Stability of bicarbonate in normal saline: a technical report

Thummaporn Naorungroj, Ary Serpa Neto, Tomoko Fujii, Briony Jude, Andrew Udy and Rinaldo Bellomo

ABSTRACT

Background: The benefit of intravenous sodium bicarbonate administration in patients with severe metabolic acidosis remains controversial, partly due to lack of double-blind trials. From a practical viewpoint, such blinding requires testing of the stability of sodium bicarbonate in polyolefin bags.

Methods: We examined seven samples of 100 mL 8.4% sodium bicarbonate diluted in 150 mL normal saline within a 250 mL polyolefin bag at time 0, 24 and 48 hours after preparation. We measured pH, P_{CO_2}, and bicarbonate concentration.

Results: Over a period of 48 hours, both pH and P_{CO_2} decreased significantly (hourly rate of change, –0.001 [$P = 0.043$) and –0.098 [$P < 0.001$] respectively). However, the concentration of bicarbonate did not decrease, with an hourly rate of change of only –0.009 ($P = 0.42$).

Conclusion: When 100 mL of 8.4% sodium bicarbonate are diluted in 150 mL of normal saline within a 250 mL polyolefin bag, changes in pH and P_{CO_2} over a 48-hour period are small and bicarbonate concentration remains stable.

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Metabolic acidosis with acidaemia is associated with unfavourable outcomes in critically ill patients.[1,2] Intravenous sodium bicarbonate therapy to increase blood pH and bicarbonate levels is a relatively common practice in this setting.[3] However, the role of sodium bicarbonate in such patients remains controversial.[4-6] Recently, a randomised controlled phase 3 trial reported that intravenous sodium bicarbonate reduced the need for renal replacement therapy in critically ill patients with severe acidaemia.[7] However, the unblinded nature of the study raised concern about bias and suggested the need to conduct well designed double-blind randomised controlled trials.

In Australia, 8.4% sodium bicarbonate for injection is provided as a 100 mL glass bottle, making blinding problematic from a practical and logistic point of view. The storage of bicarbonate in glass bottles instead of polyolefin bags aims to prevent changes in bicarbonate concentration, which occur over time as carbon dioxide (CO_2) dissolving in the solution is then lost to the atmosphere through the polyolefin bag. However, the speed of such losses and its consequences on bicarbonate solution stability over a short period remain unclear. Moreover, if stability was maintained for 48 hours, blinding of bicarbonate therapy may become logistically and practically possible and enable the conduct of double-blind randomised controlled trials of such therapy in critically ill patients.

We hypothesised that the concentration of sodium bicarbonate diluted in 0.9% normal saline would remain stable over 48 hours and tested our hypothesis in an ex vivo study.

Methods

We obtained 100 mL of sodium bicarbonate 8.4% for injection from its 100 mL glass bottle (Phebra, Sydney, Australia). We removed 100 mL of normal saline from a 250 mL polyolefin bag (Fresenius Kabi, Sydney, Australia). Then, 100 mL of 8.4% sodium bicarbonate were added to the bag in order to replace the 100 mL of saline that had been removed. This resulted in an estimated bicarbonate concentration of between 350 and 400 mEq/L, depending on the accuracy of fluid removal and addition. This process was replicated for seven bags. The measurement of pH, bicarbonate concentration and partial pressure of CO_2 (P_{CO_2}) was performed immediately after the preparation and repeated at 24 and 48 hours. The solutions were stored at room temperature and pressure. The estimated bicarbonate concentration exceeded analyser measurement specifications. Thus, samples required dilution of 1:10 with normal saline before measurement. Accordingly, at each time point, 1 mL of solution was drawn from each bag and placed in a labelled 2 mL container and capped. Then 0.5 mL from each such sample was added to its labelled tube containing 4.5 mL of normal saline before bicarbonate and CO_2 measurement. Bicarbonate level was measured with the Roche Cobas c702 analyser (Roche Australia, Melbourne, Australia) by an enzymatic assay. Moreover, all diluted samples were measured by an arterial blood gas machine after dilution to estimate pH (ABL800 FLEX blood gas analyser, Radiometer Pacific, Melbourne, Australia).

Table 1. Stability of 8.4% sodium bicarbonate diluted in normal saline at different time points

	Measurements		
	0 hours	24 hours	48 hours
pH (analyser after dilution)			
Sample 1	8.2	8.3	8.1
Sample 2	8.3	8.3	8.1
Sample 3	8.2	8.3	8.2
Sample 4	8.2	8.2	8.2
Sample 5	8.2	8.2	8.2
Sample 6	8.2	8.2	8.1
Sample 7	8.2	8.3	8.1
Mean ± SD	8.21 ± 0.03	8.25 ± 0.05	8.14 ± 0.05
Bicarbonate (mEq/L) (analyser)			
Sample 1	36	34	33
Sample 2	36	35	33
Sample 3	33	34	34
Sample 4	35	34	35
Sample 5	36	36	37
Sample 6	35	34	35
Sample 7	35	35	36
Mean ± SD	35.1 ± 1.1	34.6 ± 0.8	34.7 ± 1.5
P_{CO_2} (mmHg) (ABG machine)			
Sample 1	20.2	18.4	16.1
Sample 2	19.4	18.1	15.1
Sample 3	22.0	17.6	14.7
Sample 4	19.8	18.7	15.7
Sample 5	21.6	20.5	17.1
Sample 6	19.8	19.1	15.7
Sample 7	20.1	19.2	15.7
Mean ± SD	20.4 ± 1.0	18.8 ± 0.9	15.7 ± 0.8

ABG = arterial blood gases; P_{CO_2} = partial pressure of carbon dioxide; SD = standard deviation.

