

MEDICAL MYTHOLOGY

Myth: Blood transfusion is effective for sickle cell anemia–associated priapism

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ABSTRACT

Objective: Priapism is a recognized complication of sickle cell anemia (SCA). When initial conventional treatments fail, simple or exchange blood transfusion has been advocated as a secondary intervention. However, recent literature suggests this may not be an effective therapy and may have significant neurologic sequelae. This paper reviews and summarizes the effectiveness and risks of blood transfusion compared with conventional priapism therapy.

Methods: All relevant papers identified from a MEDLINE search were systematically examined for data related to the use of blood transfusion in the setting of priapism due to SCA. The effectiveness of conventional therapy was compared with transfusion therapy using the outcome of “time to detumescence” (TTD). In addition, papers documenting adverse neurologic sequela were reviewed and summarized.

Results: Forty-two case reports were identified containing complete information with regard to patient age and TTD. The mean TTD was 8.0 days with conventional therapy ($n = 16$) and 10.8 days with blood transfusion therapy ($n = 26$). Adverse neurologic sequelae from blood transfusion therapy was described in 9 cases, with long term outcomes ranging from complete resolution to severe residual deficits.

Conclusion: The current literature does not support the contention that blood transfusion is an effective therapy in the treatment of priapism due to SCA, as defined by an acceleration of TTD. In fact, numerous reports suggest that serious neurologic sequelae may result from this treatment. We feel the routine use of this therapy cannot be recommended.

Key words: priapism; sickle cell disease; transfusion

RÉSUMÉ

Objectif : Le priapisme est une complication reconnue de la drépanocytose. En cas d'échec des traitements initiaux classiques, on recommande le recours à la transfusion simple ou d'échange à titre d'intervention secondaire. Cependant, la littérature récente suggère qu'une telle thérapie pourrait ne pas être efficace et qu'elle pourrait laisser des séquelles neurologiques importantes. Le présent article examine et résume l'efficacité et les risques de la transfusion sanguine comparativement à la thérapie classique pour le priapisme.

Méthodes : Tous les articles pertinents relevés lors d'une recherche de MEDLINE furent examinés de façon systématique quant aux données liées au recours à la transfusion sanguine pour les cas de priapisme dus à la drépanocytose. L'efficacité de la thérapie classique fut comparée à la

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thérapie par transfusion grâce à l'examen du résultat «délai jusqu'à la détumescence» (DJD). De plus, les articles décrivant les séquelles neurologiques indésirables furent examinés et résumés.

Résultats : Quarante-deux observations contenant l'information complète en ce qui concerne l'âge des patients et le DJD furent identifiées. Le DJD moyen était de 8,0 jours avec la thérapie classique ($n = 16$) et de 10,8 jours avec la thérapie par transfusion sanguine ($n = 26$). Des séquelles neurologiques indésirables découlant de la thérapie par transfusion sanguine étaient décrites dans neuf cas, dont la gravité variait de la résolution complète à des déficits résiduels importants.

Conclusion : La littérature actuelle n'appuie pas la théorie selon laquelle la transfusion sanguine est une thérapie efficace pour le priapisme dû à la drépanocytose, si l'on considère le critère de la réduction du DJD. En fait, de nombreuses observations suggèrent que des séquelles neurologiques importantes peuvent découler de ce traitement. À notre avis, le recours de routine à cette thérapie ne peut être recommandé.

Introduction

Priapism, a painful, prolonged penile erection, is a debilitating medical emergency that was first described in association with sickle cell anemia (SCA) in 1934.¹ The incidence of this complication in adults with SCA has been estimated at 5%–10%, but recent data suggest that it may be as high as 30%–45%.² It is also common in children; in one study of 5- to 20-year-olds, 27% of subjects reported at least 1 episode of priapism.³ *Rosen's Emergency Medicine* and literature reviews suggest beginning with conventional treatment for SCA-associated priapism, in the same manner as non-SCA low-flow priapism.^{4,5} Blood and exchange transfusions are reported to be an option if conventional therapies fail. Although the use of this adjunct therapy is physiologically appealing, there are an increasing number of case reports describing significant neurologic side effects associated with transfusion therapy for SCA.

We conducted a systematic literature review to compare conventional therapy with blood transfusion therapy for SCA-associated priapism and assess the incidence and magnitude of reported side effects.

Methods

A MEDLINE search was performed using the search criteria “anemia, sickle cell” and “priapism.” All subheadings were included, but the search was limited to human subjects and articles in English. Criteria for inclusion of identified articles in this review were the following.

1. The patient must have presented with priapism and SCA as the plausible cause.
2. The patient must have had SCA (all cases of priapism associated with sickle cell trait were considered idiopathic).

3. The patient must have had chronic, not stuttering priapism.
4. The patient must have received either conventional or transfusion therapy before any surgical or experimental procedure.
5. Time information from onset of priapism to each treatment and detumescence must have been provided.
6. If the article presented a group of patients as one data set, the entire group had to meet the above stipulations.

