<td>Double blind RCT with crossover (level 1b)</td>
<td>Stool frequency</td>
<td>Mean 3.59/week in PEG group v 1.58/week in placebo group (p&lt;0.001) after first 2 weeks</td>
<td>Used PEG with electrolytes. Adequate wash-out before cross-over. Presented at WCPGHAN 2004. Unpublished as yet.</td>
</tr>
<tr>
<td>Thomson (2004), UK</td>
<td>37 patients aged 2 to 16 years with constipation treated either PEG 3350 or lactulose for 2 weeks followed by the other agent for 2 weeks as part of an unblinded, randomised, crossover design</td>
<td>RCT with crossover (level 1b)</td>
<td>Stool frequency</td>
<td>Mean 1.7 ± 0.8/wk to 1.4 ± 0.8/wk for PEG 3350 and 1.3 ± 1.5/wk for lactulose</td>
<td>No wash out period during crossover</td>
</tr>
<tr>
<td>Gremse et al, (2002), USA</td>
<td>4 doses of PEG 3350: 0.25 g/kg/day, 0.5 g/kg/day, 1 g/kg/day, and 1.5 g/kg/day were given for 3 days in 41 children with constipation for &gt;3 months and evidence of faecal impaction</td>
<td>Individual double blind RCT (level 1b)</td>
<td>Disimpaction</td>
<td>Disimpaction achieved in 30 children (75%), 95% of higher dose patients (1–1.5 g/kg/day) achieved disimpaction v 55% of low dose patients (0.25–0.5 g/kg/day)</td>
<td>Demonstrated the use of PEG 3350 for disimpaction and dose response relation</td>
</tr>
<tr>
<td>Youssef et al (2002), USA</td>
<td>28 children with constipation treated with PEG (0.5–1 g/kg/day) were compared with 21 children treated with milk of magnesia (1–2.5 ml/kg/day)</td>
<td>Individual case-control study (level 3b)</td>
<td>Efficacy</td>
<td>On 3 monthly follow ups for a year, bowel movement frequency increased and soiling frequency decreased significantly in both groups. But compared to children on milk of magnesia those on PEG were soiling more frequently (p&lt;0.01) and fewer had improved (p&gt;0.01) at the 1 month follow up. This difference disappeared at subsequent follow ups</td>
<td>Not randomised. Demonstrated a high level of compliance to PEG</td>
</tr>
</tbody>
</table>

Adverse effects

| Voskuijl et al (2004), Netherlands | No serious adverse effects recorded. Those taking lactulose reported significantly more adverse events like flatulence |
| Thomson (2004), UK | Frequency of adverse effects similar to placebo |
| Gremse et al, (2002), USA | Frequency of adverse effects similar to placebo |

Stool frequency

| Voskuijl et al (2004), Netherlands | Mean 3.59/week in PEG group v 1.58/week in placebo group (p<0.001) after first 2 weeks |
| Thomson (2004), UK | Mean 1.7 ± 0.8/wk to 1.4 ± 0.8/wk for PEG 3350 and 1.3 ± 1.5/wk for lactulose |
| Gremse et al, (2002), USA | Similar for both laxatives |

Stool consistency and ease of passage

| Voskuijl et al (2004), Netherlands | Total transit time was 47.6 ± 2.7 h (mean ± SE) for PEG 3350 and 55.3 ± 2.4 h for lactulose (p = 0.038) |
| Thomson (2004), UK | PEG 3350 was effective in 31/37 patients (84%; 95% CI 68%–94%) and lactulose was effective in 17/37 (46%; 95% CI 30%–63%) (p = 0.002). PEG 3350 was preferred by 27/37 respondents (73%) compared to lactulose |
| Gremse et al, (2002), USA | Total transit time was 47.6 ± 2.7 h (mean ± SE) for PEG 3350 and 55.3 ± 2.4 h for lactulose (p = 0.038) |

Palatability and efficacy (as reported by child and parent)

| Voskuijl et al (2004), Netherlands | No patient had clinically significant abnormalities found in any of the stool characteristics |
| Thomson (2004), UK | No patient had clinically significant abnormalities found in any of the stool characteristics |
| Gremse et al, (2002), USA | No patient had clinically significant abnormalities found in any of the stool characteristics |

