Critical Review Form
Therapy

Vukmir RB, Katz L; Sodium Bicarbonate Study Group. Sodium bicarbonate improves outcome in prolonged prehospital cardiac arrest. Am J Emerg Med. 2006 Mar;24(2):156-61.

Objectives: **To evaluate the efficacy of sodium bicarbonate in the treatment of prolonged out-of-hospital cardiac arrest (OHCA).**

Methods: **This prospective, randomized controlled trial enrolled patients cared for by seven EMS systems in Western Pennsylvania between 1994 and 1998. Adult patients aged 18 years or older suffering cardiac arrest "refractory to defibrillation" were eligible for enrollment. Exclusion criteria included "overt respiratory" arrest, traumatic arrest, or inability to obtain IV access after multiple attempts.**

Patients were randomized to receive either an empirical dose of sodium bicarbonate (50 mEq/L) early in the care of the patient or an equal amount of normal saline. All patients received standard ACLS interventions, including CPR, epinephrine, and antiarrhythmic or pressor agents as warranted. The outcomes being assessed included return of spontaneous circulation (ROSC) and survival to ED admission with a pulse. Outcomes were further assessed based on length of resuscitative efforts, divided into short-term (0-15 minutes) and long-term (>15 minutes) groups.

A total of 874 subjects were enrolled, of whom 82 were deemed ineligible due to issues with documentation or data collection. This left 792 patients in the analysis, of whom 110 (13.9%) survived to ED admission. The mean age was 67 years.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis?**	
1.	Were patients randomized?	Yes. Patients were randomized (apparently in a 1:1 fashion) to receive either 1 ampule of sodium bicarbonate or an equivalent dose of normal saline.
2.	Was allocation concealed? In other words, was it possible to subvert the randomization process to ensure that a patient would be “randomized” to a particular group?	Likely yes. "Randomization was accomplished by blinded packaging by the manufacturer (Abbott Laboratories), and every patient received study intervention." (p. 157) Although no information is given as to how packages were chosen by EMS personnel or how packaging was tracked, this would likely be sufficient to maintain allocation

		concealment.
3.	Were patients analyzed in the groups to which they were randomized?	Yes. The authors note that every patient received the study intervention, but it would appear that additional doses of sodium bicarbonate were administered outside of the study protocol. Although not specifically mentioned, it does seem that patients were analyzed by intention to treat, rather than by whether or not they received bicarbonate. Unfortunately, the authors did a poor job specifying how many patients received bicarbonate outside of protocol in each group, or the amount of bicarbonate administered.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Unclear. While patients were similar with respect to age and weight, no other demographic information was provided and no information regarding medical comorbidities was provided. More importantly, the initial and subsequent cardiac rhythms were not mentioned, despite well-documented differences in prognosis for schockable versus non-shockable rhythms.
B.	**Did experimental and control groups retain a similar prognosis after the study started?**	
1.	Were patients aware of group allocation?	No. They were in cardiac arrest and hence not aware of anything.
2.	Were clinicians aware of group allocation?	No. Patients were either given sodium bicarbonate or saline bolus and blinded packaging was used to keep clinicians unaware of group allocation.
3.	Were outcome assessors aware of group allocation?	No. The outcomes were ROSC and survival to ED admission, both assessed by paramedics who were blinded to group allocation.
4.	Was follow-up complete?	Yes. Outcome data were available for all enrolled patients.
II.	**What are the results ?**	
1.	How large was the treatment effect?	• There was no overall difference in ED survival between those who received bicarbonate compared to those who did not: 13.8% vs. 13.9%, relative risk 0.99; 95% CI 0.70 to 1.40. ○ Among patients with prolonged cardiac arrest (> 15 minutes), there was a trend toward improved survival: 12% vs. 5.9%, RR 2.0; 95% CI 0.92 to 4.5.

		○ Among patients with cardiac arrest < 15 minutes, there was no difference in survival: 14.9% vs. 18.6%, RR 0.8; 95% CI 0.54 to 1.2.
2.	How precise was the estimate of the treatment effect?	See above.
III.	**How can I apply the results to patient care?**	
1.	Were the study patients similar to my patient?	Yes. This study was conducted in the US and enrolled nontraumatic cardiac arrest patients who received standard ACLS interventions. Some of the involved EMS systems were rural and suburban, and hence transport times may have been longer that those we see, but otherwise patients were likely similar.
2.	Were all clinically important outcomes considered?	No. The only outcome assessed was survival to ED admission. The Research Working Group of the American Heart Association Emergency Cardiovascular Care Committee has recommended that large trials designed to have a major impact should use longer-term endpoints at least 90 days out coupled with some neurological and quality-of-life assessment. Survival to ED admission is not a patient-centered outcome.
3.	Are the likely treatment benefits worth the potential harm and costs?	Unclear. Based on this study alone, in which sodium bicarbonate did not have a statistically significant effect on outcomes and in which a non-patient centered outcome was evaluated, bicarbonate should not routinely be used in cardiac arrest.

Limitations:

1. **The article's title is misleading and is not supported by the results, which did not demonstrate a statistically significant difference in outcomes between groups at any time interval.**

2. **The authors provide very little information about the enrolled patients; specifically, there is no documentation of the presenting rhythm, which has a profound effect on prognosis.**

3. **No measures of effect size (i.e. relative risk) or corresponding 95% confidence intervals were provided.**

4. **Despite a planned sample size of 1000 patients, only 792 were enrolled.**

5. **The study measured only short-term outcomes, including survival to ED admission. The Research Working Group of the American Heart Association Emergency Cardiovascular Care Committee has recommended that large trials designed to have a major impact should use longer-term endpoints at least 90 days out coupled with some neurological and quality-of-life assessment.**

Bottom Line:

This prospective, randomized controlled trial conducted in Western Pennsylvania found no difference in survival rates to ED admission between groups given sodium bicarbonate and placebo early in the EMS course (relative risk 0.99; 95% CI 0.70 to 1.40. While there was a trend toward improved survival in those patients with prolonged cardiac arrest (> 15 minutes), this did not achieve statistical significance.