Effects of sodium bicarbonate ingestion on prolonged running performance and recovery in trained runners

Lew Ka Shing, Ler Hui Yin*, Gee Yong Yong, Wee Eng Hoe

ABSTRACT

Background: While the effects of sodium bicarbonate on buffering capacity have been repeatedly examined on short-term and high-intensity exercise performance, studies on prolonged endurance performances such as running are scarce. Thus, the purpose of this study was to investigate the effect of NaHCO₃ (0.3 g/kgBW) ingestion 60-minutes prior to the prolonged running testing and recovery in trained runners.

Methods: A total of 10 trained male runners (age: 20.70±1.10 years; weight: 61.30±6.20 kg; height: 166.10±3.70 cm; VO₂peak, 58.43±5.62 mL/kg/min) were recruited in this study. Subjects underwent 1 preliminary testing and 2 experimental trials: Sodium Bicarbonate (SB) and Placebo (PLA) trials, which consisted of: (i) a 60-minutes Prolonged Exercise Testing (PET) (30-minutes of constant speed run at 65% of VO₂peak followed by a self-selected speed of 30-minutes maximum distance run) and (ii) 30-minutes of the recovery period in randomized order. Data were analyzed using SPSS version 23 for Windows.

Results: Subjects ran further during the SB trial than the PLA trial (5,233.60±524.70 m vs. 5,021.40±440.10 m; p=0.012) associated with a greater blood lactate level (5.66±1.09 mmol/L vs. 3.68±0.71 mmol/L). Ingestion of SB drinks significantly increased urine pH during PET and recovery period (p<0.01). During post-recovery, a greater decrease in blood lactate level was found in the SB trial (2.53±0.91 mmol/L; 55%) as compared to the PLA trial (2.17±0.50 mmol/L; 41%) (p<0.01).

Conclusion: The ingestion of NaHCO₃ (0.30 g/kgBW) 60-minutes prior to the PET improved prolonged running performance associated with a faster lactate removal rate during the 30-minutes recovery period.

Keywords: Prolonged Running Performance, Lactate Removal, Urine pH, Abdominal Discomfort and Fullness.


INTRODUCTION

Sodium Bicarbonate (NaHCO₃) serves as one of the leavening agents and it is used for baking products such as cakes and breads. NaHCO₃ can be easily obtained at any mart or supermarket as it comes in the form of baking soda. It is known that the use of NaHCO₃ can increase the pH levels in the human body and also increase the bicarbonate (HCO₃⁻) concentrations in the blood to enhance the blood-buffering effects in the body to control the acid-base balance, which significantly contribute to fatigue.1 2 3 Sports or training involving large muscle groups and fast motor-unit activities may also benefit from the buffering effects of NaHCO₃ as exercises that recruit fast motor units and large muscle groups may also induce lactic acid production.2 Lancha Junior AH and coworkers concluded that NaHCO₃ is one of the effective agents in enhancing the extracellular buffering capacity when ingested prior to high-intensity exercise performance.2 The ingestion of NaHCO₃ results in blood hydrogen (H⁺ ion), which facilitates the removal of lactic acid from active muscles during the recovery process.3 It is also interesting to note that the use of NaHCO₃ as ergogenic aids is legal and permitted by the World Anti-Doping Agency code.4

Most of the research findings support the ingestion of NaHCO₃ in high-intensity sports performance such as swimming.3 5 6 7 All the protocols used in these studies were in high-intensity modes, and the effects of NaHCO₃ ingestion were proven positive in enhancing the high-intensity exercise performance. The ingestion of NaHCO₃ can improve extracellular buffer capacity, enabling the efflux of lactate and H⁺ ions, which will alleviate muscular fatigue and promote a better recovery process during high intensity and all-out exercises.1 4

Long-distance endurance events like road cycling, triathlon, and long-distance running are typically determined by the ability to outperform remaining competitors in the race’s final stage through short bursts of all-out effort. The pre-exercise alkalosis induced by the ingestion of NaHCO₃ may benefit the acid-base balance maintenance in the body, which can be crucial for recovery. The effects of NaHCO₃ ingestion have been proven to be effective in buffering the blood pH and increasing blood HCO₃⁻ concentration, which increases the tolerance of acidosis and enhances sports performance.9 Hence, with the possibility of increasing acidosis tolerance and improving the muscles working capacity, the ingestion of NaHCO₃ may benefit long-distance exercise performance. However, little is
known regarding the effect of NaHCO₃ ingestion on prolonged endurance exercises and during recovery. Therefore, this study aimed to investigate the effects of NaHCO₃ ingestion on prolonged running performance and recovery in trained runners.

