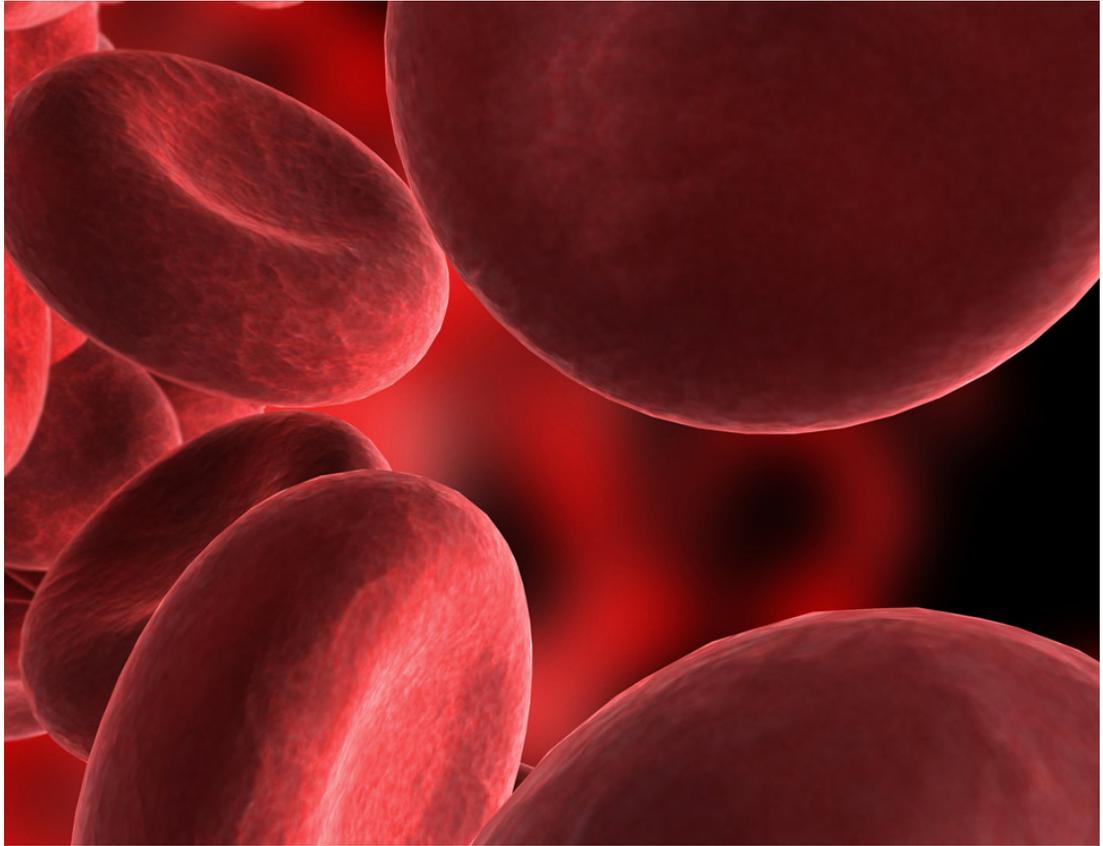


Prehospital management of sickle cell crisis

By Kenneth Navarro, LP



Case Review

You respond to a residence in the early morning hours to evaluate a boy, age 15, complaining of severe back pain. The patient denies trauma but reports a history of sickle cell disease with many previous vaso-occlusive episodes. The pain began about four hours ago and the patient took 60 milligrams of codeine. Without experiencing much relief, the patient took an additional 120 milligrams of codeine about one-and-a-half hours ago. The patient still describes the pain as a nine on a one to ten scale.

The patient is conscious, alert and appears to be in distress. The patient's blood pressure is 146/94 mmHg, pulse rate is 128 bpm, shallow respirations are 22 bpm, and the room-air pulse oximetry reading is 95 percent. The patient is warm to the touch and the breath sounds are clear and equal.