Results

All samples were macroscopically identical, clear and with no precipitation. The concentration of diluted bicarbonate for each bag is shown in Table 1. Over 48 hours, pH and P_{CO_2} levels decreased slightly, with a rate of change of –0.001 (P = 0.043) and –0.098 (P < 0.001) per hour respectively (Figure 1 and Table 1). However, there was no significant change in bicarbonate concentration over 48 hours, with a rate of change of –0.009 (P = 0.420) per hour. The mean concentration of bicarbonate remained stable at about 35 mmol/L after 1:10 dilution, thus extrapolating to a non-diluted (actual) approximate concentration of 350 mmol/L.

Discussion

We investigated the stability of 3.36% sodium bicarbonate solution in a 250 mL polyolefin bag. We found that the bicarbonate concentration remained stable over 48 hours. Our findings are in line with previous stability studies showing that sodium bicarbonate diluted in either sterile water or 5% dextrose contained in polyolefin bags (0.05, 0.1, 0.15 mEq/mL) remained stable for about 2–7 days when stored at room temperature.[8,9] In this experiment, we reported that bicarbonate was stable in normal saline and at higher concentrations (0.4 mEq/mL) for up to 48 hours. However, we also confirmed a slight and slow decrease in P_{CO_2} supporting loss of CO_2 to the atmosphere.

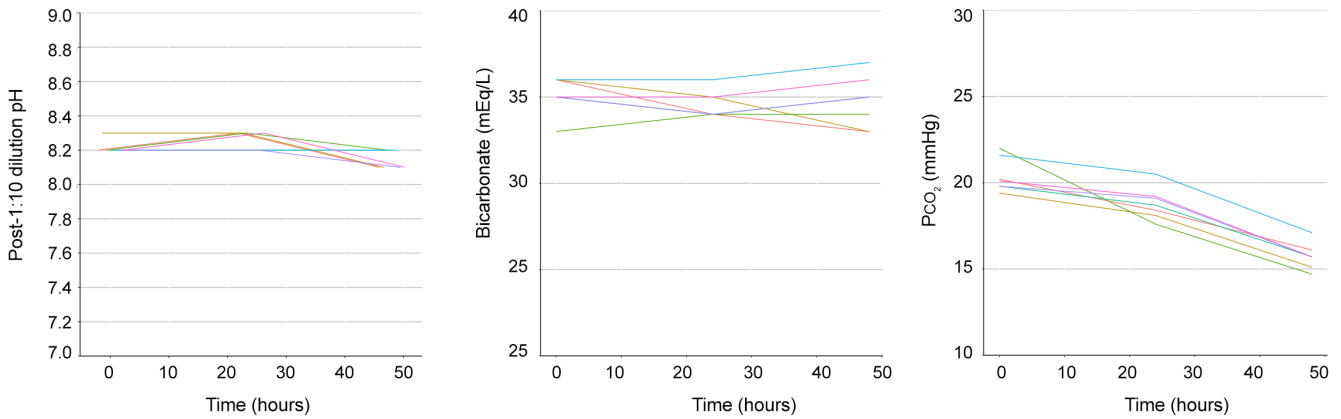
Our findings imply that it is possible to conduct double-blinded studies of bicarbonate therapy using normal saline as diluent. The use of saline instead of 5% dextrose as diluent is of interest, as hypotonic solutions such as 5% dextrose could not be safely given as placebo in patients with acidaemia and at risk of or with intracranial hypertension.[10,11] Moreover such dilution provides only an additional 23 mmol of sodium.

Although pH changed slightly from baseline to 48 hours and the theoretical bicarbonate level should be 400 mEq/L, errors in dilution from removing and adding fluid by syringe can easily account for a close to 10% error and the final estimated concentration of about 350 mmol/L. Nonetheless, such changes in concentration do not materially affect the ability to deliver the equivalent of about 100 mmol of bicarbonate reliably and rapidly if necessary. Finally, the pH remained within the acceptable stability range for injection (pH, 7.0–8.5).[8,9]

Conclusion

We found that 100 mL of sodium bicarbonate solution can be added to a 250 mL polyolefin normal saline bag after 100mL have been removed and that its concentration remains stable for up to 48 hours. These findings support the notion that a double-blinded randomised controlled trial of sodium bicarbonate therapy is logistically possible in critically ill patients using this method.

Figure 1. Individual changes in pH, partial pressure of carbon dioxide (Pco_2) and bicarbonate concentration over 48 hours after 1:10 dilution to measure concentrations by analyser. The changes in pH an Pco_2 were small and bicarbonate levels were stable



Competing interests

None declared.

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