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### Table 1: Continued

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<tr>
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<tbody>
<tr>
<td>Loening-Baucke et al (2004), USA²</td>
<td>75 children from age 1–24 months (mean age 17 mth) with constipation were started on PEG; average dose of 1 g/kg/day</td>
<td>Case series (level 4)</td>
<td>Stool frequency</td>
<td>Increased from 3.7 ± 3.2/wk to 12.4 ± 7.0/wk in the initial 4 months and then 8.6 ± 3.1/wk over long term. Also significant improvement in signs and symptoms of constipation. Constipation relieved in 85% with short-term and 91% with long-term therapy.</td>
<td>Demonstrated the efficacy, tolerability and safety of PEG use for constipation in &lt;2 year olds</td>
</tr>
<tr>
<td>Erickson et al (2003), USA²</td>
<td>46 children with constipation and dysfunctional voiding were given PEG 3350 to evaluate efficacy, compliance and side-effects</td>
<td>Case series (level 4)</td>
<td>Stool frequency</td>
<td>Increased from 0.42 ± 0.2/day to 1.25 ± 0.42/day (p = 0.0001)</td>
<td>Addressed efficacy in those with constipation and resulting disorders in micturition</td>
</tr>
<tr>
<td>Pashankar et al (2003), USA³</td>
<td>74 children with chronic constipation (31 also had encopresis) were given PEG for 3–30 mth (mean 8.4 mth) to assess long-term efficacy</td>
<td>Case series (level 4)</td>
<td>Efficacy in constipation</td>
<td>Average dose 0.78 g/kg/day. Stool frequency increased from 2.9 ± 0.3/wk to 9.9 ± 0.7/wk (p&lt;0.001). Stool consistency score (from 1 to 5) increased from 1.4 ± 0.1 to 3.1 ± 0.1 (p&lt;0.001). Also significant improvement in signs and symptoms of constipation.</td>
<td>Efficacy and compliance over long term was studied</td>
</tr>
<tr>
<td>Pashankar et al (2003), USA³</td>
<td>28 patients younger than 18 months (range 7 weeks to 17 months) with constipation were started on PEG and mean duration of therapy was 6.2 ± 5 months</td>
<td>Case series (level 4)</td>
<td>Efficacy in constipation and encopresis</td>
<td>Average dose 0.69 g/kg/day. Stool frequency increased from 3.0 ± 0.5/wk to 12.5 ± 1.5/wk (p&lt;0.001). Stool consistency score (from 1 to 5) increased from 1.4 ± 0.1 to 3.1 ± 0.1 (p&lt;0.001). Also significant improvement in signs and symptoms of constipation.</td>
<td>Good daily compliance in 93%</td>
</tr>
<tr>
<td>Pashankar et al (2003), USA³</td>
<td>83 children (&gt;2 y) with chronic constipation (39 also had encopresis) were given PEG for 3–30 mth (mean 8.7 mth) to assess safety profile of long-term therapy</td>
<td>Case series (level 4)</td>
<td>Clinical adverse effects</td>
<td>Dose-related diarrhoea in 10%, flatulence and bloating in 6% and abdominal pain in 2%</td>
<td>Long-term compliance and safety for PEG studied</td>
</tr>
</tbody>
</table>

**Side effects:**
- 9/46 had diarrhoea and 1 stopped therapy
- 1 (3.6%) infant had flatulence and bloating

**Efficacy changes:**
- Biochemical changes: Nine subjects had transient mild elevation in ALT and 3 in AST which self-corrected in 11 later.
- Patient acceptance: Good daily compliance in 90%. Caretaker reported improvement in 91% and liked by 73% of children.

**Adverse effects:**
- 5 had diarrhoea which improved on decreasing the dose. PEG was not stopped in anyone.
- 1 (3.6%) infant had flatulence and bloating.

**Efficacy in constipation:**
- Mean initial dose was 0.88 kg/day. Mean effective maintenance dose was 0.78 kg/day.

**Efficacy in constipation and encopresis:**
- Post-void residual volume decreased from 92 ml to 48 ml (p<0.0001). Also significant improvement in signs and symptoms of constipation.
  - Good daily compliance in 90%.