You place the patient on nasal cannula

oxygen at 2 lpm. While your partner attempts an IV, you assist the patient with the self-administration of nitrous oxide. The patient says the nitrous helps, but not very much. Once the IV is established, you begin a fluid bolus. You estimate the child's weight to be about 60 kilograms, so you administer 600 milliliters of normal saline. Medical control authorizes the slow administration of four milligrams of intravenous morphine, and you begin transport to the children's hospital, where the patient receives routine care. En route, you administer an additional four milligrams of morphine by slow IV push. The transport is uneventful and the care is transferred to the emergency department staff.

Introduction

Sickle cell disease, sometimes called sickle cell anemia, is a collection of blood disorders that produces abnormally shaped

red blood cells. The abnormal shape alters cellular flexibility, causing them to lodge in and eventually occlude small blood vessels. Sickle cell disease is a chronic condition, although many patients lead relatively normal lives. However, periodic acute episodes of vaso-occlusion produce severe pain along with several other potentially life-threatening risks.

In the United States, 1 in every 600 African Americans has sickle cell disease (Steinberg 1999). About eight percent of the African American population carry the sickle cell trait but do not require treatment or experience physical restrictions (Steinberg 1999). In 1973, the median life expectancy for patients diagnosed with sickle cell disease was 14 years, with very few surviving to see their 30th birthday (Diggs 1973). Deaths in children with sickle cell disease peak between the ages of one and three years; pneumococcal sepsis is the predominate cause (Leikin et al. 1989). The majority of the adults die during a classic crisis episode from a variety of factors, including fat embolism (Hutchinson, Merrick and White 1973), complication of narcotic administration (Cole et al. 1986), cardiovascular collapse (Platt et al. 1994), or multi-organ failure (Platt et al. 1994). Because of modern treatment, patients with sickle cell disease living in industrialized nations frequently survive into their fifth or sixth decade (Platt et al. 1994).

Pathophysiology

Under normal conditions, oxygen absorbed from the alveoli attaches to a hemoglobin molecule within the red blood cells. A normally functioning circulatory system transports the red blood cells throughout the body, thereby delivering the oxygen to the tissues. In sickle cell disease, a genetic mutation produces abnormal hemoglobin known as hemoglobin S.

When saturated with oxygen, hemoglobin S floats around in the bloodstream without any problems. However, after releasing oxygen to the body's tissues, the desaturated hemoglobin molecules polymerize, or link together in a chain. This polymer chain reduces the flexibility of the red blood cell, causing it to assume a sickle-shape. These rigid sickles do not easily pass through small blood vessels and soon obstruct blood flow.

In addition, the polymerization alters the surface of the affected blood cells, causing them to stick to the lining of blood vessels (Hebbel et al. 1980). This adhesion changes the normal balance of chemicals that keeps blood flowing freely. As a result, the affected area begins to constrict. The combination of the altered cell shape, the adhesion to vessel lining and vasoconstriction work to create blood flow obstructions in larger vessels, resulting in multiple organ ischemia and infarction.

The speed with which polymerization begins following desaturation appears to be directly related to the concentration of hemoglobin S present within the individual red blood cell. If the ratio of hemoglobin S to normal hemoglobin is high, polymerization may occur in milliseconds (Steinberg 1999). Individuals with the sickle cell trait but not the disease have a concentration of hemoglobin S too low to produce polymerization under most conditions (Steinberg 1999). However, dehydration or prolonged exposure to low oxygen environments as one might experience when climbing a mountain can cause significant hemoglobin S polymerization.

Sickled cells that make it back to the lungs can pick up a fresh supply of oxygen, causing the red blood cell to resume its normal appearance. However, frequent sickling of the same cell produces irreversible changes that ultimately make

the sickling permanent. A permanently sickled cell will eventually lodge somewhere within the capillary system, unless it can be destroyed by the body's natural defenses.

Sickle Cell Disease Origin

Experts believe that sickle cell disease originated in areas of the world with a high incidence of malaria. In those regions mosquitoes transmit a parasite that enters human red blood cells. The parasite completes its life cycle there and, in the process, destroys the cell. As the parasites destroy the red blood cells, the infected patient becomes anemic and ultimately dies.

