Pertussis prevention and treatment: a call for wider access to azithromycin

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ABSTRACT

- Azithromycin is recommended as the first-line antibiotic for the prophylaxis and treatment of pertussis, a common vaccine-preventable communicable disease.
- Azithromycin is better tolerated than other macrolide antibiotics.
- Access to azithromycin is limited, as the product information and the Pharmaceutical Benefits Scheme do not include azithromycin for pertussis.
- Issues regarding access to azithromycin are highlighted in a case report of pertussis exposure in a tertiary paediatric hospital.

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Pertussis remains the most common vaccine-preventable disease in Australia, with notification rates of 39.6 cases per 100 000 population per year; 75 458 notifications occurred across Australia between 1995 and 2005.[1] Pertussis infection should be considered in individuals presenting with a coughing illness of over 2 weeks' duration. To prevent transmission, close contacts of the confirmed index patient should be given prophylaxis.[2] Neonates and children are vulnerable to pertussis morbidity and mortality.

Equity of access: azithromycin for pertussis treatment and prophylaxis

Although the current national recommendation for the prevention of secondary cases of pertussis in susceptible contacts includes the prophylactic administration of azithromycin,[2,3] neither the product information approved by the Therapeutic Goods Administration (TGA) nor the Pharmaceutical Benefits Scheme (PBS) include azithromycin for this indication. The recommended first-line antibiotic for pertussis prophylaxis and treatment is azithromycin 10 mg/kg/dose (maximum 500 mg) on Day 1, then 5 mg/kg/dose (maximum 250 mg) daily on Days 2–5.[2,3]

Suggested alternatives include clarithromycin, erythromycin and trimethoprim–sulfamethoxazole.[2,3] However, azithromycin

Pertussis exposure in an oncology ward of a tertiary paediatric hospital and the measures taken to minimise the spread of infection

The index patient, an HCW, had a prolonged coughing illness. Fourteen days after the HCW's initial contact with patients, IgA serology performed by the HCW's clinician was positive for pertussis. The illness and positive serology fulfilled the case definition of a confirmed case,[8] and the HCW was considered a transmission risk. The HCW commenced antibiotic treatment with erythromycin and was relieved from duties until no longer infectious (5 days of treatment).

An urgent meeting of the hospital Outbreak Management Team was convened to arrange contact tracing and PEP. All patients who had attended the unit during the HCW's 8-hour shift were considered exposed. Although there were theoretically 6 days for PEP, an upcoming long weekend imposed a 48-hour period in which staff experienced in managing contact tracing were available. These staff were required to contact the families of the 88 potentially exposed paediatric haematology and oncology patients and 22 HCWs within this timeframe. The hospital pharmacy was also closed over the long weekend. Exposure risk needed to be determined, susceptibility to pertussis assessed, and prescriptions organised and dispensed for PEP.

Azithromycin was chosen as the prophylactic agent as per current recommendations.[2,3] Contacts deemed to be at risk (and therefore requiring PEP) were defined as: exposed patients with malignancy or immunodeficiency; patients' siblings under the age of 1 year; patients and siblings with incomplete vaccination status; and pregnant women in the last trimester of pregnancy.[8,9] The decision to provide pertussis prophylaxis to the haematology and oncology cohort was based on three parameters: (i) evidence of waning pertussis immunity in the context of immunosuppressive chemotherapy — recent studies estimate that pertussis vaccine protection is reduced in 27%–82% of children undergoing chemotherapy;[10] (ii) the impact on hospital resources if a significant number of these children were to develop pertussis and require isolation in hospital; and (iii) high levels of family anxiety — although there are currently no reports of more severe pertussis in children with suppressed immunity.

Sixty-two at-risk individuals were identified as requiring PEP. Two patients were taking trimethoprim–sulfamethoxazole or roxithromycin for other indications, and two pregnant HCWs opted to receive erythromycin; the remaining HCWs had been immunised. Fifty-eight individuals (57 patients, including eight inpatients [14%], and one sibling) were prescribed azithromycin PEP. Oral suspension was indicated for 25 (43%).

As pertussis PEP is not an indication for PBS subsidy, families would have had to pay the recommended retail price for azithromycin (approximately $43.72 per course).[11] The hospital pharmacy dispensed the prescriptions at a lower cost. The total cost of azithromycin was $1666.55 (mean, $28.75/child). Fifty families were inconvenienced — 29/50 families (58%) living within an hour of the hospital collected their medications from the hospital pharmacy at their own expense. Medications were delivered to 21/50 children (42%) who lived outside metropolitan Sydney by courier or post at a cost of approximately $100, or by hospital families and employees (at no cost). Over 130 person-hours were involved, including evening or overtime shifts and diversion of staff from routine services to ensure contact tracing and PEP dispensing occurred within the restricted timeframe. Extra staffing costs were estimated to exceed $4000. Thus, the total cost to the hospital incurred by this public health measure was approximately $5800. Azithromycin dispensing through the hospital contributed most of the person-hours involved. To our knowledge, none of the contacts who received PEP became symptomatic.

HCW = health care worker. PEP = post-exposure prophylaxis. PBS = Pharmaceutical Benefits Scheme. ◆

is equally efficacious,[4,5] and has the advantages of daily dosing, excellent bioavailability and a shorter duration of therapy (5 days, compared with 7 days for other agents). It is the preferred agent for newborns, as it is available as an oral suspension and is not associated with infantile hypertrophic pyloric stenosis.[4,6] Unlike other macrolides, it has few gastrointestinal side effects and does not interact significantly with the hepatic cytochrome P450 system.[4,5] All of these factors increase compliance.

Currently, azithromycin 500 mg tablets are subsidised by the Repatriation Pharmaceutical Benefits Scheme for use for specific respiratory tract infections, not including *Bordetella pertussis*.[7] The powder for oral suspension is only PBS-listed for the treatment of trachoma.

Our experience with ensuring that patients at risk and family members received timely pertussis post-exposure prophylaxis highlighted a major gap in access to azithromycin (Box). The consequences of this were extra staff time, cost to the hospital and inconvenience for families who returned to obtain azithromycin, which would otherwise have been accessible through their local pharmacies and affordable because of PBS subsidisation. Courier delivery of medications before a public holiday added further costs. The inclusion of pertussis as an indication for azithromycin on the PBS subsidy has previously been raised.[6] Azithromycin access for preventing and treating pertussis is relevant to both hospital and community settings, as the number of pertussis notifications continues to rise.[1]

Thus, we urge that the prevention and treatment of pertussis with azithromycin formulations be incorporated in product information[11] and be considered for PBS subsidy,[7] in alignment with national recommendations. This process is dependent on pharmaceutical manufacturers applying to the TGA for this indication to be approved before PBS listing. Given the strength of the evidence for the use of azithromycin for treatment of pertussis,[4,5] we call for manufacturers to support the wider access for this treatment specifically, and for suitable medicines to treat paediatric-related illnesses in general.

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Competing interests

None identified.

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