Does This Child Really Have a Penicillin Allergy?

Abstract:

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Abstract

Penicillins, the most prescribed paediatric medications worldwide, are also the most commonly reported cause of medication allergy, although this is rarely confirmed. An oral penicillin challenge is considered the gold standard in assessing children with suspected allergy but is seldom performed due to lack of appropriately trained staff and insufficient facilities. We introduced a standardised nurse-led protocol to evaluate children with suspected penicillin allergy fulfilling low risk criteria. In total, 40 children participated, including 22 girls and 18 boys, of which 38 met study criteria. There were 36 (95%) negative challenges completed, allowing these children to be safely prescribed oral penicillin in the future. There were 2 (5%) positive challenges developing similar signs to their initial reaction. This standardised protocol appears to be safe for use and efficient in the evaluation of low risk children with suspected penicillin allergy.

Introduction

Penicillin and penicillin-based antibiotics are the most frequently prescribed antibiotics in children worldwide[1-3]. However, penicillin allergy or hypersensitivity is also the most common medication allergy reported[1-7]. Anaphylaxis is the most severe form of allergic reaction to penicillin and can be fatal, although occurring very rarely (1/100,000 treated patients)[1,2,6,8]. The most common reaction reported in children is a delayed non-IgE, T-cell mediated response, usually presenting with a maculopapular or morbilliform rash during treatment[5,7-10]. Penicillin allergy is rarely confirmed[1-3,5] and research indicates that 80-90% of people with suspected penicillin allergy are found not to be allergic when tested[1,2,5,11,12]. When a child is diagnosed with a suspected penicillin allergy, they are then prescribed non-penicillin based antibiotics which are frequently more expensive, may be less effective, and are more likely to give rise to antibiotic resistance.[2,3,5,9,13,14] Thus, highlighting the importance of confirming or out-ruling penicillin allergy. Traditionally, penicillin allergy was assessed by obtaining a detailed history of the reported allergic event in combination with expensive and invasive skin prick testing (SPT) and/or specific IgE blood testing. Research has demonstrated that SPT and specific IgE blood tests have poor sensitivity and specificity in children[1,4-7,9,11,14,15]. Furthermore, SPT reagents have been inconsistently available for commercial use[4,6,9,14]. Oral penicillin challenges remain the gold standard for diagnosing penicillin allergy in low risk children,[1,4,5,7,12,15] but are very rarely performed due to the lack of dedicated services and appropriately trained staff to carry out the challenges[3]. The purpose of this study is to assess whether a standardised protocol for the evaluation of children (<16years) with suspected penicillin allergy, fulfilling a low risk criteria (Table 1), can be safely and efficiently used in the day ward of an acute paediatric hospital.

Methods

Ethical approval for this study was obtained from the Ethics Committee of the National Childrenâ s Hospital, Tallaght, Ireland, and St. Jamesâ s Hospital, Ireland in December 2011. Children under the age of 16 years were recruited by a paediatric doctor and nurse from the emergency department, inpatient wards and out-patient clinics at the National Childrenâ s Hospital, Tallaght, Dublin. The children were recruited over a period of thirteen months, beginning in February 2013 and ending in March 2014. Initially, a letter of invitation to the study was given to the parents/guardians of the child with a suspected allergy. This letter was followed up with a phone call to the parents/guardians from a paediatric clinical research nurse to answer any questions and facilitate a date for first visit. At first visit, informed written consent was obtained from the parents/child, a questionnaire gathering demographic details and background to the childâ s suspected penicillin allergy was completed, and a thorough history about allergic reactions/history of atopy was taken by a trained nurse or doctor. Based on this information, the child was assigned into a high or low risk group. Children within the high risk group were then excluded from the study. For inclusion and exclusion criteria[3] please refer to Table 1.

Children classified as low risk took part in an oral penicillin challenge, carried out in the paediatric day ward with a trained nurse in attendance and a duty doctor available at all times. Oral amoxicillin was the penicillin of choice for the challenge as it is the most widely prescribed penicillin in children. Baseline observations including blood pressure, heart rate, respiratory rate and oxygen saturation were recorded prior to commencing the challenge, and thereafter every 15 minutes until discharge home. Doses were administered as per protocol (Table 2). If the child developed a skin reaction or other symptoms during the dose escalation, the challenge was stopped. Emergency medication for the management of both mild reactions and anaphylaxis was readily available. Otherwise, the child was observed for 2 hours following their final dose and if no allergic reaction was observed, they were discharged home on 48 hours of the antibiotic to assess for any delayed reactions as per previous protocols[1]. Discharge information was provided to parents/guardians on what to do if a delayed reaction occurred and a follow-up phone call was conducted by a paediatric clinical research nurse two days after the challenge. Correspondence was then made with the childâ s General Practitioner to inform them of their participation in the oral penicillin challenge and their result. Data was entered into a Microsoft Excel spreadsheet for statistical analysis.