However, the parasite cannot continue its life cycle in red blood cells affected by hemoglobin S. The presence of a single mutated gene in the hemoglobin gene pair provides the carrier with some resistance to malaria, a clear survival advantage in a malaria-prone region. The carrier will still have some sickling, but no widespread problems. Therefore, this individual is a carrier of the sickle cell trait, but does not have the disease.

Unfortunately, if both the mother and father are carriers, there is a one-in-four chance that the offspring will receive two of the defective genes. When both of the paired genes are defective, the child has inherited sickle cell disease and may not live to his or her reproductive years.

Complications of Sickle Cell Disease

The spleen assists in maintaining immunity against infection, but the organ also plays a major role in removing damaged and abnormal red blood cells from circulation. The spleen, along with other tissues, helps to destroy sickled cells. In many cases however, the spleen destroys the abnormal cells faster than the

body can create new ones, resulting in a reduced oxygen-carrying capacity of the blood, or anemia.

Because most of the vasculature in the spleen is very narrow, sickled red blood cells easily occlude the vessels and splenic injury is common. In fact, in most individuals with sickle cell disease, the spleen has become nonfunctional by the end of childhood, which then predisposes them to infections.

If the body cannot remove the sickled red blood cells from the circulatory system, the abnormal cells lodge in blood vessels throughout the body, which is sometimes referred to as a vaso-occlusive event. Blockages of cerebral vessels produce strokes; blockages of peripheral vessels produce extreme pain in the extremities; blockages of vessels in the penis produce a painful prolonged erection known as a priapism. Eventually, vaso-occlusion damages almost every major organ, resulting in multiple-organ failure.

Acute chest syndrome is a sometimes fatal complication of sickle cell disease. Acute chest syndrome affects about 40 percent of all people with sickle cell anemia (Steinberg 1999) and is more common in children. Patients usually present with pleuratic chest pain, fever, referred abdominal pain, hypoxia and a cough. X-ray examinations frequently reveal infiltrates. With frequent episodes, chronic respiratory insufficiency develops.

Assessment

Improving morbidity and mortality in sickle cell disease patients requires that medical personnel identify at-risk patients early in order to provide timely and effective care (Platt et al. 1994). In any given year, 60 percent of individuals with sickle cell disease will experience an extremely painful crisis episode (Platt et al. 1991). The duration of the vaso-

occlusive episodes range from a few days to several weeks (Vichinsky and Lubin 1980). Common triggers are infection, temperature extremes, or physical or emotional stress (Steinberg 1999). However, a significant number of vaso-occlusive episodes occur spontaneously with no identifiable triggers.

Signs and Symptoms

Among the more common complaints is pain in the chest, back, extremities and abdomen. Acute episodes rarely present with isolated pain. When extremity pain is present, it is common for the pain to be symmetrical (Steinberg 1999). In many cases, fever accompanies the pain (Serjeant et al. 1994).

EMS personnel do not have clinical tests or assessment findings to determine the degree of pain in any individual. As a result, pain assessment during a vaso-occlusive crisis relies on self-reporting data from the patient. Several pain intensity scales are available, including a common one-to-ten numerical scale and the Wong-Baker FACES Pain Rating Scale (Wong et al. 2001). EMS personnel should document the described pain intensity and alter prehospital treatment based on the patient's perception of the pain, not the medic's judgment of how much pain the patient is actually experiencing.

Management

Prehospital management of sickle cell crisis will focus on support of airway, breathing, circulation, pain control and rapid transport to an appropriate facility. Cardiac arrest in sickle cell crisis is relatively uncommon and usually only develops following respiratory arrest related to respiratory failure.

Administer supplemental oxygen as necessary, but 2 lpm by nasal cannula is probably adequate in most cases.

The results of two small, randomized investigations did not demonstrate any reduction in pain intensity or duration in non-hypoxic crisis patients following oxygen administration (Zipursky et al. 1992; Robieux et al. 1992). Use a pulse oximeter to help determine the effectiveness of oxygen therapy and attempt to maintain oxygen saturation levels above 93 percent (Ellison and Shaw 2007).