The treatment protocol from *Rosen's Emergency Medicine* was used to categorize the identified papers by treatment modality.⁴ Information on adverse sequelae was also captured. The treatment categories used were: conventional, transfusional, surgical and experimental, which were chosen because of the traditional progression in treatment for SCA-associated priapism from conventional to transfusion to surgical therapies. Experimental therapies were excluded from this review because our intent was to compare the most common treatment modalities.

The conventional treatments reviewed were those recommended by standard texts for treatment of non-SCA-associated low-flow priapism, as these same techniques are typically recommended for the initial management of SCA associated priapism. Examples include, but are not limited to, intravenous fluids, oxygen, vasodilators, analgesics, caudal anesthesia, sedation, ice and hot packs, decompression, and aspiration. Some sources consider aspiration a surgical technique, but for the purposes of this review we differentiated aspiration (conventional therapy) from surgical shunting (surgical therapy), because of aspiration's frequency of use and emergency department availability.

Historically, simple blood transfusions have been advocated, but exchange transfusions are increasingly used and recommended to reduce the sickle cell hemoglobin (HbS) levels during crisis. Surgery is usually a last resort therapy, and the most common procedure is a corpus cavernosum-

spongiosum shunt. Experimental techniques usually employ drug irrigation during aspiration.

Results

We identified 126 papers published between 1966 and September 2004. Of these, 4 were unobtainable for review. The remaining 122 papers were reviewed for relevance, resulting in a total of 14 case reports or studies meeting the above inclusion criteria^{6–19} and 5 papers describing adverse sequelae.^{20–24} These papers contained information on 42 individuals who were then stratified by treatment modality into the following categories:

1. those who received only conventional treatment; and
2. those who received any type of conventional treatment and a blood transfusion or exchange transfusion.

To determine the effectiveness of each treatment, the time from onset of priapism to complete detumescence was calculated. In most papers the data required for this calculation was provided, but in some cases an estimate of the time was required. The range of times to detumescence and the mean time to detumescence (TTD) for each treatment modality were then determined.

The evidence: conventional therapy

There were 16 subjects with SCA-associated priapism who received conventional therapy without any form of transfusion therapy. The range of TTD in this group was 1 to 16 days, with a mean of 8.0 days. The mean age of subjects receiving conventional treatment was 15 years, with a range of 3.5–33 years.

The evidence: blood transfusion and exchange transfusion

There were 26 subjects with SCA-associated priapism who received one or more blood and/or exchange transfusions. The range of TTD in this group was 3 to 26 days, with a mean of 11 days. The mean age of subjects receiving transfusion therapy was 14 years, with a range of 2.2–33 years.

Adverse sequelae to transfusion therapy

The first association between hemoglobinopathies and neurologic sequelae after transfusion was reported in 1978 in thalassemia patients.²⁰ Eight patients developed a syndrome of hypertension, convulsions and cerebral hemorrhage after receiving multiple blood transfusions in preparation for a splenectomy. These sequelae persisted for up to 15 days post-transfusion. A similar association between

SCA and this syndrome was subsequently described in 2 patients.²¹ One patient was treated for priapism and was transfused with 2 units of packed erythrocytes. Four days later he complained of a headache, appeared lethargic, and experienced multiple generalized seizures. The second patient received 2 units of packed erythrocytes over 9 hours during and after an elective dental procedure. She later developed a headache and vomiting. After returning to sleep she became obtunded with left-side deviation of both eyes and left hemiplegia. She died 6 days later from cardiorespiratory arrest.

More recent reports have also described neurologic sequelae associated with blood transfusions for treatment of priapism. In a report of 6 severe cases, headache was the initial complaint in 5 patients, and 4 had seizures.²² One patient was discharged with mild neurologic deficits, and all others recovered fully. A recent case report described a patient treated with exchange transfusion for priapism who developed right-sided weakness 9 days after treatment and was diagnosed with a stroke when he presented 6 days later with right hemiparesis.²³ Another recent report describes a child who received multiple exchange transfusions for priapism and, upon commencement of the 4th transfusion, complained of nausea and headache.²⁴ The transfusion was discontinued, but the patient became obtunded and nonresponsive with left deviation of both eyes and right hemiparesis. Bradycardia and apnea developed and the patient had a tonic-clonic seizure. The patient had complete resolution of the neurologic deficits over 48 hours.

This association of neurologic sequelae and the treatment of priapism from SCA has been named the ASPEN syndrome by Seigel and coworkers.²⁴ This is an acronym for Association of Sick cell disease, Priapism, Exchange transfusion, and Neurological events. This syndrome has been reported 9 times in the literature with outcomes ranging from complete resolution, in the majority of cases, to severe neurologic deficits.

Limitations

An important limitation to consider in our methodology of comparing the 2 priapism treatment regimens is whether cases of comparable severity were represented in each treatment group and what role selection or publication bias may have played. If less severe cases were successfully managed with conventional therapy alone, and only more severe cases progressed to blood transfusion therapy, the results would be dramatically affected. The fact that treatment for priapism typically involves a step-wise progression, starting with conventional treatment and continuing

to transfusion therapy and ultimately surgical intervention, supports this hypothesis. Further evaluation of this possibility is complicated by the fact that in reports where blood transfusion was used, the transfusion was typically commenced within the first couple of days, when the degree of severity is difficult to determine. We believe the literature is more consistent with the hypothesis that the modality chosen for therapy is predominately determined not by disease severity, but by the protocol of the hospital or physician. The fact that that most of the transfusion subjects began receiving transfusions within the first 5 days of therapy, while the average TTD for the conventional group was 8.0 days, supports such a conclusion.