**Adverse effects:**
- 5 had diarrhoea which improved on decreasing the dose. PEG was not stopped in anyone.
- 1 infant had flatulence and bloating.

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- Mean initial dose was 0.88 kg/day. Mean effective maintenance dose was 0.78 kg/day.

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**Adverse effects:**
- 5 had diarrhoea which improved on decreasing the dose. PEG was not stopped in anyone.
- 1 infant had flatulence and bloating.
Are antiemetics helpful in young children suffering from acute viral gastroenteritis?

Report by
S M Borowitz, Division of Pediatric Gastroenterology, University of Virginia, Charlottesville, Virginia 22908, USA; Witz@virginia.edu
doi: 10.1136/adc.2004.064972

An 18 month old female is brought to the emergency department by her mother. She has been suffering from repeated vomiting and diarrhoea for the past 24 hours. Over the past eight hours she has vomited approximately 12 times. The vomitus has not contained any bile or blood. The little girl appears mildly dehydrated. Her stool tests positive for rotavirus. You wonder whether administration of an antiemetic may lessen her symptoms and increase the likelihood that oral rehydration therapy will be successful.

Structured clinical question
In an 18 month old girl with rotavirus gastroenteritis [patient], does the administration of antiemetic medication [intervention] decrease vomiting and increase the likelihood that oral rehydration therapy will be successful [outcome]? Limits: human, English language, all infant (birth to 23 months) or preschool child (2 to 5 years) or child (6 to 12 years).

No systematic reviews. Seventy papers were identified, four of which were relevant. See table 2.

Commentary
No study expressly answered the question as to whether antiemetics lessen the vomiting associated specifically with rotavirus gastroenteritis infection in children and increase the likelihood that oral rehydration therapy will be successful. In the one study in which the authors attempted to identify the cause of gastroenteritis, approximately half of the enrolled children were suffering from rotavirus gastroenteritis. It is reasonable to assume that at least similar numbers of children in the other studies were suffering from rotavirus infection.

In one study, oral ondansetron (1.6–4 mg/dose depending on the child’s age) or placebo was administered in the emergency department and then every eight hours for up to two days. Compared to the controls, children that received ondansetron experienced less vomiting while they were in the emergency department, were less likely to require intravenous fluid therapy, and were less likely to be admitted to the hospital. In another study, a single dose of intravenous ondansetron (0.15 mg/kg) or placebo was given in the emergency department. All of the children in this study also received intravenous fluids. The children who received ondansetron had significantly less vomiting in the emergency department than did the children who received placebo. Hospitalisation rates were comparable in the two groups; however when the authors excluded children who had a serum CO₂ less than 14 mEq/l or had received intravenous fluids prior to their emergency room visit, those who received ondansetron were significantly less likely to be admitted to the hospital than were children who were treated with placebo.

Cubeddu and colleagues showed that in children hospitalised with gastroenteritis, a single dose of intravenous ondansetron (0.3 mg/kg) decreased the frequency of vomiting over the subsequent 24 hours compared to a single dose of metoclopramide (0.3 mg/kg) or placebo. Van Egan and colleagues showed that in children hospitalised with gastroenteritis, 30 mg domperidone suppositories decreased the amount of vomiting compared to 10 mg metoclopramide suppositories or placebo. In both of these two studies, metoclopramide was not superior to placebo.

In these four studies comprising 358 patients, no serious side effects were associated with the administration of antiemetics.

