

# Sodium bicarbonate in 5% dextrose: can clinicians tell the difference?

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The role of intravenous sodium bicarbonate in the treatment of metabolic acidosis is controversial.<sup>1</sup> BICAR-ICU, a multicentre, open label, randomised controlled trial, has reignited this debate<sup>2</sup> by reporting a significant reduction in 28-day mortality with sodium bicarbonate treatment in the pre-specified subgroup of patients with severe acidaemia and acute kidney injury.<sup>2</sup> However, as the study was open label, the results are at risk of bias. Blinding of sodium bicarbonate therapy would be important in any future randomised controlled trial, the feasibility of which must be established first. Therefore, we aimed to test the hypothesis that clinicians would be unable to correctly identify a 250 mL polyolefin bag containing 100 mL of 8.4% sodium bicarbonate and 150 mL of 5% dextrose (D5W) from a 250 mL bag of D5W only.

## Methods

Three identical 250 mL bags of D5W were used. The first test bag had 100 mL aspirated and 100 mL of 8.4% sodium bicarbonate injected. The second test bag had 100 mL aspirated, and the same volume then immediately returned via the injection port. The third (control) bag was not altered in any way. All three bags were connected to an intravenous giving set and primed.

This process was performed at two different metropolitan intensive care units (ICUs) by two separate teams. At the first institution, the sodium bicarbonate test bag was labelled "1" and the non-sodium bicarbonate test bag was labelled "2". This was reversed at the second site. The teams then went to the clinical area, where staff were recruited. The control bag was left on a stand and, following a computer-generated random sequence, either test bag 1 or bag 2 was hung next to the control bag.

Participants were informed about the nature of the study before making any assessment. Participants were allowed to inspect, touch and shake the bag. Finally, they were asked if their answer was based on a clue or simply a guess. If they indicated a clue, this was recorded in detail. Participants were never told the correct answer. Low-risk ethical approval to conduct the study was obtained from the Alfred Hospital Human Research Ethics Committee, Melbourne, Australia (reference 491/19).

## ABSTRACT

**Background:** Due to the lack of double-blind randomised controlled trials, the true effect of intravenous sodium bicarbonate therapy in ICU patients with metabolic acidosis remains unclear.

**Methods:** We diluted 100 mL 8.4% sodium bicarbonate in 150 mL 5% dextrose (D5W) within a 250 mL polyolefin bag after removing 100 mL. We asked ICU clinicians to inspect a 250 mL bag containing sodium bicarbonate or a 250 mL bag where 100 mL of D5W had been removed and then returned. The bags were attached to intravenous giving sets. We asked participants to identify the contents of the bags.

**Results:** Among 60 participants (39 nursing staff [65%], 20 medical staff [33.3%] and one pharmacist), 36 (60%) answered correctly. The Cohen  $\kappa$  for agreement between test bag content and participants' answers was 0.20 (95% CI, -0.05 to 0.45;  $P = 0.12$ ), implying the answers were correct by chance. In the group of 28 participants who indicated they used a clue to help them decide their answer, 15 (53.6%) answered correctly, whereas in the remainder ( $n = 32$ ), 21 (65.6%) answered correctly ( $P = 0.49$ ).

**Conclusion:** When 100 mL of 8.4% sodium bicarbonate were diluted in 150 mL of D5W within a 250 mL polyolefin bag, clinicians were unable to correctly identify the contents of the bags. Our findings imply that sodium bicarbonate therapy can be successfully blinded.