Results

During the study period, 40 children were recruited with suspected penicillin allergy. We excluded 2 children as on detailed questioning they hadnâ t suffered a clinical reaction themselves but their parents perceived them to be at risk because of a family history of penicillin allergy. There were 22 girls and 18 boys with a mean age of 3 years at the time of the suspected allergic reaction, and a mean age of 6.2 years at the time of oral challenge. The majority of children, 30 cases, were direct referrals from General Practitioners and Consultants regarding penicillin allergy. The remaining 8 children were opportunistic cases with a history of suspected penicillin allergy noted during history taking. All children presented with a history of a delayed rash on exposure to penicillin, with 2 (5%) also reporting vomiting. There were 2 children with non-specific rash to penicillin on the first day of treatment. However as their symptoms were not severe they were deemed low risk. The implicated antibiotics received by the children are displayed in Figure 1. Thus 38 children were deemed to be low risk and suitable for challenge under the

protocol.

Of the 38 children who were deemed low risk, 36 (95%) had a negative challenge result, while 2 (5%) had a positive challenge result. The two positive challenge results included one child who developed erythematous patches over their back following two doses of amoxicillin. The challenge was stopped and the rash resolved with oral anti-histamine administration. Subsequently, the child was re-challenged at a later date with a single therapeutic dose of amoxicillin and developed the same mild reaction requiring no intervention, but confirming penicillin allergy. The second child developed a generalised rash on their torso after three doses of amoxicillin identical to their initial reaction. The rash resolved following treatment with oral anti-histamine. Two other participating children developed a delayed maculopapular rash after completing 48 hours of the antibiotic. However, both children developed the rash coupled with symptoms of vomiting and diarrhoea, leading us to believe it was unrelated to the penicillin and confirming a negative challenge result. Both children have had penicillin since their challenge with no adverse events.

Discussion

Our results confirm that this standardised protocol can be safely used to assess suspected penicillin allergy in children fulfilling a low risk criteria, in a day ward setting. The majority of children tolerated amoxicillin and thus could be safely prescribed oral amoxicillin in the future. Furthermore, the protocol can be performed by an appropriately trained paediatric nurse, in a cost effective and time efficient way. Our results support the findings of Moral et al[9], who introduced this protocol, challenging 50 low risk children with suspected penicillin allergy, resulting in only 1 mild delayed reaction. Similarly, a study evaluating Skin Prick Testing (SPT) versus Drug Provocation Testing (DPT) concluded that oral challenges in children who meet a certain criteria (low risk) are the preferred option for penicillin allergy diagnosis[15]. In addition, a large scale 20 year study carried out in France, involving 1865 children, investigated penicillin allergy diagnosis through detailed history taking, SPT, and DPT. The authors concluded that in low risk children in whom penicillin allergy is unlikely, SPT has minimal value[12] and following a detailed history, proceeding to oral challenge is safe[12]. Likewise, Caubet et al[1], whose study involved 88 children undergoing SPT, blood testing and DPT, out of whom 7 developed a rash, highlighted the inaccuracy of SPT and specific IgE blood testing in assessing delayed reactions to penicillin, but confirming the safety of DPT. They also suggest a single dose DPT in children within a low risk group; however this has yet to be validated[1,16].