**METHODS**

**Subjects**

Ten male middle-distance runners (age: 20.70±1.10 years; Body Weight (BW): 61.40±6.20 kg; height: 166.10±3.70 cm; \( \text{VO}_{2\text{max}} 58.40±5.60 \text{ mL/kg/min} \) were recruited for this study. Inclusion criteria were: (i) \( \text{VO}_{2\text{max}} \) greater than 50 mL/kg/min; (ii) free from injury for the past 3 months; (iii) currently in training with training, defined as at least 2-4 days/week of running. Subjects were informed of the nature of the study and the possible benefits and risks associated with the experimental procedures before giving their written informed consent to participate. Subjects also completed a Physical Activity Readiness Questionnaire (PAR-Q). Subjects who participated were willing to hold their ongoing consumption of nutritional supplementation for at least 2 weeks prior to this study until they completed the study.

**Experimental Design**

This was a crossover, randomized order, double-blind research design study. Subjects were required to perform preliminary testing, which comprised a submaximal exercise test and a maximal oxygen uptake (\( \text{VO}_{2\text{max}} \)) test to determine the running speed at 65% \( \text{VO}_{2\text{max}} \) during the experimental trials. For the experimental trials, subjects completed a Prolonged Exercise Testing (PET) consisting of a submaximal test and a maximal test. The submaximal test was performed to determine the running speed at 65% \( \text{VO}_{2\text{max}} \) and the maximal test was performed to determine the running speed at 100% \( \text{VO}_{2\text{max}} \). For the maximal test, subjects underwent a 4 x 4 minutes of continuous steady-state running on a motorized treadmill (H/P/ Cosmos Quasar, Germany) and metabolic cart (QUARK CPET, Cosmed, Italy). The speed of each stage increased by 1.5 km/hour every 4 minutes with a 0% gradient. Oxygen uptake (\( \text{VO}_{2} \)), Respiratory Exchange Ratio (RER), Rating of Perceived Exertion (RPE) and Heart Rate (HR) were recorded during the last 15 seconds of each stage. After the submaximal test, the subjects were allowed to rest for 5 minutes followed by an incremental treadmill run with an increment of 2% every 2 minutes until exhaustion. \( \text{VO}_{2} \), RER, RPE, and HR were collected for every last 15 seconds in each stage. In the previous stage of the running, HR \( \text{max} \) \( \text{VO}_{2\text{max}} \) time to exhaustion, and RPE were obtained at the point of volitional fatigue within the final ~10 seconds of running. The submaximal and \( \text{VO}_{2\text{max}} \) tests were used to determine the running speed of 65% \( \text{VO}_{2\text{max}} \) via the regression equation.

**Experimental Trials**

**Supplementation Protocol**

Prior to ingesting the supplement drinks, the finger-pick blood sample and urine sample was required to determine the subject's blood glucose level (4.40-6.10 mmol/L) was at fasting state and hydration status (USG<1.020). Besides that, the blood lactate analysis and urine pH were also recorded prior to the ingestion of supplement drinks. A standardized breakfast was given (two pieces of bread) to the subjects to ensure their blood glucose level was similar and reduced the chance of unwanted GI symptoms for the two experimental trials. After the ingestion of drinks, subjects were instructed to drink either supplement or placebo drinks. Subjects were required to rest at the laboratory for 60-minutes prior to the PET. The laboratory assistant prepared the supplements and placebo drinks; the researcher was blinded to the type of drinks given to the subjects during the experimental trials.