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## Sample size and statistical analysis

We tested agreement between each test bag content and participants' answers using the Cohen  $\kappa$  statistic. A Cohen  $\kappa$  greater than 0.4 was adjudicated to demonstrate at least moderate agreement. The null hypothesis was that participants answered correctly only by chance. Statistically, 47 participants were required to detect a Cohen  $\kappa$  of 0.4 (moderate agreement), with an 80% power and a 0.5 probability that participants reported the test bag contained sodium bicarbonate. Otherwise, group comparisons were made using  $\chi^2$  tests for equal proportions and Student  $t$  tests

**Table 1. Comparison of participants based on whether a correct answer was provided**

	Incorrect	Correct	P
Number of answers	24	36	
SB solution	10 (41.7%)	16 (44.4%)	> 0.99
Participants			0.63
Doctor	9 (37.5%)	11 (30.6%)	
Nurse	15 (62.5%)	24 (66.7%)	
Pharmacist	0 (0)	1 (2.8%)	
Years worked in ICU, mean (SD)	10.2 ± 9.7	10.0 ± 8.5	0.96
Clue	13 (54.2%)	15 (41.7%)	0.49
Bubble	5 (38.5%)	3 (20.0%)	
Volume	3 (23.1%)	5 (33.3%)	
Colour	3 (23.1%)	3 (20.0%)	
Puncture	1 (7.7%)	1 (6.7%)	
Other	1 (7.7%)	3 (20.0%)	

ICU = intensive care unit; SB = sodium bicarbonate; SD = standard deviation

sodium bicarbonate ( $P > 0.99$ ) (Table 1). There was no statistically significant difference in occupation or years of ICU experience between these groups. In the group of 28 participants who indicated they used a clue to help them decide their answer, 15 (53.6%) answered correctly, whereas in the remainder ( $n = 32$ ), 21 (65.6%) answered correctly ( $P = 0.49$ ). Clues were distributed similarly between those who answered correctly and incorrectly (Table 1).

### Discussion

In assessing 60 staff members, with an average 10-years' clinical experience, working at two independent metropolitan ICUs, 100 mL 8.4% sodium bicarbonate diluted in 150 mL D5W and presented in a 250 mL polyolefin bag could not be differentiated from an unaltered 250 mL D5W bag. Moreover,

any correct choices were by chance alone. Therefore, our results imply that it is possible to blind clinical staff to the presentation of sodium bicarbonate, which may help reduce bias in future clinical trials. However, as noted by Forni and colleagues,<sup>3</sup> there is the potential for sodium bicarbonate to be unblinded due to the multiple blood gas measurements performed in the ICU.

### Conclusion

Clinical staff were unable to accurately distinguish 100 mL 8.4% sodium bicarbonate diluted in 150 mL D5W and presented as a 250 mL polyolefin bag, compared with an unaltered 250 mL bag of D5W.

### Competing interests

None declared.

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for continuous variables, with results presented as frequency (%) and mean (standard deviation [SD]) respectively. A two-tailed  $P < 0.05$  was used to indicate statistical significance. Statistical analysis was performed using R version 3.5.1 (R foundation for Statistical Computing, Vienna, Austria).

### Results

#### Participants

A total of 60 participants, 30 per site took part in the study. The majority were ICU nursing staff (65%) and 33.3% were medical staff of varying seniority. One ICU pharmacist was also included. The mean number of years worked in ICU was 10.1 (SD, 9.0). Twenty-six participants were allocated to a test bag with sodium bicarbonate and 34 to one without sodium bicarbonate. Overall, 60% of participants ( $n = 36$ ) answered correctly. Most had a guess (53%), with the remainder ( $n = 28$ ) basing their assessment on a variety of clues (Table 1).

#### Agreement

The Cohen  $\kappa$  for agreement between the test bags and participants' answers was 0.20 (95% CI, -0.05 to 0.45;  $P = 0.12$ ), implying the answers were correct by chance. In those who answered correctly, 44.4% were presented a bag containing sodium bicarbonate, whereas 41.7% of those who were incorrect also examined a bag containing

## TECHNICAL NOTES

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### References

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- 3 Forni LG, Hodgson LE, Selby NM. The Janus faces of bicarbonate therapy in the ICU: not sure! *Intensive Care Med* 2019. doi: 10.1007/s00134-019-05885-7. [Epub ahead of print]