



Antibiotic Prophylaxis for Children with Sickle Cell Disease: A Survey of Pediatric Dentistry Residency Program Directors and Pediatric Hematologists

Anupama Rao Tate, DMD¹ Chelita Kaye Norris, DDS² Caterina P. Minniti, MD³

Abstract

Purposes: The purposes of this study were to: (1) investigate the current clinical practice regarding the use of antibiotic prophylaxis by pediatric dentistry residency program directors and pediatric hematologists for children with sickle cell disease (SCD) requiring dental treatment; and (2) evaluate the perceived relative risk of bacteremia following specific dental procedures, as defined by pediatric dentistry residency program directors and pediatric hematologists.

Methods: A written survey depicting various clinical scenarios of SCD children requiring common dental procedures was mailed to directors of pediatric dental advanced education programs and distributed to pediatric hematologists attending the 2003 Annual Sickle Cell Disease Association of America conference in Washington, DC.

Results: Surveys were returned by 60% (N=34/57) of the pediatric dentistry residency program directors. The surveys were obtained from 51% of pediatric hematologists at the meeting (N=72/140). At least 50% of all respondents recommended prophylaxis for the following clinical situations: dental extractions, treatment under general anesthesia, and status post splenectomy. The perceived risk of infectious complication was highest for extractions, followed by restorative treatment and tooth polishing. Dental residency program directors were more likely (71%, N=24/34) to recommend additional antibiotic therapy for patients taking penicillin prophylaxis if they required an invasive oral surgical procedure. Conversely, only 38% (N=25/66) of pediatric hematologists recommended additional antibiotic therapy ($P=.001$). Eighty-six percent of dental residency program directors (N=25/29) chose amoxicillin for prophylaxis whereas only 62% of pediatric hematologists (N=36/58) recommended amoxicillin. ($P<.05$).

Conclusions: There is a lack of consensus on the appropriate use of antibiotic prophylaxis in SCD children undergoing dental treatments. Further research and risk/benefit assessment is needed to create a unified approach. (Pediatr Dent 2006;28:332-335)

KEYWORDS: SICKLE CELL DISEASE, ANTIBIOTIC PROPHYLAXIS REGIMEN, DENTAL TREATMENT

Received September 26, 2005 Revision Accepted February 16, 2006

Sickle cell disease (SCD) is a term describing a group of inherited disorders characterized by the predominance of hemoglobin S (HbS). These blood disorders include homozygous HbSS and mixed heterozygous conditions such as HbSC, Hb S β thalassemia, Hb SD, and Hb SO Arab. SCD is the most common single gene disorder among African Americans. Frequent infarcts of the sickled red blood cells with reduction of end organ perfusion cause the reduction in size or removal of the spleen, leading to an increased risk of widespread bacterial infections. Although the actual incidence of bacterial complications for

SCD children following dental procedures is not known, it is often assumed to be greater than that of the general population.

Since the macrophages of the spleen play an important part in protection against pneumococcal infection, SCD children who lose splenic function early in life are more susceptible to infections—particularly those caused by capsulated organisms such as *Streptococcus pneumoniae*. In 1986, the Prophylactic Penicillin Study (PROPS) demonstrated that antibiotic prophylaxis in SCD children ages 3 to 36 months reduced the rate of pneumococcal bacteremia by 84% compared to placebo.¹ As a result of these findings, investigators recommended twice-daily prophylactic oral penicillin therapy in SCD children.

In 1995, a subsequent study (PROPS II)² re-evaluated the need for the prophylactic antibiotic regimen in children older than 5. This follow-up study showed that

Drs. ¹Tate and ²Norris are assistant professors of Pediatrics, Department of Dentistry, and ³Dr. Minniti is associate professor of Pediatrics, Division of Pediatric Hematology/Oncology, Children's National Medical Center, all at the George Washington University School of Medicine, Washington, DC.

Correspond with Dr. Tate at atate@cnmc.org

Table 1. Antibiotic Prophylaxis Recommendations of Surveyed Pediatric Dentistry Residency Program Directors and Pediatric Hematologists for Children With Sickle Cell Disease Undergoing a Variety of Dental Procedures

Procedure	Clinicians recommending prophylaxis (N=106)	Recommending prophylaxis (%)
Tooth polishing	15	14
Patient <2 ys old	26	25
History of pneumococcal infection	31	30
Restorative	32	30
Dental treatment under general anesthesia	53	50
Splenectomized patient	55	52
Extractions	68	64
Cardiac history	75	71

SCD children who have not had a prior severe pneumococcal infection or a splenectomy and who have received 2 Pneumococcal vaccinations and reliable care by dedicated sickle cell health care providers may safely discontinue the antibiotic prophylaxis at the age of 5.³

Most dental procedures produce some form of bacteremia, with streptococcal species accounting for over half the aerobic bacteria isolated from blood cultures postdental extraction.⁴ There is no standard regimen, however, regarding the circumstances under which antibiotic prophylaxis is needed prior to dental treatment, nor the drug or dosage. There have been no published studies recommending specific antibiotic prophylaxis protocols in SCD children requiring dental treatment.

The purposes of this study were to:

1. investigate the current clinical practice regarding the use of antibiotic prophylaxis by pediatric dentistry residency program directors and pediatric hematologists for SCD children requiring dental treatment;
2. evaluate the perceived relative risk of bacteremia following specific dental procedures, as defined by pediatric dentistry residency program directors and pediatric hematologists.

Methods

Permission was obtained from the Institutional Review Board of the Children's National Medical Center, Washington, DC. A convenience sample was obtained by mailing a written survey to 57 directors of pediatric dental advanced education programs identified in 2003.⁵ The survey was redistributed 3 months later to those who did not initially respond to ensure maximum participation. The same survey was distributed to 140 pediatric hematologists attending the 2003 Annual Sickle Cell Disease Association of America

Table 2. Antibiotic Recommendation for Dental Prophylaxis Indicated by Surveyed Pediatric Dentistry Residency Program Directors and Pediatric Hematologists for Children With Sickle Cell Disease Undergoing Dental Procedures*

Antibiotic	Pediatric dentistry residency program directors (n=29)	Pediatric hematologist (n=58)	Total responders (n=87)
Amoxicillin	25 (86%)	36 (62%)	61 (70%)
Penicillin	4 (14%)	22 (38%)	26 (30%)

*P=.0204; chi-square=5.38; DF=1.

conference in Washington, DC. The majority of the pediatric hematologists worked in academic settings. The attendants were asked to complete the survey anonymously, which was made available to them at a booth during the meeting.

The survey depicted various clinical scenarios of SCD pediatric patients requiring common dental procedures. Participants were asked to determine an antibiotic regimen, if any, for SCD patients undergoing routine cleaning, fillings, and dental extractions. Cases included SCD children:

1. currently on a daily penicillin prophylaxis regimen (125 mg penicillin twice a day until age 3 and 250 mg penicillin twice a day after age 3);
2. with penicillin allergy; or
3. off penicillin prophylaxis because they are older than 5.

Participants were asked to specify what disease process (endocarditis, generalized systemic infection, etc) they were attempting to avoid by recommending antibiotic prophylaxis.

All of the data were recorded and evaluated using the SAS JMP statistics program (SAS Institute, Cary, NC). The differences between dental residency program directors and hematologists were assessed using chi-square and Fisher exact tests, with corrections for continuity.

Results

Surveys were returned via mail by 60% (N=34/57) of the pediatric dentistry residency program directors. The surveys were obtained in person at the 2003 Annual Sickle Cell Disease Association of America conference in Washington, DC from 51% (N=72/140) of pediatric hematologists. Not all scenarios were answered by each clinician; therefore, the total number of respondents for each question is variable. The participants were allowed to give written comments regarding the type or antibiotic regime they recommended.

There was no statistically significant difference in the reported recommendation of antibiotic prophylaxis between pediatric dentistry residency program directors and pediatric hematologists for patients with various presentations of SCD requiring common dental procedures (Table 1). Clinicians were most likely to recommend prophylaxis for SCD patients with cardiac disease. At least 50% of both dental residency program directors and pediatric hematologists would recommend prophylaxis for the following scenarios:

Table 3. Antibiotic Recommendation for Dental Prophylaxis Indicated by Surveyed Pediatric Dentistry Residency Program Directors and Pediatric Hematologists for Children With Sickle Cell Disease Undergoing Invasive Oral Surgery Procedure, on Daily Penicillin Prophylaxis Regimen*

Antibiotic	Pediatric dentistry residency program directors (n=20)	Pediatric hematologist (n=17)	Total responders (n=37)
Clindamycin	13 (65%)	0 (0%)	13 (35%)
Amoxicillin or penicillin	7 (35%)	17 (100%)	24 (65%)

* $P < .0001$; Fisher exact test.

Table 4. Antibiotic Recommendation for Dental Prophylaxis Indicated by Surveyed Pediatric Dentistry Residency Program Directors and Pediatric Hematologists for Children With Sickle Cell Disease, Penicillin Allergy, Undergoing Dental Procedures*

Antibiotic	Pediatric dentistry residency program directors (n=26)	Pediatric hematologist (n=41)	Total responders (n=67)
Clindamycin	23 (88%)	10 (24%)	33 (49%)
Erythromycin	3 (12%)	31 (76%)	34 (51%)

* $P < .0001$; chi-square test.

(1) dental extractions; (2) status post splenectomy; and (3) those needing treatment under general anesthesia. Only 25% recommend antibiotic prophylaxis for SCD patients younger than 2 (pre-pneumococcal vaccination) and 30% would use prophylaxis for SCD patients with a history of pneumococcal infection. The perceived risk of infectious complications was highest for extractions ($N=68/106$; 64%), followed by restorative treatment ($N=32/106$; 30%), and lastly for tooth polishing ($N=15/106$; 14%).

Respondents were asked open-ended questions; therefore, there was a wide range of protocols recommended. When recommending prophylaxis for dental procedures, 86% of pediatric dentistry residency program directors ($N=25/29$) chose amoxicillin as their preferred regimen of prophylaxis, whereas only 62% of the pediatric hematologists recommended amoxicillin ($N=36/58$; $P < .05$; Table 2).

There was a statistically significant difference between the pediatric dentistry residency program directors' and the hematologist's recommendations for management of the SCD patient needing invasive oral surgical procedures on a daily penicillin prophylaxis regimen. The pediatric dentistry residency program directors were more likely (71%, $N=24/34$) to recommend additional antibiotic prophylaxis for patients on penicillin prophylaxis requiring invasive oral surgical procedures. Only 38% ($N=25/66$) of pediatric hematologists, however, recommended additional antibiotics ($P = .001$). There was a statistically significant difference in the choice of drug recommended for SCD

patients receiving daily penicillin prophylaxis when dental residency program directors were compared to pediatric hematologists (Table 3). Sixty-five percent ($N=13/20$) of pediatric dentistry residency program directors recommended additional clindamycin, while none of the pediatric hematologists recommended clindamycin. The drug chosen by 71% ($N=12/17$) of pediatric hematologists was additional amoxicillin.

Evaluating dental residency program directors separately from pediatric hematologists, there was a statistically significant difference in the choice of drug recommended for those SCD patients with penicillin allergy ($P < .0001$; Table 4) Eighty-eight percent ($N=23/26$) of dental residency program directors recommended clindamycin, while only 10% of pediatric hematologists recommended clindamycin. The drug chosen by 76% ($N=31/41$) of pediatric hematologists was erythromycin.

To determine the perceived infectious risk for SCD children, the clinicians were asked to define the primary negative outcome they were trying to prevent by giving antibiotic prophylaxis. Eighty-two percent of the pediatric dentistry residency program directors ($N=28/34$) ascribed the primary risk to generalized systemic infection vs 63% of pediatric hematologists ($N=43/68$). This was a statistically significant difference ($P = .02$). Seventy-two percent of the pediatric hematologists ($N=49/68$) ascribed the primary infectious risk to endocarditis compared to 21% of the dental residency program directors ($N=7/31$; $P < .01$).

Discussion

Antibiotic prophylaxis to prevent systemic infection and/or bacterial endocarditis in at-risk patients undergoing invasive dental procedures has become an accepted standard of care, despite lack of controlled studies substantiating effectiveness or risks/benefits.⁶ The National Institutes of Health recommend standard antibiotic prophylaxis be used to cover SCD children undergoing dental procedures such as extractions and root canal therapy.⁷ It is known that a variety of dental procedures cause bacteremia. De Leo showed dental prophylaxis (cleanings) resulted in bacteremia, mainly diphtheroids species, in 28% of cases.² A total of 257 children treated with dental filling showed a 31% positive prevalence of blood cultures was baseline.⁸ Bacteremia was noted in 43% to 54% of children undergoing dental extractions ranging from simple 1-tooth to multiple-teeth extractions.⁹

In a study of pediatric cardiac patients receiving prophylactic penicillin, streptococcal species accounted for over half the aerobic bacteria isolated from blood cultures postdental extraction.⁴ Although the American Heart Association (AHA) has established guidelines recommending amoxicillin for the antibiotic prophylaxis of patients at risk for endocarditis, this study's respondents varied in their choice of antibiotic prophylaxis.¹⁰ There was a statistically significant difference between pediatric dentistry residency program directors and pediatric hematologists in the choice

of drug recommended for antibiotic prophylaxis. The pediatric dentistry residency program directors were significantly more likely to recommend additional prophylaxis for those patients on daily penicillin prophylaxis.

Evaluating pediatric dentistry residency program directors separately from pediatric hematologists, there was a statistically significant difference in the choice of drug recommended for those SCD patients with penicillin allergy. The majority of dental residency program directors recommended clindamycin, while only 10% of the pediatric hematologists recommended clindamycin, which is the drug recommended by the current AHA guidelines for prevention of endocarditis.¹⁰ Erythromycin is recommended for daily antibiotic therapy in SCD patients with penicillin allergy.¹ Perhaps this explains the hematologist's preference to use erythromycin instead of clindamycin, as recommended by the AHA guidelines.

A statistically significant difference was found in ascribing the primary infectious risk for patients with SCD undergoing dental treatment was found. The majority of the pediatric dentistry residency program directors ascribed the primary risk to general systemic infection, whereas the majority of the pediatric hematologists ascribed the primary infectious risk specifically to endocarditis. This difference may explain the lack of consensus on antibiotic choices, since the pediatric hematologists concerned about endocarditis chose the regimen recommended by the AHA for "cardiac" patients. Further studies need to be done to assess the true risk of endocarditis and/or systemic infection in SCD children during dental treatments.

The perceived risk of infectious complications was reported to be most for SCD children needing dental extractions, followed by restorative treatment and then tooth polishing. The pediatric dental residency program directors were more likely to recommend additional antibiotic therapy for patients on penicillin prophylaxis requiring invasive oral surgical procedures, compared to pediatric hematologists. The majority of pediatric dentistry residency program directors attributed the need for additional antibiotic therapy to the risk of systemic infection, whereas the majority of pediatric hematologists felt the greatest risk was bacterial endocarditis.

Definitive guidelines regarding SCD patient prophylaxis are lacking. This survey confirms the wide range of responses among pediatric hematologists and pediatric dentistry residency program directors. Although the actual incidence of bacterial complications in SCD children following dental procedures is not known, it is reasonable to assume it would be at least equal to or greater than that of the general population due to the known immunologic defects found in SCD children. Only scientific analysis of the incidence of infectious complications for SCD children undergoing dental procedures and a risk/benefit assessment can lead to a unified approach in the management of SCD children undergoing dental treatment.

Conclusions

Based on this study's results, the following conclusions can be made:

1. Although there was a wide range of responses, at least 50% of respondents would recommend prophylaxis for the following patients:
 - a. sickle cell disease (SCD) patients needing dental extractions;
 - b. splenectomized patients; and
 - c. those needing treatment under general anesthesia.
2. Perceived risk of infectious complication was highest for SCD children needing dental extractions, followed by restorative treatment, and then tooth polishing.
3. The pediatric dentistry residency program directors were more likely to recommend additional antibiotic prophylaxis for patients on daily penicillin requiring invasive oral surgical procedures, compared to pediatric hematologists.
4. The majority of pediatric dentistry residency program directors indicated that the primary risk to SCD patients undergoing dental procedures was generalized systemic infection, whereas the majority of pediatric hematologists felt the primary risk was endocarditis.

References

1. Gaston MH, Verter JI, Woods G, et al. Prophylaxis with oral penicillin in children with sickle cell anemia. A randomized study. *N Engl J Med.* 1986;314:1593-1599.
2. DeLeo AA, Schoenknecht FD, Anderson MW, Peterson JC. The incidence of bacteremia following oral prophylaxis on pediatric patients. *Oral Surg* 1974;37:36-45.
3. Falletta JM, Woods RM, Verter JI, et al. Discontinuing penicillin prophylaxis in children with sickle cell anemia. *J Pediatr* 1995;127:685-690.
4. Hess J, Holloway Y, Dankert J. Incidence of post extraction bacteremia under penicillin cover in children with cardiac disease: *Pediatrics* 1983;71:554-558.
5. American Academy of Pediatric Dentistry Web site. Pediatric Dentistry Residency Programs Section. Available at: www.aapd.org/training. Accessed February 19, 2003.
6. Acs G, Cozzi E. Antibiotic prophylaxis for patients with hydrocephalus shunts: A survey of pediatric dentistry and neurosurgery program directors. *Pediatr Dent* 1992;14:246-250.
7. National Institutes of Health. The management of sickle cell disease. NIH publication no. 02-2117. Bethesda, Md: NIH; 2002.
8. Roberts GJ, Gardner P, Longhurst P, Black AE, Lucas VS. Intensity of bacteraemia associated with conservative dental procedures in children. *Br Dent* 2000;188:95-98.
9. Roberts GJ. Bacteremia of dental origin and antimicrobial sensitivity following oral surgical procedures in children. *Pediatrics* 1998;20:28-36.
10. Dajani AS, et al. Prevention of bacterial endocarditis: Recommendations by the American Heart Association. *J Am Dent Assoc* 1997;128:1142-1151.