An additional limitation is that some of the times were estimates because the subject was not fully flaccid upon hospital discharge or the paper used vague language such as "a couple of days." This problem arose in the evaluation of both treatment groups.

Conclusions

The current literature does not support the contention that blood transfusion is an effective therapy in the treatment of priapism due to SCA, as defined by an acceleration of TTD. Moreover, numerous reports suggest that serious neurologic sequelae may result from this treatment. There are 9 case reports that directly relate blood transfusion therapy for treatment of SCA-associated priapism to neurologic sequelae (the ASPEN syndrome). In the absence of prospective studies, and given the difficulty of controlling for selection or publication bias, it is impossible to rigorously determine the merit, if any, of transfusion therapy for SCA-associated priapism from the existing literature. However, given the paucity of evidence that currently exists and the potential for iatrogenic harm, we feel the routine use of this therapy cannot be recommended.

Competing interests: None declared.

References

- Diggs LW, Ching RE. Pathology of sickle cell anaemia. *South Med J* 1934;27:839-45.
- Bruno D, Wigfall DR, Zimmerman SA, et al. Genitourinary complications of sickle cell disease. *J Urol* 2001;166:803-11.
- Mantadakis E, Cavender JD, Rogers ZR, et al. Prevalence of priapism in children and adolescents with sickle cell anemia. *J Pediatr Hematol Oncol* 1999;21:518-22.
- McCullough M, Sharieff G. Renal and genitourinary tract disorders. In: Marx J, Hockberger R, Walls R, editors. *Rosen's Emergency medicine: concepts and clinical practice*. 6th ed. St. Louis (MO): Mosby; 2006. p. 2635-56.
- Maan Z, Arya M, Patel HR. Priapism – a review of medical management. *Expert Opin Pharmacother* 2003;4:2271-7.
- Al Jam'a AH, Al Dabbous IA. Hydroxyurea in the treatment of sickle cell associated priapism. *J Urol* 1998;159:1642.
- El Mauhoub M, El Bargathy S, Sabharwal HS, et al. Priapism in sickle cell anaemia: a case report. *Ann Trop Paediatr* 1991;11:371-2.
- Enwerem EO, Endeley EML, Holcombe C, et al. Priapism in children with sickle cell disease. *Indian Pediatr* 1992;29:1048-9.
- Fich A, Rachmilewitz EA. Priapism in a non-black with sickle cell anemia associated with α -thalassemia. *Am J Hematol* 1981;10:313-5.
- Grace DA, Winter CC. Priapism: an appraisal of management of twenty-three patients. *J Urol* 1968;99:301-10.
- Gradisek RE. Priapism in sickle cell disease. *Ann Emerg Med* 1983;12:510-2.
- Hasen HB, Raines SL. Priapism associated with sickle cell disease. *J Urol* 1962;88:71-6.
- Karayalcin G, Imran M, Rosner F. Priapism in sickle cell disease: report of five cases. *Am J Med Sci* 1972;264:289-93.
- Kinney TR, Harris MB, Russell MO, et al. Priapism in association with sickle hemoglobinopathies in children. *J Pediatr* 1975;86:241-2.
- Maconochie IK, Scopes JW. Priapism in a 6½-year-old boy with sickle cell disease. *J R Soc Med* 1988;81:606.
- Seeler RA. Intensive transfusion therapy for priapism in boys with sickle cell anemia. *J Urol* 1973;110:360-3.
- Seeler RA. Priapism in children with sickle cell anemia. *Clin Pediatr (Phila)* 1971;10:418-9.
- Sousa CM, Catoe BL, Scott RB. Studies in sickle cell anemia: priapism as a complication in children. *J Pediatr* 1962;60:52-4.
- Walker EM, Mitchum EN, Rous SN, et al. Automated erythrocytapheresis for relief of priapism in sickle cell hemoglobinopathies. *J Urol* 1983;130:912-6.
- Wasi P, Na-Nakorn S, Pootrakul P, et al. A syndrome of hypertension, convulsion, and cerebral haemorrhage in thalassaemic patients after multiple blood-transfusions. *Lancet* 1978;2:602-4.
- Royal JE, Seeler RA. Hypertension, convulsions, and cerebral hemorrhage in sickle-cell anemia patients after blood-transfusions. *Lancet* 1978;2:1207.
- Rackoff WR, Frempong KO, Month S, et al. Neurologic events after partial exchange transfusion for priapism in sickle cell disease. *J Pediatr* 1992;120:882-5.
- Miller ST, Rao SP, Dunn EK, et al. Priapism in children with sickle cell disease. *J Urol* 1995;154:844-7.
- Siegel JF, Rich MA, Brock WA. Association of sickle cell disease, priapism, exchange transfusion and neurological events: ASPEN syndrome. *J Urol* 1993;150:1480-2.

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