

Clinical evidence

Urinary tract infection in children

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This review of the effects of treatment for urinary tract infection in children and of preventive interventions is one of over 60 chapters in the first issue of *Clinical Evidence*, published by the BMJ Publishing Group.

Background

Definition: Urinary tract infection is defined by the presence of a pure bacterial growth $>10^5$ colony forming units/ml. Lower counts of bacteria may be clinically important, especially in boys and in specimens obtained by urinary catheter. Any growth of typical urinary pathogens is considered clinically important if obtained by suprapubic aspiration. In practice, three age ranges are usually considered on the basis of differential risk and different approaches to management: under 1 year old; young children (1 to 4, 5, or 7 years old, depending on the source); and older children (up to 12-16 years old). Recurrent urinary tract infection is defined as a single further infection by a new organism. Relapsing urinary tract infection is defined as a further infection with the same organism.

Incidence/prevalence: Boys are more susceptible before the age of 3 months; thereafter the incidence is substantially higher in girls. Estimates of the true incidence of urinary tract infection depend on rates of diagnosis and investigation. At least 8% of girls and 2% of boys will have a urinary tract infection in childhood.¹

Aetiology: The normal urinary tract is sterile. Contamination by bowel flora may result in urinary infection if a virulent organism is involved, if the child is immunosuppressed, or both. In neonates, infection may originate from other sources. *Escherichia coli* accounts for about three quarters of all pathogens. *Proteus* is more common in boys (around 30% of infections). Obstructive anomalies are found in 0-4% and vesicoureteric reflux in 8-40% of children being investigated for their first urinary tract infection.² Although vesicoureteric reflux is a major risk factor for adverse outcome, it is likely that other as yet unidentified triggers also need to be present.

Prognosis: After first infection, about half of girls have a further infection in the first year and three quarters within two years; we found no figures for boys. Renal scarring occurs in 5-15% of children within one to two years of their first urinary tract infection, although 32-70% of these scars are noted at the time of initial assessment.³ The incidence of new renal scars rises with each episode of infection.³ Renal scarring is associated

Interventions for urinary tract infections in childhood

Beneficial:

- Seven to 10 days of antibiotics (better than shorter courses)

Likely to be beneficial:

- Immediate empirical antibiotic treatment
- Prophylactic antibiotics after first or subsequent urinary tract infection
- Diagnostic imaging in children at high risk of morbidity after first urinary tract infection

Unknown effectiveness:

- Routine diagnostic imaging in all children with first infection

Unlikely to be beneficial:

- Surgical correction of moderate vesicoureteric reflux (similar benefits to medical management)
- Surgical correction of minor functional anomalies

Likely to be ineffective or harmful:

- Delaying treatment while awaiting results of microscopy or culture
- Surgical correction of mild vesicoureteric reflux

with future complications: poor renal growth, recurrent adult pyelonephritis, impaired glomerular function, early hypertension, and end stage renal failure.⁴⁻⁶ A combination of recurrent urinary infection, severe vesicoureteric reflux, and the presence of renal scarring at first presentation is associated with the worst prognosis.

Aims: To relieve acute symptoms, to eliminate infection, and to prevent recurrence, renal damage, and long term complications.

Outcomes: Acute: clinical symptoms (dysuria, frequency, fever); urine culture; incidence of new renal scars. Chronic: incidence of recurrent infection; prevalence of renal scarring; renal size and growth; renal function; prevalence of hypertension and renal failure.

Methods

Systematic reviews were extracted from validated searches of Medline, Embase, and the Cochrane database in July 1999. Randomised controlled trials (RCTs) and controlled cohort studies were also identified. We gave priority to studies on the basis of their methodology, relevance, and applicability.

Question: What are the effects of different antibiotic regimens in acute urinary tract infection in children?

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We found little evidence on the effects of delaying treatment while awaiting microscopy or culture results, but retrospective studies suggest that delayed treatment may be associated with increased rates of renal scarring. Placebo controlled trials of antibiotics for symptomatic acute urinary tract infection in children would be considered unethical. One systematic review found that antibiotic treatment for seven days or longer was more effective than short courses.⁷

Benefits

Immediate empirical versus delayed treatment: We found no RCTs comparing immediate empirical treatment versus treatment delayed while awaiting microscopy or culture results. Five retrospective observational studies found increased rates of scarring in children in whom diagnosis was delayed from four days in acute urinary tract infection to seven years where a child presented with chronic non-specific symptoms.²

Long versus short courses: We found one systematic review of 14 RCTs comparing short course (range single dose to four days) versus conventional treatment (range 7-10 days).⁷ Short courses were less effective than courses of seven days or longer. No RCTs were found comparing five day courses of antibiotics with other regimens.

Harms

The studies did not report comparative harms from long compared with short courses of antibiotics, nor from immediate compared with delayed treatment. Potential harms include the risk of unnecessary or inappropriate antibiotic prescription.

Comment

We found no good evidence from which to predict which children are at high risk of complications after an acute urinary tract infection.⁸

Question: Which children benefit from diagnostic imaging?

We found no convincing evidence of benefit from routine diagnostic imaging of all children with a first urinary tract infection. However, subgroups of children at increased risk of future morbidity may benefit from investigation. Because such children cannot be identified clinically, investigation of all young children with urinary tract infection may be warranted.

Benefits

We found no RCTs. One systematic review of 63 descriptive studies found no direct evidence to support the effectiveness of routine diagnostic imaging in children with urinary tract infection.² The quality of studies was generally poor and none included clinically important long term outcome measures.

