

Compliance with Intramuscular Penicillin Prophylaxis in Children with Sickle Cell Disease in Jamaica

L King, S Ali, J Knight-Madden, M MooSang, M Reid

ABSTRACT

Objective: Penicillin prophylaxis is important in the defence against invasive pneumococcal disease in sickle cell disease (SCD). Penicillin may be administered by the oral route or by the intramuscular (IM) route. Compliance with the oral route, although difficult to assess, has been reported to be highly variable and often poor. We sought to determine the compliance rate with intramuscular penicillin (IM) prophylaxis in children with sickle cell disease.

Methods: Children followed at the Sickle Cell Unit in Jamaica were recruited. Good compliance was deemed if patients received at least 10 injections over the preceding 12-months. Children on IM prophylaxis for less than a 12-month period were deemed to be compliant if they received 80% of injections since commencing prophylaxis.

Results: Data were available for 78 (HB SS 73; male 42) patients attending the clinic during the period of observation. Sixty-nine (88.5%) of the children were compliant with IM penicillin prophylaxis.

Conclusion: This study reports a high compliance (88.5%) to IM penicillin prophylaxis which was associated with an incidence rate of invasive pneumococcal disease lower than what is seen in other comparable studies, reflecting the route of administration. Intramuscular penicillin prophylaxis, despite challenges, is a practical option. It can contribute to better patient compliance and thus significantly impact global rates of invasive pneumococcal disease and its complications in children with SCD and other similar conditions.

Keywords: Compliance, intramuscular, penicillin prophylaxis, sickle cell

Cumplimiento de las Normas Terapéuticas en la Profilaxis con Penicilina Intramuscular en Niños Jamaicanos con Anemia Falciforme

L King, S Ali, J Knight-Madden, M MooSang, M Reid

RESUMEN

Objetivo: La profilaxis con penicilina es importante en la defensa contra la enfermedad neumocócica invasiva de la enfermedad de células falciformes (ECF). La penicilina puede administrarse por vía oral o por vía intramuscular (IM). El cumplimiento terapéutico por vía oral – aunque es difícil de evaluar – se ha reportado como altamente variable y a menudo pobre. Se buscó determinar la tasa de cumplimiento terapéutico con la profilaxis de penicilina intramuscular (IM) en niños con enfermedad de células falciformes.

Métodos: Se reclutaron niños bajo seguimiento en la Unidad de Células Falciformes en Jamaica. Se consideraba un buen cumplimiento el que los pacientes recibieran al menos 10 inyecciones en los últimos 12 meses. Se consideraba que los niños bajo profilaxis IM por un período menor de 12 meses habían cumplido las normas terapéuticas, siempre que hubiesen recibido el 80% de las inyecciones desde el comienzo de la profilaxis.

Resultados: Hubo datos disponibles para 78 (HB SS 73; 42 hombres) pacientes que asistieron a la clínica durante el período de observación. Sesenta y nueve (88,5%) de los niños cumplieron con las normas de la profilaxis con penicilina IM.

Conclusión: Este estudio reporta un alto cumplimiento (88,5%) con la profilaxis de la penicilina IM, asociado con una tasa de incidencia de la enfermedad neumocócica invasiva, inferior a la que se observa en otros estudios comparables que reflejan la vía de administración. A pesar de los desafíos, la profilaxis con penicilina intramuscular, es una opción práctica. Puede contribuir a un mejor cumplimiento del paciente, y así afectar significativamente las tasas globales de la enfermedad neumocócica invasiva y sus complicaciones en niños con ECF y otras condiciones similares.

