Financial analysis of chronic transfusion for stroke prevention in sickle cell disease

Alan S. Wayne, Steve E. Schoenike, and Charles H. Pegelow

Chronic red blood cell transfusion can prevent many of the manifestations of sickle cell disease. The medical costs of chronic transfusion and management of associated side effects, especially iron overload, are considerable. This study was undertaken to evaluate the financial impact of chronic transfusion for stroke prevention in patients with sickle cell anemia. Outpatient charges pertaining to hospital-based Medicare uniform bill (UB-92) codes, professional fees, and iron chelation were evaluated. Data were collected on 21 patients for a total of 296 patient months (mean, 14; median, 14 months/patient). Charges ranged from $9828 to $50 852 per patient per year. UB-92, chelation, and physician-related charges accounted for 53%, 42%, and 5% of total charges, respectively. Of UB-92 charges, 58% were associated with laboratory fees and 16% were related to the processing and administration of blood. Charges for patients who required chelation therapy ranged from $31 143 to $50 852 per patient per year (mean, $39 779; median, $38 607). Deferoxamine accounted for 71% of chelation-related charges, which ranged from $12 719 to $24 845 per patient per year (mean, $20 514; median, $21 381). The financial impact of chronic transfusion therapy for sickle cell disease is substantial with charges approaching $400 000 per patient decade for patients who require deferoxamine chelation. These data should be considered in reference to cost and efficacy analyses of alternative therapies for sickle cell disease, such as allogeneic bone marrow transplantation. (Blood. 2000;96:2369-2372)

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Introduction

The medical care required for persons with sickle cell disease (SCD) has been recognized as a significant burden in regard to health care expenditures. Chronic transfusion therapy can prevent many of the complications of SCD, including stroke. Monthly red cell transfusion is required to adequately suppress hemoglobin-S production. With long-term administration, complications eventually develop, most notably iron overload that in turn requires treatment with deferoxamine (DFO) chelation. This approach to managing SCD, although effective, is expensive, and no systematic analysis of the costs of such management has been published. This study was undertaken to evaluate the financial impact of chronic transfusion therapy for stroke prevention in SCD.

Materials and methods

Patients

Study subjects included all patients with the diagnosis of sickle cell anemia who were receiving outpatient chronic transfusion therapy for stroke prevention at Jackson Children’s Hospital and at the University of Miami Division of Pediatric Hematology Oncology. Sixteen patients had experienced a prior stroke and 5 patients were enrolled in the Stroke Prevention (STOP) Trial in Sickle Cell Anemia. This study was approved by the institutional review board.

Data collection

A retrospective review was conducted for the period from January 1997 to April 1998. Outpatient hospital charges were generated from the hospital database, using Medicare uniform bill (UB-92) charge codes. All UB-92 charges were reviewed, and those charges related to emergency room visits, inpatient hospitalization, or management of comorbid conditions were excluded from the analysis. Monthly charges for chelation therapy were estimated, based on the prescribed patient dose for 30 days/month, DFO average wholesale price of $11.19/500 mg, and standard allowed fees for dispensing and home care administration based on State of Florida Agency for Health Care Administration Medicaid guidelines. Patient records were reviewed to verify the number of outpatient visits, DFO dose, and number of packed red blood cell units administered during the study period. Hematology attending physician charges were estimated by using a fee of $108 per clinic visit, which is the standard University of Miami professional charge for an established outpatient receiving the level of service provided (CPT code 99213).

Statistical analysis

Total patient charges for the study period were tabulated, and the percentage of expenditures was calculated by UB-92, chelation, and physician charge categories. Monthly patient charges were calculated as follows: Total UB-92 code charges ÷ number of data collection months, total physician charges ÷ number of data collection months, and DFO chelation-associated monthly charges.

Patient charges were analyzed in 3 groups: all patients, patients not receiving DFO chelation, and patients receiving DFO chelation. Charges were annualized and regressed by group against the variables of patient age, weight, annualized transfusion volume in units, and annualized DFO dose in grams. Parametric and nonparametric measures of association were calculated, using the methods of Pearson and Spearman. Descriptive statistics, analysis of variance, and regression calculations were performed, using SAS System for Windows (Release 6.12 SAS Institute Inc.).
Results

Patient and treatment characteristics

Data were collected on 21 patients for a total of 296 patient months (mean, 14; median, 14 months/patient; Table 1). Patient age ranged from 6 to 22 years (mean, 13; median, 14) and weight from 18 to 66 kg (mean, 42; median, 43). Patients received 1 to 3 units (mean, 2.5; median, 2.2) of packed red blood cells every 3 to 4 weeks as needed to maintain the hemoglobin-S level ≤30%. Red cell units were leukodepleted by filtration for 17 patients and by washing for the remaining 4. To decrease the risk of alloimmunization, the 19 patients with known red cell phenotype received blood matched for ABO, Rh(C, c, D, E, e), and Kell antigens. Routine laboratory studies performed at each visit included a complete blood count, reticulocyte count, type and crossmatch, and hemoglobin electrophoresis. In addition, chemistry panels with liver function tests and iron indices were monitored at least every 3 months. DFO chelation therapy was administered via nightly subcutaneous injection to 14 patients with confirmed iron overload in doses ranging from 750 to 2500 mg/day (mean, 43 mg/kg/day). Patients treated with DFO tended to be older, to weigh more, and to require larger transfusion volumes than those not on chelation therapy (Table 1).