Patients in crisis often stop hydrating because of an increased focus on the event. Dehydration can worsen a vaso-occlusive event, highlighting the need for vascular access. EMS personnel should establish intravenous access with normal saline at a keep-open rate (Yale, Nagib and Guthrie 2000). If the assessment evidence suggests dehydration, administer a fluid bolus of 10 mL/Kg. Exercise caution, however, as excessive fluids can induce pulmonary edema, especially if the patient suffers from cardiac or renal failure or pulmonary vascular injury (Yale, Nagib and Guthrie 2000).

Acetaminophen and non-steroidal anti-inflammatory agents may be useful to control pain in mild to moderate vaso-occlusive episodes (Ellison and Shaw 2007). For moderate to severe episodes, EMS personnel should consider the use of opioids (Ellison and Shaw 2007). For patients requiring parenteral narcotics, morphine is the first-line analgesic.

If there is a delay in establishing IV access, the paramedic may allow patients to self-administer nitrous oxide to assist in pain management. If the patient cannot cooperate with nitrous administration, if its use is contraindicated or if the pain is not relieved, medics should administer intravenous morphine in small increments (2 to 4 milligrams at a time). Meperidine, a popular analgesic in some EMS systems, is controversial and has fallen out of favor



in the treatment of vaso-occlusive crisis. In patients suffering from sickle cell disease, the drug is associated with an increased incidence of seizure activity, although researchers have not established a causal link (Ballas 2008).

An unfortunate but pervasive attitude among health care personnel is that patients with sickle cell disease are narcotic dependent, and this attitude might influence treatment decisions (Waldrop 1995; Pack-Mabien et al. 2001; Shapiro et al. 1997). Emergency department studies demonstrate significant delays in analgesia administration for sickle cell disease patients presenting for treatment (Tanabe et al. 2007). It is never a good idea for EMS personnel to make a value judgment as to whether a patient really needs an analgesic. If the patient has a history of sickle cell disease and is in pain, treat the pain.

The most serious complication of pain control in sickle cell patients is sedation and respiratory depression. Reversal agents should be reserved for life-threatening complications of opioid administration and then administered in small increments to preserve some of the analgesic properties (Shannon and Berde 1989).

Be careful when evaluating the respiratory rate and effort in crisis patients following analgesic administration. Initially, the patient may present with tachypnea resulting from the pain. Narcotic administration may relieve the pain, thereby reducing the respiratory rate, but the decrease in rate may also be a result of the respiratory depressant effects of the narcotics. Patients receiving narcotics, especially those receiving the maximum prehospital dose should have ECG rate, pulse oximetry and capnography values monitored very closely.

Additionally, tachypnea produces a slight hyperventilation, which reduces the amount of carbon dioxide in the patient's blood. Narcotic administration reduces the

pain, causing a reduction in the patient's respiratory rate. This action promotes a slight retention of carbon dioxide in the alveoli and in the bloodstream. Carbon dioxide retention promotes oxygen unloading from the hemoglobin and increases sickling (Bunn and Forget 1986).

Conclusion

Vaso-occlusive crisis is a frequent and painful complication of sickle cell disease. Most of these patients seek medical attention for pain control, although many times the medical community does not manage the pain well. EMS personnel must guard against judging whether patients are actually experiencing pain and care for the patient appropriately.