Palabras claves: Cumplimiento terapéutico, intramuscular, profilaxis con penicilina, célula falciforme

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INTRODUCTION

Bacteraemia and meningitis due to *Streptococcus pneumoniae* are a major cause of mortality and morbidity in the early childhood period in persons with sickle cell disease (SCD). Penicillin prophylaxis has been well established as an important preventive measure in the defence against invasive pneumococcal disease (IPD) in these persons. Its use has resulted in a ~ 85% reduction in mortality and morbidity (1). Penicillin may be administered either by the oral route twice daily (penicillin V) or by the intramuscular (IM) route every 21 – 28 days (benzathine penicillin). Compliance with the oral route, although difficult to assess, has been reported to be highly variable and often poor (2, 3). Poor compliance with penicillin prophylaxis in this high-risk group of patients may impact on public health goals of decreasing the prevalence of pneumococcal disease and its associated morbidity/mortality, as well as limiting the emergence of penicillin resistant strains of *Streptococcus pneumoniae*. There is a paucity of information on compliance with the intramuscular route of administration in the medical literature.

In Jamaica, penicillin prophylaxis is given from age four months to four years in children with severe genotypes of SCD (homozygous, Hb SS or sickle-thalassaemia, Hb S β^0 thal disease). The majority of children receive penicillin via the IM route every 28 days. Their first injection is given at the Sickle Cell Unit (SCU). They are issued with an injection card which records the date the injection was given and also the date that the next injection is due. They are able to report either to the SCU or for greater convenience, to their local health centre for subsequent injections. Injection cards are updated at each injection visit by the healthcare provider and can record data for up to five years. Penicillin prophylaxis is discontinued at age four years only after pneumococcal polysaccharide vaccine (PPV) has been administered. The PPV is not subsidized by the government and due to financial difficulties of parents, the vaccine may not be administered at precisely age four years. Lifelong penicillin prophylaxis is recommended in persons with previous invasive pneumococcal disease.

The aim of this study was to determine the compliance rate with IM penicillin prophylaxis in a cohort of patients with a severe form of disease diagnosed by newborn screening. Most of these patients have been followed at the SCU,

a comprehensive care unit, since shortly after birth. Counselling and education, including the importance of penicillin prophylaxis and the need for compliance in the early childhood period, with an emphasis on age-appropriate complications are a routine part of clinic visits. Children are seen for routine visits every three months until age four years and, thereafter, every six months.

SUBJECTS AND METHODS

The current newborn screening programme in Jamaica started in 1995 and occurs at three-main hospitals in Kingston and its neighbouring parish of St Catherine. Infants with an initial screening diagnosis of homozygous sickle cell disease (Hb SS) are collectively grouped as a cohort of patients. Because of the laboratory technique used for diagnosis (4), a few infants with an initial diagnosis of Hb SS will have their diagnosis revised to a form of sickle-thalassaemia as they age. A convenience sample of children age four-months to four-years, on IM penicillin prophylaxis, who had not received their final pneumococcal polysaccharide vaccine at the start of the study, was obtained over a four-month period (November 2008 – February 2009). All children were actively followed at the SCU and were attending the SCU either for a doctor's visit or for an injection visit.

The injection card for children on IM prophylaxis was examined at their clinic visit. Good compliance was deemed if patients had received at least 10 injections over the preceding 12-months. Children on IM prophylaxis for less than a 12-month period were deemed to be compliant if they had received 80% of injections since commencing IM prophylaxis. Children who had received only their first injection were deemed ineligible as this would not be a reflection of their compliance. Over the three-month period, if a child had data collected on more than one occasion, the data obtained on first entry into the study was used for analysis. Data were analysed using Stata version 9. The study had ethical approval from the Faculty of Medical Sciences, The University of the West Indies/University Hospital of the West Indies Ethics Committee.

RESULTS

Ninety-nine eligible patients attended the clinic during the period of observation. Data were available for 78 (HB SS 73; male 42). Sixty-nine (88.5%) of the children were compliant

with IM penicillin prophylaxis. The mean ages of the compliant and non-complaint groups were 2.45 ± 0.99 and 2.74 ± 1.10 years, respectively. There was no statistically significant difference between the two groups (Table).

