frontiers in Nutrition

ORIGINAL RESEARCH
published: 08 September 2020
doi: 10.3389/fnut.2020.00154

Sodium Bicarbonate Ingestion Improves Time-to-Exhaustion Cycling Performance and Alters Estimated Energy System Contribution: A Dose-Response Investigation

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Specialty section:
This article was submitted to Sport and Exercise Nutrition, a section of the journal Frontiers in Nutrition

Received: 29 May 2020
Accepted: 29 July 2020
Published: 08 September 2020

Citation:
Gurton WH, Gough LA, Sparks SA, Faghy MA and Reed KE (2020) Sodium Bicarbonate Ingestion Improves Time-to-Exhaustion Cycling Performance and Alters Estimated Energy System Contribution: A Dose-Response Investigation. Front. Nutr. 7:154. doi: 10.3389/fnut.2020.00154

This study investigated the effects of two sodium bicarbonate ($NaHCO_3$) doses on estimated energy system contribution and performance during an intermittent high-intensity cycling test (HICT), and time-to-exhaustion (TTE) exercise. Twelve healthy males (stature: 1.75 ± 0.08 m; body mass: 67.5 ± 6.3 kg; age: 21.0 ± 1.4 years; maximal oxygen consumption: 45.1 ± 7.0 ml.kg.min^{-1}) attended four separate laboratory visits. Maximal aerobic power (MAP) was identified from an incremental exercise test. During the three experimental visits, participants ingested either 0.2 g.kg^{-1} BM $NaHCO_3$ (SBC2), 0.3 g.kg^{-1} BM $NaHCO_3$ (SBC3), or 0.07 g.kg^{-1} BM sodium chloride (placebo; PLA) at 60 min pre-exercise. The HICT involved 3 × 60 s cycling bouts (90, 95, 100% MAP) interspersed with 90 s recovery, followed by TTE cycling at 105% MAP. Blood lactate was measured after each cycling bout to calculate estimates for glycolytic contribution to exercise. Gastrointestinal (GI) upset was quantified at baseline, 30 and 60 min post-ingestion, and 5 min post-exercise. Cycling TTE increased for SBC2 (+20.2 s; $p = 0.045$) and SBC3 (+31.9 s; $p = 0.004$) compared to PLA. Glycolytic contribution increased, albeit non-significantly, during the TTE protocol for SBC2 (+7.77 kJ; $p = 0.10$) and SBC3 (+7.95 kJ; $p = 0.07$) compared to PLA. GI upset was exacerbated post-exercise after SBC3 for nausea compared to SBC2 and PLA ($p < 0.05$), whilst SBC2 was not significantly different to PLA for any symptom ($p > 0.05$). Both $NaHCO_3$ doses enhanced cycling performance and glycolytic contribution, however, higher doses may maximize ergogenic benefits.

Keywords: anaerobic, ergogenic aid, high-intensity exercise, alkalosis, fatigue, extracellular buffer

INTRODUCTION

High-intensity interval training (HIIT) involves near maximal exercise bouts (>80–100% maximum heart rate) separated by brief recovery periods (1). The high anaerobic demand associated with maximal efforts results in the accumulation of hydrogen cations (H^+) within the cytosol (2). Whilst these are mostly removed by intramuscular and/or extracellular buffering mechanics, production overwhelms neutralization, and this contributes toward a reduced intramuscular pH (3), causing exercise-induced acidosis. Such a biochemical state has been suggested to reduce glycolytic energy production and may disrupt calcium ion cross-bridge formation (4). A common strategy to mitigate these deleterious effects of exercise is to enhance circulating level of extracellular blood bicarbonate (HCO_3^-), which subsequently allows for sustained efflux of H^+ from intramuscular environments during high-intensity exercise (5). Increases in [HCO_3^-] of ∼5.0–6.0 mmol.l^{-1} are suggested to be ergogenic and can be achieved via the ingestion of extracellular buffers, such as sodium bicarbonate ($NaHCO_3$) in doses of 0.2–0.3 g.kg^{-1} BM, respectively (6, 7).

Common practice is to ingest 0.3 g.kg^{-1} BM $NaHCO_3$ at 60–90 min prior to exercise, which is based on historical research showing time to peak pH or HCO_3^- occurs at this time point at the group mean level (6, 8). It is, however, likely that through following this strategy the dissociation of $NaHCO_3$ within stomach acid will cause gastrointestinal (GI) upset (9), which may impair performance or dissuade athletes from using $NaHCO_3$ (10, 11). Whilst, some authors have observed ergogenic benefits despite moderate GI upset (12, 13), in some cases the upset has been severe or the participant has not been able to continue with the study procedures (14, 15). The administration of smaller $NaHCO_3$ doses (0.2 g.kg^{-1} BM) might therefore be preferable, as it can mitigate GI upset and also reduce the sodium load per dose which might alleviate the health risks of ingesting this supplement; although these risks are more associated with long term use of $NaHCO_3$ (12, 16). McNaughton (17) reported exacerbated GI upset following higher $NaHCO_3$ doses, while Gough et al. (12) observed reduced occurrence of bowel urgency and bloating for 0.2 g.kg^{-1} compared to 0.3 g.kg^{-1} BM $NaHCO_3$. Reducing the dose is a simple strategy that might remove some of the negative connotations of ingesting this supplement, whilst it is far more cost effective than some of the recent strategies employed to reduce the GI upset following $NaHCO_3$ ingestion, such as in enteric-coated capsules (18, 19).