Patient charges

Total charges for the 21 patients during the study period were $678,559 (Table 2). UB-92, chelation, and physician-related fees accounted for 53%, 42%, and 5% of the total charges, respectively. Of the UB-92 charges, 58% were associated with laboratory fees, 25% with chelation, and 16% were related to the processing and administration of blood. Physician fees were the smallest charge category, representing less than 10% of the total charges for each patient group.

Annualized charges for the 14 patients who received chelation therapy ranged from $31,143 to $50,852 per patient per year (mean, $39,779; median, $38,607) and were greater than those for the 7 patients not on DFO (range, $9828-$25,922; mean, $17,378; median, $19,652; \( P = .0001 \)). Charges related to iron chelation therapy ranged from $12,719 to $24,845 per patient per year (mean, $20,514; median, $21,381). Of chelation-related charges, 71% were associated with DFO and 29% with home health care services. Patient age, transfusion volume, and DFO dose were all strongly correlated with charges for those on chelation therapy (parametric correlation data not shown; Table 3).

Discussion

Survival in SCD has improved dramatically over the past decades because of the change in living conditions and improvements in supportive care. The current cost of care for individuals with SCD is substantial, varying with the severity of disease manifestations. A recent study by the National Association of Children’s Hospitals and Related Institutions (NACHRI) found that annual expenditures. The total direct yearly cost of hospitalization in the United States for children with SCD was estimated to be between $24,300,000 and $119,800,000 (in 1996 U.S. dollars) with an annualized figure of $70,000 per year. This figure amounted to 8.8 times the mean expenditure for all pediatric patients because of an increased frequency of certain

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<th>Table 2. Patient charges</th>
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<td>Total UB-92 charges</td>
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<td>UB-92-300 (lab)</td>
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<td>UB-92-391 (transfusion)</td>
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<td>Total charges</td>
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Data represent 1997-1998 U.S. dollars (%).
*Percentage of total charges.
†Percentage of UB-92 charges.

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<th>Table 3. Correlation analysis of patient variables with annualized charges</th>
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<td>Age (yr)</td>
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<td>Weight (kg)</td>
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<td>Blood transfused (units)</td>
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<td>DFO dose (grams)</td>
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Data represent Spearman correlation coefficients (probability).
complications as well as greater costs of treatments based on weight (eg, medications, transfusions). Notably, a study of adults with SCD found charges for health care use exceeded $100,000 per patient year (1991 U.S. dollars).1

Stroke, a frequent and devastating complication of SCD, has an estimated lifetime prevalence of 5%-17%.16-19 Children most commonly develop ischemic infarction because of occlusion of large cerebral blood vessels. Without chronic red cell transfusion, the risk of recurrent stroke is extremely high with reported prevalence rates of 50%-90%.5,16,20 Maintenance of the hemoglobin-S level below 30% with chronic transfusion dramatically decreases the recurrence risk to about 10%5,21; however, prolonged transfusion is required.21,22 Chronic transfusion has also been shown to prevent first-time strokes in pediatric patients at high risk.7

To our knowledge, an analysis of the cost of chronic transfusion therapy for preventing complications of SCD has not been previously reported. The median charge of approximately $40,000 per year for patients receiving chelation therapy is within the general range of data from the NACHRI14 and Washington State2 studies. Our data also correspond with previous estimates of the cost of chronic transfusion and DFO chelation for patients with homozygous beta-thalassemia and SCD that were believed to exceed $30,000 per patient year (1990 U.S. dollars).23,24

The true societal costs of this therapy are difficult to assess. Our data reflect patient charges rather than actual health care costs. At our institution, cost-to-charge ratios averaged 66% (range, 20%-184%) for services provided for similar patients (DRG 396) in fiscal year 1997 (data not shown). However, this study underestimates total patient charges for several reasons. The calculated charges include conservative professional fees and Medicaid reimbursement rates for chelation therapy below those customarily charged to private insurance carriers. Furthermore, we attempted to exclude health care services provided for comorbid conditions and restricted our analysis to those charges associated with the delivery of outpatient chronic transfusion therapy, treatment of overload, and monitoring for associated complications (eg, hepatic dysfunction).

Notably, approximately 30% of patient charges in this study were related to laboratory testing. Efforts to modify the frequency of laboratory monitoring for patients on chronic transfusion are likely to offer the greatest opportunity for cost containment in this setting. DFO accounted for 30% of total patient charges. Although charges were substantially lower for those who did not require chelation therapy, all patients who remain on chronic transfusions were expected to eventually need DFO. Although oral chelators may someday decrease the costs associated with combating iron overload, currently DFO is the only medication proven effective for the prevention and management of transfusional hemochromatosis. Exchange rather than simple transfusion can be employed to reduce iron accumulation, but this approach incurs the additional expense of apheresis.25 Ultimately, the most effective way to reduce costs would be to limit the duration of chronic transfusion therapy, stopping before iron chelation becomes necessary. However, at least for patients who have sustained a previous stroke, prolonged, possibly lifelong transfusion appears to be required.21,22

A modest cost reduction could be achieved by decreasing the volume of transfusion and allowing higher hemoglobin-S levels,26 although the long-term efficacy of this approach in preventing different complications of SCD is unknown. Finally, even though the specialized blood products employed for patients with SCD are more expensive than standard red cell units, their use decreases the incidence of a number of transfusion-associated complications that might otherwise increase future costs.3

The financial impact of transfusion therapy for SCD is substantial with charges approaching $400,000 per patient decade. Furthermore, the benefits of chronic transfusion are not permanent, and toxicity can limit long-term effectiveness. These factors should be considered in reference to cost and efficacy analyses of alternative therapies for SCD, such as hydroxyurea27,28 and allogeneic bone marrow transplantation.29

Acknowledgments

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