**Experimental Protocol**

Prior to the PET, 2nd finger-pick blood samples were taken for blood glucose (ACCU-CHEK® Advantage III, USA) and blood lactate (YSI 1500, YSI Incorporated, The Netherlands) analysis. Urine samples were collected in a disposable urine container to determine the urine specific gravity (USG) (Atago*UG-a, Japan) and urine pH (Eutech pH 2700, Thermo Fisher Scientific, USA). The ratings of Abdominal Discomfort (AD) scale from 0 to 10 (completely comfortable to unbearable pain) and Gut Fullness (GF) scale from 0 to 10 (empty to bloated) were rated by the subjects. An HR monitor (Garmin HRM3-SS, USA) was placed in the front chest of the subject and the \( \text{VO}_{2} \) testing mask connected to the metabolic cart was placed on the face of the subject. Subject was required to run at a constant speed on the treadmill for 30-minutes at 65% \( \text{VO}_{2\text{max}} \), followed by a self-selected speed of 30-minutes maximum distance running. The 30-minutes maximum distance running speed was manually adjusted by the subject's own preference pace. The administrator informed the elapsed time to complete the run; however, no feedback was given to the subject regarding the distance covered during the maximum distance running. No encouragement was provided to the subject throughout both trials to ensure consistency. All subjects were encouraged to run as far as possible. HR, \( \text{VO}_{2} \), RER, and RPE were recorded every 5-minutes throughout the Prolonged Endurance Testing (PET). After 60-minutes PET (Post-Exercise),
Table 1. Distance (m) covered during Self-selected Speed of 30-minutes Maximum Distance Run.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Distance (meters) (mean±SD)</th>
<th>p</th>
<th>Diff (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SB</td>
<td>5,233.60±524.70</td>
<td>0.012*</td>
<td>4.14</td>
</tr>
<tr>
<td>PLA</td>
<td>5,021.40±440.20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SB: Sodium Bicarbonate; PLA: Placebo; *Significantly different if p-value less than 0.05

Table 2. Oxygen Uptake (VO_{2}) Responses during 60-minutes PET.

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Oxygen Uptake (VO_{2}) (ml/kg/min) (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10</td>
</tr>
<tr>
<td>SB</td>
<td>36.50±2.80</td>
</tr>
<tr>
<td>PLA</td>
<td>36.10±3.00</td>
</tr>
</tbody>
</table>

SB: Sodium Bicarbonate; PLA: Placebo; *Significantly different if p-value less than 0.05

Table 3. Heart Rate (HR) Responses and RPE during 60-minutes PET and 30-minutes Recovery Period.

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>PET (mmol/L)</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>HR (beats/minutes)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SB</td>
<td>140±12</td>
<td>146±14</td>
</tr>
<tr>
<td>PLA</td>
<td>135±24</td>
<td>144±15</td>
</tr>
<tr>
<td>RPE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SB</td>
<td>10.7±1.5</td>
<td>11.7±1.4</td>
</tr>
<tr>
<td>PLA</td>
<td>11.0±0.9</td>
<td>12.0±1.1</td>
</tr>
</tbody>
</table>

SB: Sodium Bicarbonate; PLA: Placebo; HR: Heart Rate; RPE: Rating of Perceived Exertion; *Significantly different if p-value less than 0.05

Results

Table 1 showed subjects significantly improved their running distance by 4.14% on a 30-minutes maximum running distance during the Sodium Bicarbonate (SB) trial (5,233.60±524.70 meters; p=0.012) as compared with the PLA trial. In addition, the VO_{2} responses were similar throughout the 60-minutes PET during PLA and SB trials (p>0.05) (Table 2). After 30-minutes of the recovery period, the heart rate responses remained similar during both trials (SB trial: 88±14 beats/minutes; PLA trial: 85±12 beats/minutes; p=0.638) (Table 3).