Table: Demographics of patients on IM penicillin prophylaxis

	Compliant n = 69	Noncompliant n = 9	p value
Age (years)	2.45 ± 0.99 (0.63 – 4.21)	2.74 ± 1.10 (0.95 – 4.48)	0.40
Sex			0.36
M	38	4	
F	31	5	
Genotype			0.70
HbSS	64	9	
Hb S β 0	5	0	

DISCUSSION

Patient compliance with medication is a complex issue and there are many factors which contribute to improved compliance especially in the paediatric population (5). Methods of reliably detecting patient compliance are difficult. Reported rates also often vary widely from measured compliance. With regards to children with SCD and penicillin prophylaxis, compliance rates vary from 43 to 67% (2, 3). However, most of these studies have been small with patients on oral prophylaxis. Even when techniques such as increased counselling/education have been employed, compliance rates have not changed significantly (6). Two small studies have demonstrated improved compliance with the IM route (7, 8). In the present study, a compliance rate of 88.5% was seen in children four-years and under on IM penicillin prophylaxis providing further support for the recommendation of this route.

Penicillin prophylaxis *via* the IM route has its challenges, the common ones encountered at our unit relate to pain associated with the injection and the fear of health professionals which may develop in children receiving injection. The latter can be minimised if injections are given at a location other than at the primary healthcare provider. On the positive side, IM prophylaxis removes a significant portion of the responsibility of parents to administer oral medication twice daily as well as problems related to children, especially the younger age group, taking medications. The convenience to patients of being able to receive injections at their local health centre is an additional factor contributing to good compliance. In our experience, the decreased responsibility of drug administration, the convenience of attending a local health clinic and the reduced cost of IM penicillin are significant determinants of why parents continue to opt for the IM route even when healthcare providers offer the oral route as an option. In comparison, parental perceptions of burdens such as remembering to collect refills and administer medica-

tion negatively impacted compliance for children on oral penicillin (9).

The prevalence of invasive pneumococcal disease in children four years and under in the same cohort of patients diagnosed by newborn screening in Jamaica and with a severe form of disease was 0.32 per 100 patient-years (10). This rate is much lower than rates reported in comparable groups (3) [2.9 per 100 patient-years] and in the intervention group in the Prophylactic Penicillin Study (PROPS) (1) [1.5 per 100 patient-years]. Altogether, these rates demonstrate the benefit of penicillin prophylaxis in the early childhood period in SCD. The lower rate of IPD in our setting is most likely a reflection of compliance with the route of administration. Compared to our compliance rate of 88.5%, Teach *et al* (3) reported a compliance rate of 43.1% for their patients who were on oral penicillin prophylaxis.

The pneumococcal conjugate vaccine (PCV) has resulted in a significant reduction in the incidence of IPD and as such has contributed to the recommendations for the administration of the pneumococcal conjugate vaccine in the early childhood period (11). With regards to SCD, Halsa *et al* (12) attributed a 93% reduction in incidence of IPD, to a low rate of 0.13 per 100 patient-years, in patients with SCD less than five-years to the introduction of PCV vaccine. Despite this evidence which provides support for the good alliance of penicillin prophylaxis and PCV in the fight against IPD, most of our patients have not received the PCV. The PCV is a costly vaccine and in Jamaica it has not been integrated into the routine childhood immunization schedule. It is therefore not subsidized by the government. In developing countries where the burden of SCD is greatest and where there are resource challenges which might preclude the use of PCV, emphasis on good compliance with penicillin prophylaxis becomes crucial in decreasing mortality and morbidity from IPD in this vulnerable population.

Intramuscular penicillin prophylaxis, despite commonly perceived drawbacks, is a practical option for long-term penicillin administration which can contribute to better patient compliance and in so doing have a significant effect on global rates (especially in developing countries) of invasive pneumococcal disease and its complications in children with SCD and other similar conditions.

There are some limitations to this study. Data were not obtained for 21 patients. Whereas injection cards are requested for perusal at doctors' visit, patients such as those who received IM prophylaxis at their local health centre, sometimes forget cards at home. Verbal communication however implied compliance in most cases. In addition, there was a lack of blinding of investigator and patient. However, the study collected retrospective information using robust criteria that was established before the commencement of the study thereby reducing the bias inherent in a non-blinded study.

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