ARTICLE

Pertussis prophylaxis

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SUMMARY

Pertussis has significantly increased in Australia, particularly in older children and adults. These patients do not always exhibit classical symptoms and are an important source of infection for young infants.

Antibiotic treatment, isolation of index cases and timely vaccination are important strategies to prevent transmission of pertussis.

Evidence of the efficacy of chemoprophylaxis for pertussis is limited. Assessing efficacy is often confounded by a delay in diagnosis of the index case.

Antibiotic prophylaxis after exposure to pertussis aims to limit transmission to non-immune contacts. It is recommended for high-risk groups such as unimmunised infants, women in late pregnancy and individuals who may be a source of infection.

Introduction

Pertussis, also known as whooping cough, is caused by the bacterium *Bordetella pertussis*. Humans are the only known host for this pathogen.

There has been a recent resurgence of pertussis notifications in Australia and developed countries unrelated to changes in immunisation rates, particularly in adolescents and adults. Suggested reasons for the increase include:

- increased diagnosis and reporting
- waning immunity after childhood vaccination
- underdiagnosis of infection because of atypical presentations, which has resulted in an adult reservoir of circulating *B. pertussis*.[1]

Clinical presentation

In its classical form, young children with pertussis present with a non-specific coryzal illness associated with a mild cough (catarrhal phase) after an incubation period of approximately one week. This is followed 1–2 weeks later by a spasmodic cough with an inspiratory whoop commonly associated with post-tussive vomiting (paroxysmal phase). This phase can last up to six weeks before symptoms gradually resolve over a number of weeks. Infants in the first months of life may present with apnoea alone. Older children, adolescents and adults may have mild or no cough, or a chronic non-productive cough. They only rarely present with a classical paroxysmal cough with a whoop. This group are now the most important source of infection in young infants.

Mortality and morbidity

Mortality from pertussis is rare overall, but approaches 1% in infants under six months. However, morbidity from infection is common. It can include hospitalisation, superinfection, failure to thrive, cerebral hypoxia and encephalopathy in infants. Sleep disturbance, rib fracture and prolonged cough can occur in adults.

Transmission

B. pertussis is highly infectious and is spread by coughing or sneezing. Rates of transmission to susceptible contacts are up to 50% in the community and about 80% in susceptible household contacts.

Isolating infected cases until antibiotic treatment renders them non-infectious (five days) is the most important means of stopping pertussis circulating in the community.

Vaccination

Whole cell pertussis vaccines, introduced in the 1950s, significantly reduced pertussis in children. Acellular vaccines, introduced in Australia in 1999, have similar efficacy to whole cell vaccines with fewer adverse effects.

The current national immunisation schedule recommends primary immunisation with acellular pertussis vaccine (given in conjunction with diphtheria and tetanus immunisations – DTPa) at two, four and six months of age with booster doses at four and 15–17 years.[2] Waning immunity has been observed in older children and adults with this schedule. For this reason, booster vaccination is now also recommended for high-risk contact groups including adults planning a pregnancy, adult family members of newborns, and child and healthcare workers.

Australian guidelines[2] recommend a single dose of an acellular vaccine for contacts of pertussis older than eight years, and catch-up vaccination for unvaccinated or partially vaccinated (incomplete infant vaccination) contacts up to their eighth birthday.

Clinical trials are underway to evaluate neonatal pertussis vaccination and vaccination of pregnant mothers to limit pertussis transmission to newborns.

Management of the index case

Australian guidelines for the public health management of pertussis recommend antibiotic treatment of the index case with exclusion from childcare, school, work or other environments where high-risk contacts may be present, until they are non-infectious (that is, after five days of antibiotic treatment).[2] Treatment must be commenced in the first 21 days of illness to be effective. It does not shorten the duration of the illness, but does limit the duration of infectivity.

Guidelines for chemoprophylaxis

Chemoprophylaxis to prevent secondary transmission is not recommended in most situations because of the delayed presentation of the index case, and the cost and adverse effects of antibiotics. However, given the high risk of mortality and morbidity associated with infection of the newborn, particularly in the context of the rising incidence of pertussis in the community and the high transmission rate, chemoprophylaxis is recommended to limit transmission to those most at risk of the infection (that is, young infants). Data to support this recommendation are limited.

Australian guidelines recommend post-exposure chemoprophylaxis for contacts to whom transmission is most likely, and when there is significant risk of morbidity or mortality or risk of transmission to other high-risk groups.[2] These groups include:

- all household contacts of an index case when the household includes children less than two years who have received less than three doses of vaccine (including newborn infants)
- any woman in the last month of pregnancy
- all adults and children in a childcare arrangement with an index case, if the group contains children less than two years who have received less than three doses of vaccine
- healthcare workers in maternity and neonatal units
- infants in maternity and neonatal units where a healthcare worker was the infected case.

Therapy must be started within 21 days of exposure to the index case to be effective.

US guidelines for chemoprophylaxis[3,4] are broader than Australian guidelines and recommend prophylaxis for all household contacts and other close contacts, regardless of age and immunisation status. They also recommend prophylaxis for high-risk contacts after 21 days of illness in the index case.

UK guidelines[5] are similar to Australian guidelines, but extend 'vulnerable contact' definitions to include unimmunised and partially immunised infants or children up to 10 years of age, immunocompromised individuals and people with chronic illnesses (asthma, congenital heart disease).