Table 4 showed that blood glucose levels remained similar in both trials during PET and recovery (p>0.05). Blood lactate levels in both trials increased significantly after 60-minutes of PET (SB trial: 5.66 ± 1.08 mmol/L; PLA trial: 3.68 ± 0.71 mmol/L; p=0.001). After 30-minutes of recovery, blood lactate levels in both trials decreased (SB trial: 2.53 ± 0.91 mmol/L; PLA trial: 2.17 ± 0.49 mmol/L; p=0.291). Although no significant difference was found in blood lactate during post-recovery between trials, the lactate removal rate in the SB trial was faster than the PLA trial (55% vs. 40%) (Table 4). Urine pH level was similar prior to the ingestion of supplement drinks in both SB and PLA trials (Table 4). After 60-minutes of supplement drinks ingestion, urine pH increased significantly in the SB trial (8.37±0.13) as compared with the PLA trial (7.13±0.39); p=0.001; followed by Post Exercise (SB trial: 7.47±0.36 vs. PLA trial: 6.59±0.50; p=0.002) and at Post-Recovery (SB trial: 7.00±0.49 vs. PLA trial: 6.22±0.54; p=0.009). The urine USG analysis in Table 4 revealed that subjects remained euhydrated (<1.0200) throughout both experimental trials (p=0.011), except for post-exercise, when the USG in the SB trial was significantly higher than in the PLA trial (p=0.010) (Table 4). Table 4 also showed that subjects perceived “Fairly Comfortable” and “Slightly Full” after a supplement drink was ingested in the SB trial. In contrast, the feelings of abdominal discomfort and GUT fullness in the PLA trial were very minimal and not statistically significant different (p>0.05).

Discussion

The present study showed that subjects could run approximately 212 meters further in the SB trial (5,233.60±524.70 meters) compared to the PLA trial (5,021.40±440.20 meters). Subjects perceived “very hard” at the end of the 60-minute PET, associated with HR and VO_{2} responses, indicating that they had reached 92% of HR_{max} and 80% of VO_{2}max in both the SB and PLA trials. These results showed that the subjects were using the same effort while performing the PET for both trials. Similar to the study carried out by Siegler JC and Gleadall-Siddall DO, no effects were found on average
HR, HR\textsubscript{max} and RPE between the placebo group and the NaHCO\textsubscript{3} ingestion group (0.3 g/kg) among 10 amateur boxers. However, overall punch efficacy was significantly improved after ingestion of NaHCO\textsubscript{3} (p<0.001). The blood buffering potential from the external ingestion of NaHCO\textsubscript{3} could elevate the extracellular concentration of HCO\textsubscript{3} level throughout four rounds of boxing, thus facilitating the removal of H\textsuperscript{+} from working muscles. Furthermore, Karavelioglu MB reported that 15 female futsal players after taking NaHCO\textsubscript{3}+ supplement (0.3 g/kgBW) prior to a 120-minutes Yo-Yo intermittent recovery test level 1 showed no significant difference in the HR and blood lactate between pre-test and post-test (Pre-Test: 197 ± 6 beats/minutes; Post-test: 196±7 beats/minutes; p>0.05).13 However, a statistically significant difference was found in the running distance between pre-test (1,120.00± 320.50 meters) and post-test (1,421.30±287.60) in the experimental group. On the contrary, Freis T et al., indicated that acute ingestion of NaHCO\textsubscript{3} (0.3 g/kg) did show significant improvement in maximal running speed in the NaHCO\textsubscript{3} ingestion group (17.40±1.00 km/hours) compared to placebo (17.10±1.00 km/hours) (p=0.009) but failed to show a significant difference in time to exhaustion for prolonged high intensity running.14

The blood lactate levels were significantly greater in the SB trial (5.66 ± 1.08 mmol/L) than in the PLA trial (3.68 ± 0.71 mmol/L) during Post-Exercise (Table 4). Similar results were found in the study conducted by Freis T et al., where the blood lactate response increased in the NaHCO\textsubscript{3} trial group compared to the placebo group (NaHCO\textsubscript{3}: 11.10±2.30 mmol/L; placebo: 8.90±3.00 mmol/L; p<0.001) after prolonged high intensity running. Likewise, the effect of NaHCO\textsubscript{3} loading on sprint performance following a 3 hours simulated cycling race followed by a 90-seconds all-out. A previous study showed NaHCO\textsubscript{3} intake (0.3 g/kgBW) improved mean duration during 90-seconds by almost 3%, peak blood lactate concentration and HR at the end of 90-seconds were higher (p<0.05) than in Placebo, NaHCO\textsubscript{3} ingestion increased blood HCO\textsubscript{3} (p<0.001) and blood pH (p<0.05) prior to 90-seconds. Consumption of NaHCO\textsubscript{3} was able to increase the glycolytic contribution to elevating higher ATP resynthesis rates in high-intensity performance for longer duration.16 The lactate produced by anaerobic glycolysis during exhaustive graded activity was neutralized by the higher concentration of HCO\textsubscript{3} in blood and this weakened the decrement in myoplasmic pH which in turn enhanced the performance by allowing longer anaerobic glycolytic processes.14

