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Preoperative Use of Erythropoietin in an Adolescent Jehovah's Witness

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Strategies used increasingly to avoid heterologous blood transfusion in the operating room include autologous transfusion, directed donor transfusion, intraoperative cell salvage, and hemodilution. Patients who are Jehovah's Witnesses will not accept heterologous transfusions on religious grounds.[1] Some Jehovah's Witnesses will accept intraoperative hemodilution and cell salvage as long as the blood remains in a circuit that is always connected to the patient. The problems of Jehovah's Witnesses are magnified in children who require major elective procedures entailing significant blood loss. While the courts will act to intervene and order transfusions in a life-threatening emergency, they have not done so in elective situations. Undertaking a major elective procedure without the use of heterologous blood may place the child at risk after the procedure is started or in the postoperative period.

Within the last several years, recombinant DNA technology has produced synthetic human erythropoietin that has provided a means to increase red cell production and red cell mass in severely anemic patients.[2] The most common use for the drug has been in treating anemia associated with renal failure.[3]

We report the preoperative use of recombinant DNA erythropoietin in an adolescent of the Jehovah's Witness faith who required placement of Cotrel-Dubousset rods for correction of scoliosis.

CASE REPORT

The patient was a 14-yr-old, 40-kg girl with progressive scoliosis. Her curvature was 42 degrees. Past medical history was significant for mitral valve prolapse and infrequent bouts of asthma. Pulmonary function study results obtained 6 weeks before surgery demonstrated mild peripheral airway obstruction (decreased forced expiratory flow at 25–75% vital capacity) and hyperinflation (increased functional residual capacity). Her hematocrit had been 39.5% 2 months prior to surgery. Initial discussions with the family revealed that her parents would accept hemodilution and use of cell salvage, but they adamantly refused to allow heterologous blood transfusion and would not permit the surgery to go ahead if transfusion was contemplated. With this background, and with the family's consent, we began erythropoietin (Epogen™, Amgen Inc.) administration to increase the patient's hematocrit before surgery. She was given 100 units/kg, subcutaneously, two to three times/week with iron supplements. She was treated with erythropoietin for 7 weeks (total of 15 doses), at which time her hematocrit increased to 47%, and surgery was scheduled. Her blood pressure at the start of treatment was 106/68 mmHg and was unchanged during the course of therapy. No side-effects of treatment were observed. The increase in hematocrit is shown in the table 1. The delay in response to erythropoietin was due to the patient not taking her iron supplements at the beginning of therapy.

On the day of surgery, she was given intramuscular morphine, glycopyrrolate, hydroxyzine, and inhaled metaproterenol preoperatively. An intravenous induction was carried out with thiopental sodium, fentanyl, and midazolam. Following induction of anesthesia, an 18-G catheter was inserted into the left radial artery. Tracheal intubation was facilitated with succinylcholine. A 4-Fr central venous catheter was inserted into the right external jugular vein. Two units of whole blood

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TABLE 1. Change in Hemoglobin, Hematocrit, and Reticulocytes with Erythropoietin Therapy

Date	Hgb (g/dl)	Hct (%)	Reticulocytes (%)	Comments
11/20	13.8	39.5		
12/04	13.6	38.9	2.2	Iron not taken
12/12	13.9	39.9	1.2	Iron, 200 mg TID taken daily
12/18	14.0	41.8	2.7	
12/27	15.0	44.6	2.1	
1/02	14.8	45.7		
1/09	15.9	47.0	4.4	
1/10	11.7	34.7		Day of surgery after hemodilution
1/10	13.6	40.1		End of surgery
1/11	11.6	35.5		1 day post operative
1/16	8.4	25.3	1.4	Prior to discharge

Hgb = hemoglobin.

were collected in CPD-A collection bags *via* the arterial catheter with simultaneous replacement with 2 l of Ringer's lactate solution. There were no changes in blood pressure or central venous pressure during hemodilution. Before disconnecting the blood collection bags from the arterial catheter, they were connected to the venous infusions and very slowly opened. After removal of the blood, her hematocrit was 34.7%. Anesthesia was continued with nitrous oxide, a fentanyl infusion, intermittent midazolam, and thiopental. Sodium nitroprusside was infused as needed to maintain arterial pressure at approximately 70 mmHg. Once the corrective rods were placed and decortication achieved, the patient's blood was reinfused. Immediately prior to infusion of blood, her hematocrit was 30%. One unit of salvaged blood was also transfused. During the reinfusion of blood, furosemide (15 mg) was administered in divided doses. She left the operating room with a hematocrit of 40.1%. One week later, she left the hospital with a hematocrit of 25.3%.

DISCUSSION

The dilemmas posed by surgery in Jehovah's Witnesses have been reviewed recently.[1] Whereas competent adults of this faith may freely refuse blood transfusions, the situation in children is more complex. In emergency situations, physicians may institute therapy, including transfusion of blood, to save a child's life despite parental objection. This position has been upheld by the courts. Courts have declined to exert their authority when the procedure is felt to be elective and non-life-threatening. A paradox is created here in that a deferred elective procedure may lead to a crippling or life-threatening condition in the future.