Table 1

<table>
<thead>
<tr>
<th>Citation, country</th>
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</thead>
<tbody>
<tr>
<td>Pashankar and Bishop (2001), USA</td>
<td>24 children (18 mth–12 y) with chronic constipation (with/without soiling) were started on 1 g/kg/day of PEG (dose adjusted subsequently) for a total of 8 weeks</td>
<td>Case series (level 4)</td>
<td>Stool frequency</td>
<td>Increased from 2.3 ± 0.4/wk to 16.9 ± 1.6/wk (p&lt;0.0001)</td>
<td>Open labelled trial</td>
</tr>
<tr>
<td>Pashankar DS, Bishop WP</td>
<td>Efficacy and optimal dose of daily polyethylene glycol 3350 for treatment of constipation and encaeprosis in children. J Pediatr 2001;139:428–32.</td>
<td></td>
<td>Stool consistency</td>
<td>Score (from 1 to 5) increased from 1.2 ± 0.1 to 3.3 ± 0.1 (p&lt;0.001)</td>
<td>No controls</td>
</tr>
<tr>
<td>Ungar A.</td>
<td>Movicol in treatment of constipation and faecal impaction. Hosp Med 2000;61:37–40.</td>
<td></td>
<td>Optimal dose</td>
<td>Range 0.27–1.42 g/kg/day (mean 0.84 g/kg/day)</td>
<td></td>
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</tbody>
</table>

www.archdischild.com
Table 2: Antiemetics in acute viral gastroenteritis

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Reeves et al (2002)</td>
<td>107 children, age 1 month to 22 years</td>
<td>Double blind RCT</td>
<td>Primary outcomes: frequency of vomiting episodes after drug administration, and the need for hospitalisation</td>
<td>38 (70%) of the 54 patients in the group who received ondansetron and 27 (51%) in the group that received placebo had complete cessation of vomiting (p = 0.04)</td>
<td>The study was supported by a grant from Glaxo Wellcome Inc. who manufacture ondansetron. No testing was done to determine the cause of gastroenteritis.</td>
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<tr>
<td></td>
<td>who presented to an ED who had experienced at least three episodes of vomiting in the previous 24 hours though to be secondary to an acute gastroenteritis and required intravenous fluids</td>
<td></td>
<td>Secondary outcomes: duration of vomiting after drug administration, number and duration of diarrhoea symptoms, frequency of return visits to an urgent or emergency care centre, need for readministration of intravenous fluids, and need for later hospital admission</td>
<td>Fourteen patients (26%) who received ondansetron and 16 patients (30%) who received placebo were hospitalised (p &gt; 0.05)</td>
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<td></td>
<td>Patients were excluded if they had received any antiemetic therapy within 72 hours of enrolment, had a history of hepatic disease or had diarrhoea lasting more than 7 days</td>
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<td>Ondansetron 0.15 mg/kg IV was given as a single dose</td>
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<td>Ramsook et al (2002)</td>
<td>145 children ages 6 months to 12 years</td>
<td>Double blind RCT</td>
<td>Primary outcomes: frequency of emesis during the 48 hours after enrolment and rates of intravenous fluid administration</td>
<td>The rank sum of vomiting episodes while in the ED was significantly lower in the group who received ondansetron (p = 0.001). During the 48 hours of follow up, the median number of episodes of vomiting were not significantly different in the two groups. A lower proportion of patients receiving ondansetron required intravenous fluids (p = 0.015). The admission rate was lower in the patients receiving ondansetron (p = 0.007)</td>
<td>The study was supported in part by a grant from GlaxoWellcome Research and Development who manufacture ondansetron. The majority of children studied were less than 4 years of age. No testing was done to determine the cause of gastroenteritis.</td>
</tr>
<tr>
<td></td>
<td>who presented to an ED due to with or without diarrhoea thought to be secondary to gastroenteritis and had vomited at least five times during the preceding 24 hours and had not received any antiemetics</td>
<td></td>
<td>Secondary outcomes: hospital admission rates and frequency of diarrhoea</td>
<td>Children receiving ondansetron had significantly more diarrhoea in the 48 hour follow up period than did controls</td>
<td></td>
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<tr>
<td></td>
<td>Patients were excluded if they had any chronic illnesses, possible appendicitis, urinary tract infection, or, severe gastroenteritis requiring immediate intravenous fluid resuscitation</td>
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<td></td>
<td>The children who received ondansetron were more likely to return to the ED than were controls (p = 0.047)</td>
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<td>Ondansetron syrup was given every eight hours for up to two days. Children 6 months to 1 year of age were given 1.6 mg/dose, children 1 to 3 years of age were given 3.2 mg/dose and children 4 to 12 years of age were given 4 mg/dose. Oral rehydration was initiated 15 minutes after the first dose of ondansetron or placebo</td>
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<td>Cubeddu et al (1997)</td>
<td>36 children ages 6 months to 8 years</td>
<td>Double blind RCT</td>
<td>Frequency of vomiting over the 24 hours after treatment</td>
<td>The number of vomiting episodes was significantly less in the children who received ondansetron (mean = 2) than in controls (mean = 5). There was no statistically significant difference between children treated with metoclopramide or placebo. 58% of children who received ondansetron experienced no vomiting as compared to 17% of controls. There was no statistically significant difference between children treated with metoclopramide or placebo.</td>
<td>The study was supported by Glaxo Wellcome Research and Development who manufacture ondansetron. 47% of children enrolled had rotavirus enteritis, 11% had adenovirus enteritis, and 31% had bacterial enteritis. All 36 children completed the study.</td>
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<td>diagnosed with acute gastroenteritis with associated vomiting who had vomited twice within one hour</td>
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<td></td>
<td>Over 24 hours, the number of treatment failures was significantly greater in the children treated placebo (33%) and metoclopramide (42%) than in children treated with ondansetron (17%). Children receiving both metoclopramide and ondansetron experienced more episodes of diarrhoea than controls over the 24 hours study period (p = 0.013 and 0.004 respectively)</td>
<td>At entry, children in the placebo group were somewhat better hydrated and somewhat older than children in both treatment groups. There was no difference in the number or type of adverse events in the three groups.</td>
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<td></td>
<td>Patients were excluded if they were severely dehydrated, had a rectal temperature greater than 39°C, had experienced seizures, or had received any parenteral antiemetic medication in the six hours prior to the study</td>
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<td>Ondansetron 0.3 mg/kg, metoclopramide 0.3 mg/kg, or sterile saline were given as a single IV infusion. Oral rehydration was commenced 30 minutes after treatment administration</td>
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Table 2 Continued