Antibiotics

Macrolide antibiotics are the drugs of choice for prophylaxis. Trimethoprim-sulfamethoxazole is an alternative treatment. The duration of therapy is the same as a treatment course (Table 1). The age of the recipient, cost and availability are all important factors that determine the choice of the individual drug.

Azithromycin is the antibiotic of choice in infants under one month of age due to safety concerns about other macrolides in this age group, particularly the association between erythromycin, pyloric stenosis and cardiac arrhythmias.

Evidence

Published data on the efficacy of chemoprophylaxis for pertussis are limited. A Cochrane review of antibiotics for pertussis was updated in January 2011.[6] Two trials of antibiotic prophylaxis were included in the review. Both studies were prospective,

Table 1 **Recommended antibiotic for post-exposure prophylaxis for pertussis** [1]

Drug	Dose <1 month old	Dose 2–6 months old	Dose >6 months old	Adult dose
Azithromycin	10 mg/kg as a single dose for 5 days	10 mg/kg as a single dose for 5 days	10 mg/kg (max 500 mg) as a single dose for a day, then 5 mg/kg (max 250 mg) as a single dose for 2–5 days	500 mg day 1 250 mg days 2–5
Clarithromycin	Not recommended	7.5 mg/kg twice daily for 7 days	7.5 mg/kg twice daily (max 500 mg/dose) for 7 days	500 mg twice daily for 7 days
Erythromycin	Use if azithromycin unavailable Age <7 days: 10 mg/kg twice daily for 7 days Age 7–28 days: 10 mg/kg every 8 hours for 7 days	10 mg/kg every 6 hours for 7 days	10 mg/kg (max 250 mg/dose) every 6 hours (max 1 g/day) for 7 days	erythromycin: 250 mg every 6 hours for 7 days erythromycin ethylsuccinate: 400 mg every 6 hours for 7 days
Trimethoprim-sulfamethoxazole	Not recommended <2 months of age	4/20 mg/kg twice daily for 7 days	4/20 mg/kg (max 160/800 mg) twice daily for 7 days	160/800 mg twice daily for 7 days

randomised, controlled trials of erythromycin versus placebo for asymptomatic household contacts. In one of the trials, children less than six months old were excluded, and one of the trials had incomplete outcome data. Combined data demonstrated no statistically significant difference in *B. pertussis* culture positivity, whooping cough or paroxysmal cough in the treatment group compared to controls.

The efficacy of macrolide antibiotics for the treatment of pertussis was included in the same review.[6] Eleven randomised or quasi-randomised controlled trials were included. All trials involved only children. The review concluded that 'antibiotic treatment is effective in eliminating *B. pertussis* from the nasopharynx and thus rendering participants non-infectious, but does not alter the clinical course of the illness'. In terms of microbiological eradication and relapse, there was no difference in the efficacy of short (7 days) versus long courses (10–14 days) of erythromycin (estolate or unspecified salt of erythromycin), or short courses of erythromycin estolate (7 days) versus short courses of azithromycin (3–5 days) or clarithromycin (7 days). There is no evidence for the use of roxithromycin in the management of pertussis.

Other antibiotics that demonstrate similar efficacy to the macrolides include trimethoprim-sulfamethoxazole, oxytetracycline and chloramphenicol. Oxytetracycline and chloramphenicol are not recommended because of their more significant adverse effect profile, particularly in children.

Observational studies of post-exposure prophylaxis describe high rates of efficacy for erythromycin in reducing culture-confirmed *B. pertussis* in contacts of pertussis cases. They also report the prevention of clinical symptoms in these contacts as well as decreases in secondary transmission (attack rates) in household contacts.[6] Other studies report control of pertussis outbreaks with chemoprophylaxis in conjunction with other control measures including case isolation and treatment of cases (based on clinical and microbiological criteria).

The efficacy of prophylaxis is said to be optimal if given within 2–3 weeks of exposure (symptoms in the household contact case), but data are limited.

Safety of chemoprophylaxis

Adverse effects from therapy are of particular importance in young infants. All recommended antibiotics suggested for prophylaxis are associated with gastrointestinal adverse effects. Infantile hypertrophic pyloric stenosis may occur in neonates given erythromycin as post-exposure prophylaxis.[7]

Both clarithromycin and erythromycin inhibit cytochrome P450 3A. This is an important consideration if there is co-administration of drugs metabolised by this pathway. Azithromycin does not inhibit the P450 enzyme system to the same degree, but it is an inhibitor of P-glycoprotein. It has a better tolerability profile than the other macrolides. Trimethoprim-sulfamethoxazole is not recommended for pregnant women, nursing mothers, or infants aged less than two months. It can be associated with a range of hypersensitivity reactions, some of which are severe.

Cost and availability of azithromycin

Azithromycin is not listed on the Pharmaceutical Benefits Scheme for pertussis treatment or prophylaxis so it is expensive for the patient relative to the other macrolides. Its availability in some parts of the community is limited.[8]

Conclusion

National and international guidelines recommend prophylaxis with macrolides after exposure to pertussis in targeted groups. The efficacy of prophylaxis is limited in published trials, but observational data are encouraging. Its effectiveness in many situations may be further confounded because of delay in diagnosis of the index case.

Conflict of interest: none declared

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SELF-TEST QUESTIONS

True or false?

3. Adolescents and adults with pertussis usually present with the classical paroxysmal cough with an inspiratory whoop.

4. Clarithromycin is not recommended as prophylaxis for pertussis in newborns.

Answers on page 103

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FURTHER READING

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