Contemporary research has administered $NaHCO_3$ using an individualized time-to-peak pH or HCO_3^- approach, which is in response to studies showing that time-to-peak pH or HCO_3^- can vary between 10 and 180 min within individuals, regardless of the ingestion method (i.e., capsule vs. fluid) (7, 12–14). In using the individual time-to-peak approach, this ensures that peak [HCO_3^-] is achieved immediately before exercise, which does seem to lead to a more consistent ergogenic response (12, 14). The identification of this time-to-peak HCO_3^- response presents a logistical challenge to athletes however, as the financial cost is high and requires specialist equipment and staff. It is plausible to suggest further research is therefore required to simplify this strategy, and to assess whether ergogenic benefits still exist for smaller $NaHCO_3$ doses following administration at a standardized time point. This, in turn, could increase the practical application of this supplement, whilst also potentially limiting GI upset.

The ergogenic benefits associated with $NaHCO_3$ ingestion are somewhat related to the increased activation of glycolytic energy pathways (20, 21). Whilst this is debated (22), $NaHCO_3$ ingestion attenuates muscle acidosis during exercise thus preventing the allosteric inhibition of glycogen phosphorlyase and phosphofructokinase (5). This has been shown to increase estimated glycolytic contribution during HIIT protocols (20), while there is robust evidence suggesting enhanced glycolytic flux within the muscle (23). Strategies that elevate glycolytic energy system contribution may enhance exercise capacity during HIIT, however, research is yet to determine whether smaller $NaHCO_3$ doses elicit a similar physiological response.

The purpose of this study therefore was to investigate the effect of 0.2 and 0.3 g.kg^{-1} BM $NaHCO_3$ ingested at 60 min pre-exercise on estimated energy contribution during a high-intensity, interval cycling test (HICT), and time-to-exhaustion (TTE) cycling performance.

MATERIALS AND METHODS

Experimental Approach to the Problem

A block randomized, across subjects counterbalanced, single-blind, placebo-controlled, crossover experimental design was implemented for this study. Participants visited the laboratory on four separate occasions to complete an incremental exercise test, familiarization, and three experimental trials. All testing was conducted at the same time of day (± 2 h) to minimize the confounding effects of circadian rhythms on exercise performance (24). Participants arrived at the laboratory in a 3-h post-prandial state, having refrained from alcohol ingestion and vigorous exercise for 24 h prior. Maximal aerobic power (MAP) was determined from the incremental exercise test and used to prescribe the exercise intensities for the HICT and TTE cycling protocols (described below). Participants completed these exercise procedures for three experimental treatment arms: (a) 0.2 g.kg^{-1} BM $NaHCO_3$ (SBC2), (b) 0.3 g.kg^{-1} BM $NaHCO_3$ (SBC3), or (c) 0.07 g.kg^{-1} BM sodium chloride to ensure taste-matching (placebo; PLA) (12). Participants were instructed to maintain activity levels and dietary intake throughout the study, which were assessed via written logs. All experimental trials were separated by 7 days.

Participants

Twelve healthy males (stature: 1.75 ± 0.08 m; body mass: 67.5 ± 6.3 kg; age: 21.0 ± 1.4 years; maximal oxygen consumption: 45.1 ± 7.0 ml.kg.min^{-1}) volunteered for this study. All participants were recreationally active and completed at least 60 min of vigorous exercise per week. Participants were excluded if they had any history of hypertension (>140/80 mmHg), were currently