<table>
<thead>
<tr>
<th>Citation</th>
<th>Study group</th>
<th>Study type</th>
<th>Outcome</th>
<th>Key results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Egan et al (1979)⁴</td>
<td>60 children ages 2 to 6 years admitted to the hospital with acute gastroenteritis with vomiting.</td>
<td>Double blind RCT</td>
<td>Primary outcome was severity of nausea, vomiting, anorexia, abdominal pain, and abdominal distension as rated on a four point Likert scale. Secondary outcome was global rating of symptoms at 24 hours.</td>
<td>Children receiving domperidone required fewer additional suppositories than children who received metoclopramide (p&lt;0.05) or placebo (p&lt;0.05). The time span between suppositories was longer in children receiving domperidone than children receiving metoclopramide (p&lt;0.01) or placebo (p&lt;0.05). Children treated with domperidone had significantly less nausea, vomiting, anorexia and abdominal pain than children treated with metoclopramide or placebo.</td>
<td>No testing was done to determine the cause of gastroenteritis. All 60 children completed the trial. No drug-related side effects were identified.</td>
</tr>
</tbody>
</table>

CLINICAL BOTTOM LINE

- There is currently insufficient evidence to justify the use of oral or intravenous ondansetron in children suffering from acute viral gastroenteritis. A large, well-constructed prospective study is needed to answer this question.
- Ondansetron given intravenously (0.15–0.3 mg/kg/dose) or orally (1.2–4 mg/dose given every eight hours) probably decreases vomiting in children suffering from viral gastroenteritis.
- Serious complications appear to occur in less than 1% of children given ondansetron, but studies in gastroenteritis are limited.
- Ondansetron given intravenously (a single dose of 0.15–0.3 mg/kg) or orally (1.2–4 mg/dose given every eight hours) may decrease the need for hospitalisation in children suffering from vomiting associated with acute viral gastroenteritis.
- Metoclopramide given intravenously or as a suppository does not decrease vomiting in children suffering from viral gastroenteritis.

REFERENCES


Should acyclovir be prescribed for immunocompetent children presenting with chickenpox?