References

- Ballas, S. K. 2008. Meperidine for acute sickle cell pain in the emergency department: Revisited controversy. [Letter to the editor]. *Annals of Emergency Medicine*, 51:217.
- Bunn, H. F. and B. G. Forget. 1986. *Hemoglobin: Molecular, genetic, and clinical aspects*. Philadelphia: W. B. Saunders.
- Cole, T. B., R. H. Sprinkle, S. J. Smith and G. R. Buchanan. 1986. Intravenous narcotic therapy for children with severe sickle cell pain crisis. *American Journal of Diseases of Children*, 140:1255-1259.
- Diggs, L. M. 1973. Anatomic lesions in sickle cell disease. In *Sickle cell disease: Diagnosis, management, education, and research*, eds H. Abramson, J. F. Bertles and D. L. Wethers. St. Louis: C. V. Mosby.
- Ellison, A. M. and K. Shaw. 2007. Management of vasoocclusive pain events in sickle cell disease. *Pediatric Emergency Care*, 23:832-841.
- Hebbel, R. P., O. Yamada, C. F. Moldow, H. S. Jacob, J. G. White and J. W. Eaton. 1980. Abnormal adherence of sickle erythrocytes to cultured vascular endothelium: Possible mechanism for microvascular occlusion in sickle cell disease. *Journal of Clinical Investigation*, 65:154-160.
- Hutchinson, R. M., M. V. Merrick and J. M. White. 1973. Fat embolism in sickle cell disease. *Journal of Clinical Pathology*, 26:620-622.
- Leikin, S. L., D. Gallagher, T. R. Kinney, D. Sloane, P. Klug and W. Rida. 1989. Mortality in children and adolescents with sickle cell disease. *Pediatrics*, 84:500-508.
- Pack-Mabien, A., E. Labbe, D. Herbert and J. Haynes, Jr. 2001. Nurses' attitudes and practices in sickle cell pain management. *Applied Nursing Research*, 14:187-192.
- Platt, O. S., D. J. Brambilla, W. F. Rosse, P. F. Milner, O. Castro, M. H. Steinberg and P. P. Klug. 1994. Mortality in sickle cell disease: Life expectancy and risk factors for early death. *New England Journal of Medicine*, 330:1639-1644.
- Platt, O. S., B. D. Thorington, D. J. Brambilla, P. F. Milner, W. F. Rosse, E. Vichinsky and T. R. Kinney. 1991. Pain in sickle cell disease: rates and risk factors. *New England Journal of Medicine*, 325:11-16.
- Robieux, I. C., J. D. Kellner, M. J. Coppes, D. Shaw, E. Brown,



- C. Good, H. O'Brodovich, D. Manson, N. F. Olivieri, A. Zipursky, et al. 1992. Analgesia in children with sickle cell crisis: Comparison of intermittent opioids vs. continuous intravenous infusion of morphine and placebo-controlled study of oxygen inhalation. *Pediatric Hematology and Oncology*, 9:317-326.
- Serjeant, G. R., C. D. Ceulaer, R. Lethbridge, J. Morris, A. Singhal and P. W. Thomas. 1994. The painful crisis of homozygous sickle cell disease: Clinical features. *British Journal of Haematology*, 87:586-591.
- Shannon, M. and C. B. Berde. 1989. Pharmacologic management of pain in children and adolescents. *Pediatric Clinics of North America*, 36:855-871.
- Shapiro, B. S., L. J. Benjamin, R. Payne and G. Heidrich. 1997. Sickle cell-related pain: Perceptions of medical practitioners. *Journal of Pain and Symptom Management*, 14:168-174.
- Steinberg, M. H. 1999. Management of sickle cell disease. *New England Journal of Medicine*, 340:1021-1030.
- Tanabe, P., R. Myers, A. Zosel, J. Brice, A. H. Ansari, J. Evans, Z. Martinovich, K. H. Todd and J. A. Paice. 2007. Emergency department management of acute pain episodes in sickle cell disease. *Academic Emergency Medicine*, 14:419-425.
- Vichinsky, E. P. & Lubin, B. H. (1980). Sickle cell anemia and related hemoglobinopathies. *Pediatric Clinics of North America*, 27, 429-447.
- Waldrop, R. 1995. Health professional perceptions of opioid dependence among patients with pain. *American Journal of Emergency Medicine*, 13:529-531.
- Wong, D. L., M. Hockenberry-Eaton, D. Wilson, M. L. Winkelstein and P. Schwartz. 2001. *Wong's Essentials of Pediatric Nursing*, 6th ed. St. Louis, 1301.
- Yale, S. H., N. Nagib and T. Guthrie. 2000. Approach to the vaso-occlusive crisis in adults with sickle cell disease. *American Family Physician*, 61:1349-1356.
- Zipursky, A., I. Robieux, E. J. Brown, D. Shaw, H. O'Brodovich, J. D. Kellner, M. J. Coppes, G. Koren and N. F. Olivieri. 1992. Oxygen therapy in sickle cell disease. *American Journal of Pediatric Hematology/Oncology*, 14:222-228.