Erythropoietin is a sialoglycoprotein that is predominantly produced by the kidney and is the primary hormonal regulator of red cell hematopoiesis.[4,5] (In the fetus, this hormone is produced in the liver.[6]) Erythropoietin acts by promoting formation of red blood cell precursors, erythrocytic colony forming units, and normoblasts from more primitive pluripotential stem cells in the bone marrow. It is now commercially available as the result of recombinant DNA technology.[2] In the present case, the use of erythropoietin preoperatively allowed us to increase the patient's hematocrit above normal physiologic levels and augment her hemoglobin concentration by approximately 2 g/dl. Intraoperatively, blood conservation was aided by hemodilution and salvage of shed blood. Following surgery, blood loss continued *via* the drains, and she left the hospital with a hematocrit of 25.3%. Had she not received the erythropoietin, we estimate that her hematocrit at discharge would have been between 15 and 20%.

Erythropoietin therapy provides a way to increase hematocrit both in patients where the hematocrit is decreased because of disease, *e.g.*, chronic renal failure, and in some normal patients. Erythropoietin has been used in adult patients scheduled for elective orthopedic procedures to increase the amount of blood available for autologous transfusion and has been proposed for use in premature infants to correct the anemia of prematurity.[7,8] Autologous transfusion is not an option for Jehovah's Witnesses, nor is it an option in many children.[9] In these circumstances, erythropoietin has the potential for becoming a new and valuable tool. It should be noted that the presently available formulation of erythropoietin contains albumin, which our patient and her family accepted. It is expected that shortly a formulation will be available that does not contain albumin. This latter formulation would be of use if potential recipients object to the presence of this other protein.

Erythropoietin is not without its side-effects. In patients with renal failure, hypertension is the most common and disturbing side-effect of therapy.[3] Seizures also may occur. It is not known whether patients who do not have preexistent hypertension, as is seen in many patients with chronic renal failure, are equally at risk for developing severe hypertension with erythropoietin therapy.[7] The use of low-dose therapy may decrease the incidence of this complication.

As presently available, the drug costs $50 per 4,000 unit vial. In the present case, therapy cost $750. By comparison, for a patient in our hospital who receives a two-unit transfusion of either heterologous or autologous blood, the hospital charges would be approximately $300. (Many hospitals have additional charges for blood that is for autologous transfusion.) In nonanemic patients, it remains to be defined how high one can raise hematocrit preoperatively, how rapidly the rise can be accomplished, what the optimal dose of the drug is, and what is the best route of administration.

In summary, we reported the use of erythropoietin preoperatively in an adolescent Jehovah's Witness to augment red cell mass prior to surgical repair of scoliosis.

The drug may be of particular benefit in children when autologous donation and subsequent transfusion is not possible, and when heterologous transfusion is to be avoided. The optimal dose of the drug will need to be defined in this population where anemia is not the reason for its use.

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Anesthetic Implications of Relapsing Polychondritis: A Case Report

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Relapsing polychondritis is a rare inflammatory disorder of uncertain etiology. It is characterized by progressive destruction of cartilaginous structures.[1,2] Presenting symptoms are variable, but frequently involve inflammation and destruction of the ears, nasal cartilage, and ocular and tracheobronchial support structures. Symptomatic tracheobronchial involvement is a poor prognostic indicator and frequently represents significant intra- and extrathoracic tracheal obstruction. In this report, we present the details surrounding the anesthetic management of a patient with relapsing polychondritis and provide a review of the current literature.

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Case Report

A 34-yr-old white man, who weighed 74 kg and was 175 cm tall, had a history of relapsing polychondritis and was referred to our service for preoperative consultation before elective reconstructive surgery of his saddle-nose deformity. Relapsing polychondritis was diagnosed at age 23 yr and had been well controlled with intermittent steroid and azathioprine therapy. His disease remained in remission during treatment with oral prednisone, 17.5 mg once daily. His medical history was significant for severe dyspnea on strenuous exertion (running), tolerance of lower levels of activity (swimming), and bilateral hearing loss. One year earlier, he was hospitalized with stridorous respirations and wheezing associated with an upper respiratory tract infection.

Previous evaluation (February 1988) of his pulmonary function revealed a pattern consistent with severe obstruction. His vital capacity was 4.25 l, 82% of predicted, and forced volume in 1 s 1.58 l, 49% of predicted. The flow-volume loop (fig. 1) was consistent with a fixed airflow obstruction (tracheal stenosis), with limitation of air flow during both phases of the ventilatory cycle. Maximal voluntary ventilation was severely reduced, measuring 34% of predicted. Computerized tomography of the cervical and thoracic regions showed normal airway caliber without evidence of an obstructing mass or stenosis. Fiberoptic bronchoscopy revealed severe tracheomalacia with dynamic extrathoracic tracheal collapse on inspiration, and dynamic intrathoracic tracheal and left mainstem bronchial collapse on forced expiration. There was no evidence of a fixed tracheal stenosis.

Physical examination revealed a healthy-appearing man in no apparent distress. Notable physical findings included an obvious saddle-nose deformity and thickened and deformed ears. There was a mild pectus excavatum deformity. He had no stridor, wheezing, or other evidence of ventilatory compromise. The remainder of the physical