Report by
D Harris, Specialist Registrar, St Mary’s Hospital, London, UK
J Redhead, Consultant, St Mary’s Hospital, London, UK; julian.redhead@st-marys.nhs.uk
doi: 10.1136/adc.2005.072215

A 4 year old child is brought to the emergency department by her mother because of a rash that has developed over the preceding 24 hours. The rash is that of uncomplicated chickenpox infection and the history gives a good story of recent contact. The child has no medical history of note and is not immunocompromised. You wonder whether the prescribing of oral acyclovir would reduce the disease severity and duration compared to symptomatic control only.

Structured clinical question
In uncomplicated chickenpox infection in immunocompetent children [patient] is oral acyclovir [intervention] beneficial in reducing severity and duration of infection [outcome]?

Search strategy and outcome

Cochrane “acyclovir and chickenpox”.

The Medline search found 14 papers. Papers were excluded if they had no placebo group, which resulted in three relevant papers. These three papers have since been subject to a systematic review by the Cochrane Review Group. The review

ondansetron, metoclopramide, or domperidone; however only 140 patients received ondansetron, 32 received metoclopramide, and 20 received domperidone, and follow up was limited to no more than seven days. In the study by Cubeddu and colleagues,³ hospitalised children who received ondansetron or metoclopramide experienced more episodes of diarrhoea during the 24 hour study period than did children who received placebo. Similarly, in the study by Ramsook and colleagues,² children who received ondansetron had significantly more diarrhoea during the 48 hour study period than did children who received placebo. In two of the studies,² ³ children who received ondansetron experienced more diarrhoea than did children who received placebo.

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REFERENCES

was first published in 1999 with the most recent substantive amendment made in February 2004.

See table 3.

Commentary

Chickenpox (varicella) remains a common and highly contagious childhood illness among immunocompetent children. Although generally self-limiting, the infection usually presents with an itchy vesicular rash over the trunk and face, fever, and mild systemic upset. Disease complications include secondary bacterial infection of cutaneous lesions, encephalitis, cerebella ataxia, pneumonia, and otitis media. The economic burden is thought to come from the time taken off work by the child’s caregiver.

All three papers were randomised double blind placebo controlled trials carried out in the USA. Between them they looked at 988 patients aged between 2 and 18 years with either clinical or laboratory diagnoses of varicella.

Although the number of days to no new lesions and number of days to reduction of fever were reduced by one day in the acyclovir groups, the findings that one could consider to be more clinically relevant were less definite.

Reported adverse effects were similar in both groups and there was no significant difference between the treatment groups with respect to all skin, central nervous system, and respiratory complications arising from chickenpox infection.

Balfour and colleagues\(^1\) showed that the efficacy of acyclovir improves if treatment is initiated within 24 of rash onset, which in practical terms is a diagnostic window often difficult to achieve. Although Balfour et al also show that initiating treatment within 48 hours has greater benefit than 72 hours, one may ask oneself if the modest benefits in outcome, when weighed against the strict compliance required for four times daily medication over five days are of clinical worth.

Concerns have been raised regarding the development of resistance to acyclovir. The Cochrane Review concluded that there is evidence to suggest that strains of varicella resistant to acyclovir. The Cochrane Review concluded that there is evidence to suggest that strains of varicella resistant to acyclovir. The Cochrane Review concluded that there is evidence to suggest that strains of varicella resistant to acyclovir.

There is no published evidence to show a positive outcome in cost-benefit analysis and the Cochrane Review showed no reduction in the number of days missed from school between the treatment groups.

Possible issues with the studies were that all three had pharmaceutical sponsorship and other than the study of Dunkle and colleagues\(^2\) they comprised relatively small patient numbers.

### CLINICAL BOTTOM LINE

- **Oral acyclovir shortens time to fever reduction and time to no new lesions by one day but has no effect on complication rates secondary to infection.** (Grade A)
- **These reductions were only seen if treatment was initiated with 24 hours of rash onset.** (Grade B)
- **Use of acyclovir should not currently be recommended in immunocompetent children with chickenpox infection.** (Grade A)
ACKNOWLEDGEMENTS

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Are antiemetics helpful in young children suffering from acute viral gastroenteritis?

S M Borowitz

Arch Dis Child 2005 90: 646-648
doi: 10.1136/adc.2004.064972

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