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Three part question

P: In patients with an acute sickle cell crisis

I: Is the use of hypotonic IV solution 0.3% NaCl

C: Compared to 0.9% normal saline

O: Associated with improvement in time to resolution of the crisis

Clinical scenario

A 19 year old male with sickle cell disease presents to the ED with his typical vaso-occlusive crisis pain in his shoulders and knees. In choosing a solution for rehydration you wonder whether a hypotonic solution would be more effective than normal saline.

Search strategy

PubMed: hypotonic fluids and parenteral fluids and hyponatremia and sickle cell and pain crisis and vaso-occlusive crisis. This search was limited to full text and abstracts and English.

Search outcome

This search resulted in 18 articles. Bibliographic references found in these articles were also examined to identify related literature. Only original research articles were included. No articles directly addressing this question were found. I was able to find studies that, at least tangentially, address the subject through discussion of hydration status and cation concentrations of erythrocytes. The Cochrane library and Best Bets was also searched but no relevant results were found. Correspondence with Dr. Richard Snyder was also used as a research source.

Relevant paper(s)

| Author, date, and country | Patient group | Study type | Outcomes | Key results | Study weaknesses |
|---------------------------|-----------------------|------------------|--|---|-----------------------|
| Clark M 1982 USA | In vitro erythrocytes | Laboratory based | Change in MCHC, and effects on the deformability of ISCs and discoid cells | Reduction in MCHC, increased deformability of ISCs, and no increased deformability of discoid cells | Not a clinical trial. |
| Clark M 1980 USA | In vitro erythrocytes | Laboratory based | Deformability of high MCHC | Loss of deformability and | Not a clinical trial. |

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| | | | discoid cells and ISCs with rehydration. | morphology changes result from severe ion and water loss during sickling. | |
| Rosa R 1980 USA | Sickle cell disease | Prospective unblinded | Prevention of sickle cell crisis and resolution of acute pain crisis. | --Less sickled cells at lower partial pressures of oxygen. --Increased oxygen affinity in vivo. --Reduction in the incidence of sickle cell crisis. --Halved the duration of acute crises. | --N=3 --No control group (pts served as their own controls) --No blinding or randomization. --Protocol changed in the middle of the study (diuretics added) |
| Guy R 1971 USA | Sickle cell pain crisis | Prospective unblinded | Resolution of pain. | --Four patients improved rapidly and serum osmolality decreased. --One pt had no improvement in pain and osmolality was not seen to lower. | --N=5 --No control group --No blinding |

*MCHC = mean corpuscular hemoglobin concentration

**ISC = irreversible sickled cell

Comment(s)

There are no studies directly comparing the use of hypotonic solutions vs. NS in the

treatment of acute sickle cell crisis. An answer to the question may be inferred from the results of studies done citing the therapeutic effects of increasing the osmotic gradient leading into the affected erythrocyte. This search certainly reveals a gap in the emergency medicine literature and presents an opportunity for further research.

Clinical bottom line

Although there is a theoretical advantage to the use of hypotonic solutions in acute sickle cell crisis, there is insufficient evidence in support of the routine use of hypotonic solutions in acute sickle cell crisis.

References

- 1) Clark, M. Hydration of Sickle Cells: Using the Sodium Ionophore Monensin. A Model for Therapy *Journal of Clinical Investigation* 1982; Nov; 70 (5): 1074-80.
- 2) Clark, M. Influence of Red Cell Water Content on the Morphology of Sickling *Blood* 1980; May; 55 (5): 823-30.
- 3) Rosa, R. A Study of Induced Hyponatremia in the Prevention and Treatment of Sickle-Cell Crisis *The New England Journal of Medicine* 1980; Nov 13; 303 (20): 1138-43.
- 4) Guy, R. Treatment of Sickle Cell Crisis with Hypotonic Saline *Clinical Research* 1971; 19: 420.