Higher HCO\textsubscript{3} ingestion can contribute to a higher pH level, resulting in a more alkaline environment and a greater buffering effect, which explains the higher pH level in the urine sample after NaHCO\textsubscript{3} ingestion in the current study (8.37±0.13; p= 0.001). The ingestion of NaHCO\textsubscript{3} is also expected to reduce a drop in blood pH during and after exercise. Human body contains three primary mechanisms to regulate the acid-base balance: the chemical buffers to adjust H\textsuperscript{+} ions, pulmonary ventilation to excrete H\textsuperscript{+} ions, and the kidney to maintain body acid-base balance. The kidney and lungs play a vital role in the buffering process when the body produces acid such as lactic acid through metabolism. In the present study, results showed that the increase of urine pH was maintained after the ingestion of NaHCO\textsubscript{3} throughout the SB trial compared to the PLA trial (SB: 8.37±0.13, PLA trial: 7.13±0.39; p=0.001). The extracellular HCO\textsubscript{3} concentration increased after ingestion of NaHCO\textsubscript{3}, therefore affecting the intracellular pH level and it maintained a steady pH

### Table 4. Several parameters assessed related to the pre-Ingestion, Pre-Exercise, Post-Exercise, and Post Recovery conditions.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Pre-Ingestion</th>
<th>Pre-Exercise</th>
<th>Post-Exercise</th>
<th>Post-Recovery</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.02±0.35</td>
<td>5.75±0.64</td>
<td>5.32±0.52</td>
<td>4.65±0.14</td>
<td>0.309</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>5.10±0.38</td>
<td>6.15±1.00</td>
<td>5.31±0.53</td>
<td>4.82±0.43</td>
<td>0.004*</td>
</tr>
<tr>
<td>pH</td>
<td>1.65±0.43</td>
<td>1.73±0.30</td>
<td>5.66±1.08</td>
<td>2.53±0.91</td>
<td>0.002*</td>
</tr>
<tr>
<td>USG</td>
<td>7.26±0.39</td>
<td>8.37±0.13</td>
<td>7.47±0.36</td>
<td>7.00±0.49</td>
<td>0.011*</td>
</tr>
<tr>
<td>AD</td>
<td>1.0035±0.0022</td>
<td>1.005±0.0027</td>
<td>1.0134±0.0033</td>
<td>1.0172±0.0032</td>
<td>0.193</td>
</tr>
<tr>
<td>SB</td>
<td>1.0028±0.0017</td>
<td>1.0034±0.0020</td>
<td>1.0092±0.0048</td>
<td>1.015±0.0034</td>
<td>0.152</td>
</tr>
<tr>
<td>PLA</td>
<td>0.20±0.40</td>
<td>1.90±2.10</td>
<td>2.20±2.20</td>
<td>1.60±1.50</td>
<td>0.001</td>
</tr>
<tr>
<td>PLA</td>
<td>0.30±0.50</td>
<td>1.00±0.80</td>
<td>1.20±1.00</td>
<td>1.00±0.80</td>
<td>0.001</td>
</tr>
<tr>
<td>GF</td>
<td>0.20±0.40</td>
<td>1.80±1.00</td>
<td>1.40±1.50</td>
<td>1.30±1.30</td>
<td>0.001</td>
</tr>
<tr>
<td>SB</td>
<td>0.40±0.70</td>
<td>1.00±0.80</td>
<td>0.90±0.70</td>
<td>0.70±0.70</td>
<td>0.001</td>
</tr>
<tr>
<td>PLA</td>
<td>1.00±0.80</td>
<td>1.00±0.80</td>
<td>1.00±0.80</td>
<td>1.00±0.80</td>
<td>0.001</td>
</tr>
</tbody>
</table>

SB: Sodium Bicarbonate; PLA: Placebo; USG: Ultrasonography; AD: Abdominal Discomfort; GF: Gut Fullness; *Significantly different from respective Pre-Ingestion values at p<0.05; †Significantly different from respective Pre-Exercise values at p<0.05; ‡Significantly different from PLA values during Pre-Exercise, Post-Exercise and Post-Recovery at p<0.01 and p<0.001, respectively; §Significantly different if p-value less than 0.05.
gradient between both intracellular and extracellular compartments. For the ratings of Abdominal Discomfort (AD) and GUT fullness (GF), no significant difference was found between the SB and the PLA trials in this present study. Although no significant difference between trials was detected in the rating of AD, 30% of the subjects did experience diarrhea symptoms prior to the current study’s test. Price MJ and Cripps D reported no significant difference in cycling sprint performance one hour after ingesting a placebo, glucose, NaHCO₃, or a combined carbohydrate (CHO) and NaHCO₃ solution. A solution containing both CHO (almost 28 gram) and NaHCO₃ was shown to reduce gastrointestinal distress while increasing CHO availability. In this present study, two pieces of white bread (30.5 gram of CHO in 67 gram of white bread) were given to the subjects to co-ingest with the 0.3 g/kgBW of NaHCO₃, but gastrointestinal discomfort was still observed in a few subjects in the study. Recently, Hilton NP et al. compared the effects of NaHCO₃ ingestion (0.3 g/kgBW) in enteric-coated and gelatin capsules on performance in 4-km cycling time trials. The results showed that the subjects ingested NaHCO₃ in enteric-coated and gelatin capsules during 4-km cycling time trials (8.5 and 9.6 seconds, respectively). Out of 11 participants, only three experienced gastrointestinal discomfort after ingesting enteric-coated capsules, compared to seven after ingesting gelatin capsules. Therefore, enteric-coated capsules are one possible way to minimize the severity of side effects. Saunders B et al., conducted a study on NaHCO₃ ingestion and high-intensity cycling and the results indicated that the blood lactate concentration for NaHCO₃ ingestion cyclists was higher (p<0.05) for those who improved in the performance. The alkalosis effect induced by the ingestion of NaHCO₃ will aid in the removal of H⁺ ions from working muscles and facilitate the extracellular buffering capacity. This explains why individuals who ingest NaHCO₃ can improve their performance because the H⁺ ions in the muscles can be removed or neutralized through better acid-base balance maintenance in their muscles. This directly contributes to the faster lactate clearance in the SB trial after a 30-minutes recovery period than in the PLA trial. The efflux of H⁺ ions may be halted by intracellular acidosis. Therefore, the faster recovery rate in the SB trial proves that the alkalosis induced by the NaHCO₃ aids in the removal of lactate in the body.

CONCLUSION
NaHCO₃ (0.3g/kgBW) ingestion 60-minutes prior to the PET improved prolonged running performance associated with a faster lactate removal rate during the 30-minutes recovery period. Further investigation should incorporate various methods (Enteric-coated, gelatin capsules, combined with higher dosage CHO with NaHCO₃) to reduce gastrointestinal distress following acute and chronic bicarbonate loading.

ACKNOWLEDGMENTS
The authors wish to thank the subjects for their invaluable contribution to the study.

AVAILABILITY OF DATA AND MATERIALS
Supporting data is available for the purpose of review from the corresponding author upon reasonable request.

COMPETING INTERESTS
The authors declare that they have no competing interests.

ETHICS APPROVAL
Ethics approval was granted by Tunku Abdul Rahman University College Ethics Committee (TARUC/EC/2019/07-3).

FUNDING
Funding was provided by the TAR UC Internal Research Grant (UC/I/G2019-00056).

AUTHOR’S CONTRIBUTIONS
LKS was responsible for literature search, experimental design, data collection and analysis, manuscript preparation, and writing. LHY was responsible for experimental design, data analysis, and interpretation, and manuscript revision. GYY was responsible for literature search, data analysis & interpretation, manuscript editing and revision. WEH was responsible for experimental design, manuscript editing and revision. All authors read and approved the final manuscript.

REFERENCES
10. Carr AJ, Slater GJ, Gore CJ, Dawson B, Burke LM. Effect of sodium bicarbonate...