As noted previously, the pre-test probability of a true penicillin allergy in children is low[8]. We have shown that potentially 5% of an at-risk population may have their allergy confirmed on testing. Secondly, while most delayed reactions are minor, some children do develop severe reactions such as Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis which can be life threatening, and clearly require specialist input to assess the potential medical risks for the future[4]. Other benefits include allowing us to modernise the service where we removed the requirement for IV cannulation and could allow this protocol be nurse-led, where a junior doctor had been required in the past. This brought considerable cost savings. Other minor savings included removing the need for specific IgE blood testing to Penicillin V and G prior to oral penicillin challenge, leading to a cost saving of approximately 49.50 per patient. Finally, the protocol used is minimally invasive, causing little pain or distress to the child as IV cannulation is avoided and the children spend a minimum time of 4 hours in hospital. Our research involved a small number of children referred to an acute secondary centre. However, the risk of true penicillin allergy is likely to be even lower in the community and thus this standardised protocol could ultimately be delivered in a primary care setting with the correct education and support. This study only challenged participating children with oral penicillin, there continues to be an unquantifiable risk of an allergic reaction for a given child following intravenous administration of penicillin.

In conclusion, this standardised protocol is safe in assessing low risk children with suspected penicillin allergy. This standardised protocol could be disseminated to other acute paediatric units and in time could be utilised in a primary care setting. Further research is required to examine the pharmacoeconomic implications of a diagnosis of suspected penicillin allergy.

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References

1. Caubet JC, Kaiser L, Lemaˆfitre B, Fellay B, Gervaix A, Eigenmann PA. The role of penicillin in benign skin rashes in childhood: a prospective

study. J Allergy Clin Immunol. 2011; 127: 218-222.

2. Karabud S, Motala, C. Penicillin allergy in children. Current Allergy and Clinical Immunology. 2009 June; 22:64-66.

3. Moral L, Garde J, Toral T, Fuentes MJ, Marco N. Short protocol for the study of paediatric patients with suspected betalactam antibiotic hypersensitivity and low risk criteria. Allergol Immunopathol. 2011; 39: 337-341.

4. Blana-Lˆ‡pez N, Zapatero L, Alonso E, Torres MJ, Fuentas V, Martˆ›nez-Molero MI, Blanca M. Skin testing and drug provocation in the diagnosis of nonimmediate reactions to aminopenicillins in children. Allergy. 2009; 64: 229-233.

5. Corzo-Higueras JL. Drug provocation tests in children: indications and interpretation. Allergol Immunopathol. 2009; 37: 321-332

6. Oâ Dowd L, Atkins P. UpToDate. Waltham, MA: UpToDate. 2006. Penicillin and related antibiotic allergy; skin testing; and desensitization.

7. Romano A. Recognising antibacterial hypersensitivity in children. Paediatr Drugs. 2000 Mar-Apr; 2: 101-112.

8. Pichichero ME. A review of evidence supporting the American academy of pediatrics recommendation for prescribing cephalosporin antibiotics for penicillin-allergic patients. Pediatrics. 2005 April; 115: 1048-1057.

9. Gruchalla RS, Pirmohamed M. Antibiotic allergy. The New England Journal of Medicine. 2006 Feb; 354: 601-609.

10. Romano A, Blanca M, Torres MJ, Bircher A, Aberer W, Brockow K, Pichler WJ, Demoly P. Diagnosis of nonimmediate reactions to ˆ -lactam antibiotics. Allergy. 2004; 59: 1153-60.

11. Ponvert C, Le Clainche L, de Blic J, Le Bourgeois M, Scheinmann P, Paupe, J. Allergy to ˆ -lactam antiobiotics in children. Pediatrics. 1999 Oct; 104:1-9.

12. Ponvert C, Perrin Y, Bados-Albiero A, Le Bourgeois M, Karila C, Delacort C, Scheinmann P, De Blic J. Allergy to betalactam antibiotics in children: results of a 20-year study based on clinical history, skin and challenge tests. Pediatric Allergy and Immunology. 2011; 22: 411-418.

13. Borch JE, Andersen KE, Bindslev-Jensen C. The prevalence of suspected and challenge-verified penicillin allergy in a university hospital population. Pharmacology & Toxicology. 2006; 98: 357-362.

14. Wˆ¶hrl S, Vigl K, Stingl G. Patients with drug reactions- is it worth testing? Allergy. 2006; 69:928-934.

15. Blanca M, Romano A, Torres MJ, Fˆ'rnandez J, Mayorga C, Rodriguez J, Demoly P, Bourquet PJ, Merk HF, Sanz ML, Ott H, Atanaskovic-Markovic M. Update on the evaluation of hypersensitivity reactions to betalactams. Allergy 2009; 64: 183-193.

16. Chiriac AM, Demoly P. Drug provocation tests: up-date and novel approaches. Allergy 2013; 9: 1-5.

Comments: