

# Physicians' Perceptions of Factors Influencing Adherence to Antibiotic Prophylaxis in Children with Sickle Cell Disease

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## ABSTRACT

**Background:** Children with sickle cell disease (SCD) aged <5 years are at great risk for invasive infection with *Staphylococcus pneumoniae* and *Haemophilus influenzae* due to the inability of their spleen to protect against infection.

**Objectives:** This study examined (1) physicians' perceptions of factors associated with adherence to antibiotic prophylaxis in children with SCD and (2) how physician characteristics are associated with these perceptions.

**Methods:** A MEDLINE search of the years 1996 to 2002, using the terms *sickle cell disease*, *compliance*, *children*, *physician perceptions*, and *antibiotic prophylaxis*, was done. A survey was developed using existing literature to assess physicians' perceptions of factors associated with adherence to antibiotic prophylaxis for SCD. The survey was sent to a stratified random sample of 375 pediatricians and all 125 practicing hematologists in North Carolina. They were given a Likert-type scale to assess their perceptions of factors that influence patients' adherence to antibiotic prophylaxis for SCD. Physician demographic information was collected using the *North Carolina Health Professions Data Book*. The demographic information was matched to the survey respondent and correlated with his or her responses.

**Results:** The response rate was 56.9%. Of the respondents, 60.9% were pediatricians, and 56.5% were in a practice with at least 1 patient aged <5 years with SCD. Physician race and practice specialty were significantly associated with factors physicians considered very important to adherence.

**Conclusions:** Most physicians agree on many issues that affect adherence; however, significant and important differences exist, based on physician ethnicity. Physicians' perceptions of factors that affect adherence in this study did not always agree with factors demonstrated to actually affect adherence in SCD patients. Therefore, this study indicates a need for physician continuing-education programs that focus on factors that actually influence adherence of

antibiotic prophylaxis and the racial/ethnic backgrounds of the providers in relation to the patient. (*Curr Ther Res Clin Exp.* 2003;64:116–126) Copyright © 2003 Excerpta Medica, Inc.

**Key words:** sickle cell disease, adherence, physician perceptions, antibiotics.

## INTRODUCTION

Sickle cell disease (SCD) is potentially fatal and affects 1 in 375 black children.<sup>1</sup> Although blacks are most at risk for the disease, individuals from the Caribbean, Central America, parts of South America, Turkey, Greece, Italy, the Middle East, and East India also may be at risk.<sup>1</sup> SCD is an inherited disorder in which the hemoglobin of the red blood cells is shaped like a sickle, resulting in blockage of blood flow that can damage tissue.

Children with SCD aged <5 years are at great risk for invasive infection with *Staphylococcus pneumoniae* and *Haemophilus influenzae* due to the inability of their spleen to protect against infection.<sup>2</sup> Randomized, controlled trials have demonstrated that a twice-daily dosage of penicillin given prophylactically until age 5 years reduces the incidence of septicemia by 84%.<sup>3</sup> Studies<sup>4–6</sup> have indicated that adherence of patients with SCD to antibiotic prophylaxis is typically less than optimal. In a study by Teach et al,<sup>4</sup> fewer than half (43.1%) of patients with SCD were compliant with the recommended penicillin prophylaxis. A pilot study by the US Food and Drug Administration<sup>6</sup> showed that 16% to 20% of patients with SCD aged <5 years showed poor compliance.

Patients do not adhere to their medication regimens for many reasons. More than 200 factors that can influence adherence have been cited in the literature.<sup>7</sup> It is difficult to predict adherence using strictly demographic characteristics, such as patient age, sex, education, socioeconomic status, and ethnicity.<sup>8</sup> Other factors, such as the impact of the medication on the patient's lifestyle and the characteristics of the drug regimen (eg, twice-daily dosing), are important potential contributors to nonadherence.<sup>9</sup>

Social support and the availability of family and friends to assist with or supervise medication administration have been found to improve medication adherence in general.<sup>10,11</sup> Patient-physician interaction can also impact adherence; physicians often fail to clearly state the precise medication regimen or to explain the directions in lay terms.<sup>8</sup> Patient dissatisfaction with medical care, which can result from poor physician-patient communication, long waiting periods, and having to see a number of different physicians, can also be related to adherence.<sup>12</sup>

It is unclear whether factors that affect medication adherence in general also affect adherence to antibiotic prophylaxis in patients with SCD. Several studies have assessed specific issues related to adherence to antibiotic prophylaxis in patients with SCD. A study examining the relationship between adherence, treatment attitudes, and illness-related family stress among pediatric patients

with SCD found considerable doubt about the helpfulness of treatment and fears that the therapy might be harmful.<sup>13</sup> Davis<sup>6</sup> speculates that poor compliance with antibiotic prophylaxis for SCD could be due to parents not having or forgetting to give the medication.

To date, physicians' perceptions of factors associated with patients' adherence to antibiotic prophylaxis for SCD have not been assessed. It is important to better understand physicians' perceptions of the factors that influence adherence to antibiotic prophylaxis for SCD. This information could be compared with the findings of studies<sup>6</sup> that examined what actually influenced these patients to adhere to antibiotic prophylaxis to assess whether physicians' perceptions are correlated with actual adherence factors. Whether physicians with different demographic characteristics have varying beliefs about what factors influence adherence to antibiotic prophylaxis for SCD also needs to be examined, so that educational programs can be targeted to specific groups of physicians.

The purpose of this study was to examine physicians' perceptions of factors that contribute to patients' adherence to antibiotic prophylaxis and physician characteristics that are associated with their perceptions of factors that contribute to patients' adherence to antibiotic prophylaxis for SCD.

## **MATERIALS AND METHODS**

This study was a cross-sectional survey of hematologists and pediatricians in North Carolina. Information on the providers was obtained from the *North Carolina Health Professions Data Book*.<sup>14</sup> The demographic information was matched to the survey respondent and correlated with his or her responses. Our survey assessed physicians' perceptions of factors important to adherence to antibiotic prophylaxis. A MEDLINE search of the years 1996 to 2002, using the terms *sickle cell disease, compliance, children, physician perceptions, and antibiotic prophylaxis*, was done. The survey was developed using literature assessing adherence to antibiotic prophylaxis in patients with SCD<sup>13,15</sup> and general medication adherence.<sup>11,12</sup> A Likert-type scale, which consisted of 13 items (described later) relating to SCD and adherence to antibiotic prophylaxis, was included in the survey.

After obtaining an institutional review board exemption (because patient identifiers were not being recorded), the survey was pretested on 3 physicians (a hematologist, a pediatrician, and a general practitioner) and was subsequently modified for clarity. The survey was sent to 500 physicians: all 125 hematologists practicing in North Carolina and a stratified random sample of 375 pediatricians. The sampling frame included all pediatricians who practiced in a North Carolina county in which >20% of the population was nonwhite, to target physicians who were most likely to have cared for patients with SCD. Four weeks after the survey was mailed, it was sent again to nonresponders. A monetary incentive of \$1 was included with the survey to improve the response rate.<sup>16</sup>

## Measures

Physician characteristics included sex, race, age, practice setting, practice specialty, number of patients aged <5 years with SCD in practice, and duration of practice. Physician sex, race (nonwhite or white), and practice specialty (eg, pediatrics and hematology) were measured as dichotomous variables. Practice setting was measured as a categorical variable (group practice, medical school or university, hospital, other, and unknown). Number of patients aged <5 years with SCD in practice and duration of practice were measured as continuous variables. Some physician demographic information, such as sex, race, and age, was obtained from the *North Carolina Health Professions Data Book*,<sup>14</sup> whereas other demographic information was obtained from the survey.

Physicians were first asked about their demographic characteristics and whether they provide care to patients aged <5 years with SCD. Physicians who provided care to such patients were asked their perceptions about whether the following 13 factors influenced patients' adherence to antibiotic prophylaxis for SCD: family knowledge of the disease, physician explanation of the disease, physician explanation of medication directions, social support, family forgetting to give the child the medication, receiving guidance from an SCD counselor, family understanding of the importance of the therapy, patient satisfaction with medical care, length of the physician-patient relationship, pharmacist explanation of medication directions, family doubt of the helpfulness of the therapy, access to prescription medications, and family fearing the therapy is harmful. Physicians were asked to rate their perceptions of the importance of each factor on adherence using a Likert-type scale (very important, somewhat important, or not important).

## Statistical Analysis

The survey data were analyzed using Statistical Package for Social Sciences software version 10 (SPSS Inc., Chicago, Illinois). Bivariate analyses were used to determine the possible relationship between factors that physicians perceived to be the most influential on adherence and physicians' demographic characteristics. Correlations were performed for continuous variables, and chi-square tests were performed for categorical variables.

## RESULTS

Of the 500 surveys mailed, 64 (50 pediatricians and 14 hematologists) were returned and discarded because of incorrect addresses. A total of 248 responses were received (overall response rate, 56.9%). Of the respondents, 60.9% were pediatricians. Among these, the response rate was 58.8% ( $n = 191$ ); among hematologists, the response rate was 51.4% ( $n = 57$ ). The characteristics of the respondents are shown in Table I. The majority of respondents were male (56.9%), white (81.0%), aged 30 to 76 years (mean [SD] age, 47 [9.4] years), and specialized in pediatrics (60.9%). The characteristics of the respondents and nonrespondents were not significantly different. More than half (65.5% [140/248]) of the responding physicians cared for patients aged <5 years with SCD.

**Table I.** Demographic characteristics of the respondents (N = 248).\*

| Characteristic  | Data        |
|---|-------------|
| Sex, no. (%) of responders  |             |
| Men   | 141 (56.9)  |
| Women   | 101 (40.7)  |
| Unknown   | 6 (2.4)     |
| Race, no. (%) of responders   |             |
| White   | 201 (81.0)  |
| Black   | 11 (4.4)    |
| Asian   | 15 (6.0)    |
| Other   | 15 (6.0)    |
| Unknown   | 6 (2.4)     |
| Age, y  |             |
| Mean (SD)   | 47 (9.4)    |
| Range   | 30–76       |
| Practice setting, no. (%) of responders                               |             |
| Group practice  | 75 (30.2)   |
| Medical school or university  | 29 (11.7)   |
| Hospital  | 23 (9.3)    |
| Other   | 30 (12.1)   |
| Unknown   | 91 (36.7)   |
| Practice specialty, no. (%) of responders                             |             |
| Pediatrics  | 151 (60.9)  |
| Hematology  | 48 (19.4)   |
| Other   | 28 (11.3)   |
| Unknown   | 21 (8.5)    |
| No. of patients aged <5 years with SCD seen in practice, <sup>†</sup> |             |
| no. (%) of responders   |             |
| 0   | 76 (30.6)   |
| 1–2   | 35 (14.1)   |
| 3–5   | 34 (13.7)   |
| 6–15  | 31 (12.5)   |
| ≥16   | 40 (16.1)   |
| Mean (SD)   | 14.9 (45.5) |
| Range   | 0–500       |
| Duration of practice, y   |             |
| Mean (SD)   | 13.8 (9.5)  |
| Range   | 1–48        |

SCD = sickle cell disease.

\*Percentages may not total 100% due to rounding.

<sup>†</sup>Data unavailable for 32 (12.9%) respondents, who did not answer this question on the survey.

Physician responses to factors influencing patients' adherence to antibiotic prophylaxis are shown in Table II, which contains data only from physicians who indicated that they provided care to patients with SCD. The majority of physicians thought that family knowledge of SCD (85.2%), physician explanation of the disease (76.5%), physician explanation of medication directions (71.8%), social support (71.1%), and receiving guidance from an SCD counselor (59.7%) were very important factors influencing adherence to antibiotic prophylaxis. Of the responding physicians, 48.3%, 40.9%, and 40.3%, respectively, thought that patient satisfaction with medical care, length of physician-patient relationship, and pharmacist explanation of medication directions were very important factors influencing adherence to antibiotic prophylaxis. Six percent of physicians indicated that fear of the therapy was a very important influence on their patients' adherence to medications, and 58.4% believed that it was not important. A total of 20.8% of physicians thought that family doubt about the helpfulness of antibiotic prophylaxis was a very important factor in adherence. Furthermore, the majority of physicians thought that family understanding of the importance of antibiotic prophylaxis (57.0%) and family forgetting to give the child the medication (67.1%) were very important factors influencing adherence to antibiotic prophylaxis (Table II). A total of 40.9% of physicians did not consider difficulty getting access to prescription medication an important factor contributing to adherence, and 58.4% of physicians thought that family fearing the therapy is harmful was not an important factor contributing to adherence.

Physicians' characteristics that were significantly related to their beliefs about influences on patients' adherence to antibiotic prophylaxis are shown in Table III, which contains data only from physicians who indicated that they provided care to patients with SCD. Nonwhite physicians were significantly more likely than were white physicians to perceive social support ( $P = 0.041$ ), family doubt of the helpfulness of therapy ( $P < 0.001$ ), receiving guidance from an SCD counselor ( $P = 0.015$ ), and family fearing that antibiotic prophylaxis is harmful ( $P < 0.001$ ) as very important factors influencing adherence to antibiotic prophylaxis. Hematologists were significantly more likely than pediatricians to believe that social support was an important influence ( $P = 0.044$ ).

Female physicians were more likely than were male physicians to think that family knowledge of SCD was a very important influence on adherence ( $P = 0.006$ ). Practice specialty was associated with whether physicians believed that the family forgetting to give the child the medication was important to adherence; pediatricians were more likely than were hematologists to perceive this factor as very important ( $P = 0.022$ ). Practice specialty also was associated with whether physicians believed that social support was a very important factor in adherence; hematologists were more likely than were pediatricians to believe that this factor was very important ( $P = 0.044$ ). Physician age, years in practice, and practice setting did not significantly influence physician beliefs about influences on adherence of patients with SCD to antibiotic prophylaxis.

**Table II.** Physicians' perceptions (no. [%]) of factors influencing patient adherence (n = 149).\*†

| Factor   | Very Important | Somewhat Important | Not Important | Data Not Available |
|--|----------------|--------------------|---------------|--------------------|
| Family knowledge of SCD  | 127 (85.2)     | 9 (6.0)            | 0 (0.0)       | 13 (8.7)           |
| Physician explanation of SCD                                     | 114 (76.5)     | 19 (12.8)          | 1 (0.7)       | 15 (10.1)          |
| Physician explanation of medication directions                   | 107 (71.8)     | 26 (17.4)          | 2 (1.3)       | 14 (9.4)           |
| Social support   | 106 (71.1)     | 29 (19.5)          | 0 (0.0)       | 14 (9.4)           |
| Family forgetting to give the child the medication               | 100 (67.1)     | 34 (22.8)          | 2 (1.3)       | 13 (8.7)           |
| Receiving guidance from an SCD counselor                         | 89 (59.7)      | 43 (28.9)          | 2 (1.3)       | 15 (10.1)          |
| Family understanding of the importance of antibiotic prophylaxis | 85 (57.0)      | 47 (31.5)          | 4 (2.7)       | 13 (8.7)           |
| Patient satisfaction with medical care                           | 72 (48.3)      | 60 (40.3)          | 3 (2.0)       | 14 (9.4)           |
| Length of physician-patient relationship                         | 61 (40.9)      | 68 (45.6)          | 6 (4.0)       | 14 (9.4)           |
| Pharmacist explanation of medication directions                  | 60 (40.3)      | 62 (41.6)          | 11 (7.4)      | 16 (10.7)          |
| Family doubt of the helpfulness of therapy                       | 31 (20.8)      | 71 (47.7)          | 34 (22.8)     | 13 (8.7)           |
| Difficulty getting access to the prescription medication         | 22 (14.8)      | 54 (36.2)          | 61 (40.9)     | 12 (8.1)           |
| Family fearing the therapy is harmful                            | 9 (6.0)        | 40 (26.8)          | 87 (58.4)     | 13 (8.7)           |

SCD = sickle cell disease.

\*Percentages may not total 100% due to rounding.

†Ninety-nine respondents were excluded from this table because they indicated that they did not provide care to patients with sickle cell disease.

**Table III.** Significant physician characteristics (no. [%]) associated with perceptions of factors important to adherence (n = 149).\*

| Adherence Factor                                      | Physician Race <sup>†</sup> |                        | P      |
|---|-----------------------------|------------------------|--------|
|   | Nonwhite<br>(n = 118)       | White<br>(n = 28)      |        |
| Social support  | 113 (95.7)                  | 20 (71.4)              | 0.041  |
| Family doubt of the helpfulness of therapy            | 109 (92.3)                  | 20 (71.4)              | <0.001 |
| Receiving guidance from an SCD counselor              | 100 (84.7)                  | 17 (60.7)              | 0.015  |
| Family fearing that antibiotic prophylaxis is harmful | 65 (55.1)                   | 28 (100.0)             | <0.001 |
| Adherence Factor                                      | Physician Sex <sup>†</sup>  |                        | P      |
|   | Male<br>(n = 84)            | Female<br>(n = 62)     |        |
| Family knowledge of SCD                               | 74 (88.0)                   | 62 (100.0)             | 0.006  |
| Adherence Factor                                      | Practice Specialty          |                        | P      |
|   | Pediatrics<br>(n = 119)     | Hematology<br>(n = 30) |        |
| Family forgetting to give the child the medication    | 118 (99.1)                  | 28 (93.3)              | 0.022  |
| Social support  | 88 (74.3)                   | 30 (100.0)             | 0.044  |

SCD = sickle cell disease.

\*Ninety-nine respondents were excluded from this table because they indicated that they did not provide care to patients with SCD.

<sup>†</sup>The race and sex of 3 respondents was unknown; thus, these respondents were excluded from this part of the analysis.

## DISCUSSION

This study sought to examine physicians' perceptions of factors that contribute to a patient's adherence to antibiotic prophylaxis and the physician characteristics that are associated with these factors. Physicians' knowledge of situations that affect adherence may be beneficial in creating better educational programs, resulting in their ability to help patients increase their adherence to antibiotic prophylaxis for SCD.

Patients' satisfaction with medical care has been found to be associated with increased adherence to a pediatric asthma medication regimen.<sup>11</sup> In the current study, 48.3% of physicians thought that patient satisfaction was a very important factor contributing to their adherence to antibiotic prophylaxis. Future studies need to assess whether patient satisfaction plays a role in such compliance. Until those studies have been done, physicians should recognize that patient satisfaction with medical care may be an important influence on patients' adherence to antibiotic prophylaxis.

Only 6.0% of physicians indicated that fear that the therapy might be harmful was a very important influence on their patients' adherence to medications,



and 58.4% believed that it was not. In our study, only 20.8% of physicians thought that family doubt about the helpfulness of antibiotic prophylaxis was an important factor in adherence. Thus, there may be a need for educational programs targeted to physicians that focus on family perceptions of therapy.

Physicians' race was significantly associated with whether they believed that family fearing the antibiotic prophylaxis is harmful and doubting the helpfulness of the therapy influenced adherence. Nonwhite physicians were more likely than were white physicians to believe that family fears and doubts were important factors contributing to adherence. Because of their similar backgrounds, nonwhite physicians may be more aware of their nonwhite patients' fears and doubts.<sup>17</sup> Perhaps continuing-education programs that focus on cultural awareness, medication adherence, and SCD could be developed and targeted to white physicians who provide care to patients with SCD.

Studies<sup>10,11</sup> have shown that social support has been associated with increased adherence to medication regimens. In our study, 71.1% of the physicians surveyed thought that social support was a very important influence on patients' adherence to antibiotic prophylaxis, with hematologists being significantly more likely than pediatricians to believe this ( $P = 0.044$ ). Nonwhite physicians were significantly more likely to believe that social support was an important influence on patients' adherence to antibiotic prophylaxis than were white physicians. This finding provides further evidence that, if white physicians who provide care to patients with SCD were to become more aware of the cultural backgrounds and situations of their patients, they might be able to improve patients' adherence to antibiotic prophylaxis for SCD.

Davis<sup>6</sup> speculated that decreased adherence to antibiotic prophylaxis may be due to parents' not having antibiotics or forgetting to give them. In a study assessing compliance with penicillin prophylaxis among patients with SCD, Elliott et al<sup>15</sup> found that burdens of compliance (obtaining refills and remembering to give a child medication) were important predictors of compliance with antibiotic prophylaxis. In our study, although 67.1% of physicians thought that family forgetfulness was a very important influence on adherence to antibiotic prophylaxis, only 14.8% of physicians believed that difficulty getting access to prescription medication was a very important influence on adherence to antibiotic prophylaxis. This finding illustrates the need for physicians to better communicate with the families of patients with SCD about medication access. Physicians could work with local pharmacies, SCD counselors, and other agencies to reduce patient barriers to obtaining prophylactic antibiotics. In our study, 59.7% of physicians believed that receiving guidance from an SCD counselor was a very important influence on adherence, and 40.3% believed that pharmacist explanation of medication directions was a very important influence on adherence.

Future research should address issues in the home to determine the reasons why patients are nonadherent to antibiotic prophylaxis. Studies also need to focus on adherence to antibiotic prophylaxis from the perspective of the family and patient. Elliott et al<sup>15</sup> studied some of the factors in the home and parental

perceptions that relate to adherence to penicillin prophylaxis. The authors found that patients' self-report was not a good measure of adherence and suggest that pharmacy records would serve as a better way to detect it. Furthermore, the problem of measuring adherence should be addressed; future research should compare physicians' and patients' estimates of adherence with pharmacy records. A collaborative effort between physicians, pharmacists, and families of children with SCD might be effective in ascertaining and improving adherence and might be the best way to achieve optimal patient care.

This study has several limitations, one of which was that the survey population consisted mostly of pediatricians who practiced in an area where >20% of the population is nonwhite. By limiting the sample population in this way, some of the physicians who provide care to patients with SCD may have been missed. The characteristics of such providers may have differed from those of the providers we surveyed. However, this strategy is also a strength because it is likely that providers who see more patients with SCD were captured due to the higher percentage of nonwhites in the county population.

Although the response rate of 56.9% in this study is less than ideal, it exceeds the mean response rate of other published physician surveys (54%).<sup>18</sup> Although it is likely that physicians who responded saw more patients with SCD than those who did not respond, this could not be measured; therefore, nonresponse bias may have been introduced into the study. However, for factors that could be assessed, no significant differences were found between respondents and nonrespondents.

In using a cross-sectional study design, it is difficult to assess causal relationships between factors in the study. We could not assess the physicians' perceptions of each individual patient's factors related to adherence. Even though this study design is limited, it provided us with an estimate of the physicians' characteristics associated with adherence.

## CONCLUSIONS

Most physicians agree on many issues that affect adherence; however, significant and important differences exist, based on physician ethnicity. Physicians' perceptions of factors that affect adherence in this study did not always agree with factors demonstrated to actually affect adherence in SCD patients. Therefore, this study indicates a need for physician continuing-education programs that focus on factors that actually influence adherence of antibiotic prophylaxis and the racial/ethnic backgrounds of the providers in relation to the patient.

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