Harms

The studies reported no evidence on harms. Potential harms include those relating to radiation, invasive procedures, and allergic reactions to contrast media.

Comment

Although the studies showed no benefits overall, subgroups of children at high risk of future morbidity,

including those with vesicoureteric reflux, may benefit from early investigation. These children cannot be identified clinically.⁹ One prospective study found that the highest rates of renal scarring after an episode of pyelonephritis occurred between the ages of 1-5 years.¹⁰ Older children with more severe presentations may need careful investigation.

Question: What are the effects of preventive interventions?

Option: Prophylactic antibiotics

Two small RCTs found that prophylactic antibiotics may prevent recurrent urinary tract infections in children, particularly during the period of prophylaxis. The long term benefits of prophylaxis have not been adequately evaluated, even for children with vesicoureteric reflux.¹¹ The optimum duration of treatment is unknown.

Benefits

Versus no prophylaxis: We found no systematic review. One RCT of 45 children with either first or subsequent acute urinary tract infection compared 10 months of treatment with prophylactic antibiotics versus no treatment.¹² During the 10 month prophylaxis period, recurrent urinary tract infections were reported in none of the children in the intervention group compared with 11 in the control group. Twelve months after stopping prophylactic antibiotics, eight children (32%) in the intervention group compared with 13 (64%) in the control group had had a urinary tract infection. A further double blind crossover trial of 18 girls aged 3-13 years found two episodes of infection in one year in the treatment groups compared with 35 in the control groups ($P < 0.01$).¹³

Duration of treatment: We found no RCTs evaluating the optimum length of prophylaxis (although two studies of prolonged acute treatment were identified).

Harms

Potential harms include those of using antibiotics. In one study, although gut flora were affected by treatment, *E coli* cultured from rectal swabs from 70% of children remained sensitive to the prophylactic antibiotic (co-trimoxazole).¹⁴

Comment

The decision to stop prophylaxis may be made based on trial periods without treatment or, for children with vesicoureteric reflux, two negative cystograms.⁸ It is not possible to clinically identify children who are at high risk of subsequent urinary tract infections and long term damage.⁸ Routine prophylaxis until the results of investigations are known may therefore be warranted.

Option: Surgical correction for anomalies obstructing micturition

We found no good studies evaluating surgical correction.

Benefits

We found no systematic review or RCTs. One small observational study suggested that children with minor anomalies do not develop renal scarring and may

therefore not benefit from surgery.¹⁵ Eight of 20 children with moderate degrees of vesicoureteric reflux had renal scars compared with none of the eight children with minor anomalies.

Harms

Potential harms include the usual risks of surgery.

Comment

In the presence of major anomalies the prevention of urinary tract infections is not the prime motive of surgical intervention. Minor anomalies may not be associated with significant morbidity and surgical correction has not been evaluated in such children.

Option: Surgical correction for vesicoureteric reflux

One systematic review and a subsequent multicentre RCT found no difference between surgery for vesicoureteric reflux and medical management in preventing recurrence or complications from urinary tract infections.

Benefits

We found one systematic review of studies published before 1989 that included four RCTs (total 830 children) comparing surgical correction of moderate/severe (grades III-V) vesicoureteric obstruction versus medical management (continuous prophylactic antibiotics).¹⁶ Surgery abolished reflux, but there were no significant differences in rates of subsequent urinary tract infections, renal function, incidence of new renal scars, hypertension, or end stage renal failure between groups over a period of six months to five years. A subsequent RCT in 132 children found that the incidence of pyelonephritis was lower in children receiving surgical treatment, but there was also no difference in overall clinical outcome.¹⁷ In another arm of this study, six of 20 renal scars were thought to be associated with postoperative obstruction, which may have negated an otherwise beneficial effect of surgery over medical management.¹⁸

Long term outcome: We found no studies comparing long term outcomes (greater than five years).

Harms

The review did not mention surgical complications, and none of the individual studies was designed to compare harms.¹⁶ As noted above, postoperative obstruction may negate the benefits of surgery.¹⁸

Comment

Better results were obtained by centres handling the greatest number of cases.¹⁹ Surgery is usually considered only in children with more severe vesicoureteric reflux (grade III-V), who are less likely to experience spontaneous resolution.²⁰

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Key messages

- Treating symptomatic acute urinary tract infection in children with an antibiotic is accepted clinical practice and trials would be considered unethical
- We found little evidence on the effects of delaying treatment while awaiting microscopy or culture results, but retrospective observational studies suggest delayed treatment may be associated with increased rates of renal scarring
- One systematic review of randomised controlled trials (RCTs) has found that antibiotic treatment for seven days or longer is more effective than shorter courses
- We found no convincing evidence of benefit from routine diagnostic imaging of all children with a first urinary tract infection, but subgroups at increased risk of future morbidity may benefit from investigation. Because such children cannot currently be identified clinically, investigating all young children with urinary tract infection may be warranted
- Two small RCTs found that prophylactic antibiotics prevented recurrent urinary tract infection in children, particularly during the period of prophylaxis. The long term benefits of prophylaxis have not been adequately evaluated, even for children with vesicoureteric reflux. The optimum duration of treatment is unknown
- One systematic review and a subsequent multicentre RCT found no difference between surgery for vesicoureteric reflux and medical management in preventing recurrence or complications from UTI

Competing interests: None declared.

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