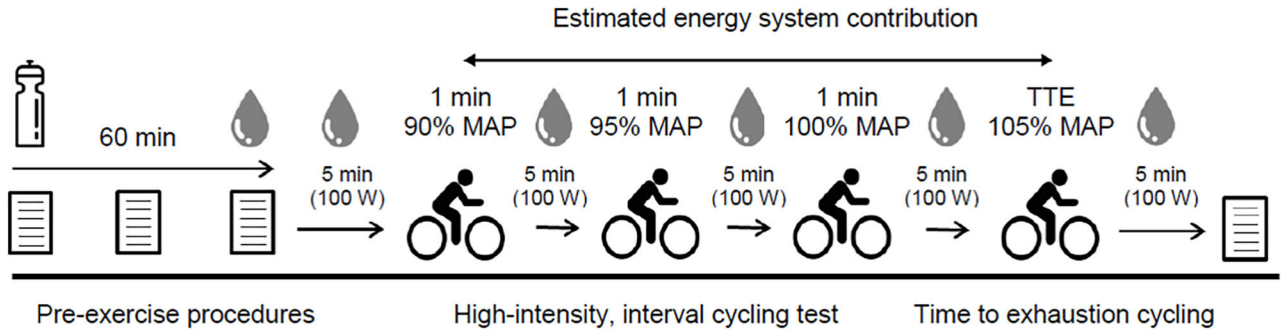

FIGURE 1 | Schematic overviewing procedures during experimental visits; MAP, maximal aerobic power; TTE, time to exhaustion.

taking any medication/sports supplements, or had ingested intra- or extracellular buffering agents within the previous 6 months. The study was approved by the institutional departmental review board. Each participant was informed of the benefits and risks of the investigation prior to signing informed consent to participate in the study. Procedures were conducted in accordance with the World Medical Association's Declaration of Helsinki.

Procedures

On the initial visit, participants performed an incremental exercise test on a cycle ergometer (Excalibur Sport, Lode, Netherlands) to determine MAP. Gaseous exchange was collected using a breath-by-breath metabolic cart (Oxycon Pro, Jaeger, Hoechberg, Germany) to determine maximal rate of oxygen consumption (VO_{2max}). To determine VO_{2max}, the highest 30 s rolling average was calculated. Following a 5-min warm-up (70 W; 70–90 rev.min^{-1}), increments of 20 W.min^{-1} were applied until volitional exhaustion. This was deemed as the failure to maintain cycling cadence >60 rev.min^{-1} despite verbal encouragement. Maximal anaerobic power was calculated as the fraction of time in the final stage divided by test increment, added to completed power (25). Familiarization to exercise procedures (HICT and TTE cycling) was completed after 30 min of passive recovery. This involved three bouts of 60 s cycling (90, 95, and 100% MAP), interspersed with 90 s of active recovery (100 W) and TTE cycling at 105% MAP. These were completed on the cycle ergometer, with handle bar and seat height position adjusted according to preference, which was subsequently replicated for all experimental trials. The TTE cycling protocol was terminated when cadence dropped 10 rev.min^{-1} below the preferred cadence, and when participants were unable to re-establish preferred cadence (range of selected cadence = 70–90 rev.min^{-1}). Participants were encouraged to exercise until volitional exhaustion, but total exercise time was not revealed.

During experimental trial visits, participants completed visual analog scales (VAS) were used for baseline GI upset (0 mm = "no symptom"; 100 mm = "severest symptom") that quantified the severity of nausea, flatulence, abdominal discomfort (AD), gut fullness (GF), bowel urgency rating (BUR), diarrhea, vomiting, and belching (12). Participants then consumed one of three experimental beverages (SBC2, SBC3, or PLA) across a 5-min period 60 min prior to exercise. Ingestion time was chosen in-line with previous work that showed the absorption kinetics between these doses are not significantly different up to this time point (14), and is the most practiced ingestion timing (6, 8). These were served as a chilled aqueous solution of 4 ml.kg^{-1} BM water and 1 ml.kg^{-1} BM squash (double strength orange squash, Tesco, UK) to increase the palatability and taste-match each beverage (26). A supplement belief questionnaire was completed post-ingestion to assess the efficacy of the single-blind design, and to ensure that no psychological bias regarding the impact of $NaHCO_3$ ingestion was transferred onto participants (27). Symptoms of GI upset were repeated at 30- and 60-min post-ingestion. Pre-exercise capillary blood samples were collected into 20 μL end-to-end sodium heparised capillary tubes (EKF Diagnostic GmbH, Germany) and analyzed for blood lactate concentration ([BLa^-]) using the Biosen C-Line (EKF Diagnostic GmbH, Germany). Participants rested for 5 min to determine baseline oxygen consumption and respiratory exchange ratio (RER), before completing the HICT and TTE protocols, during which gaseous exchange was measured throughout, and blood samples were taken after each cycling bout. Additional visual analog scales were completed immediately post-exercise for GI upset. An overview of experimental trials is displayed in **Figure 1**.

Estimated Energy System Contribution Calculations

Absolute energy demand and energy contribution from the oxidative and glycolytic energetic systems were estimated via non-invasive technique. The oxidative phosphorylation pathway (W_{AER}) was determined by subtracting resting oxygen consumption (i.e., the mean VO_2 value during the final 30 s of baseline) from the area under the oxygen consumption curve for each of the three 60 s bouts (90, 95, and 100% MAP) during the HICT (28). Area under the curve was calculated using the trapezoidal method. This approach has recently been shown to provide reliable and valid estimations for W_{AER} during intermittent exercise (20, 29). The glycolytic pathway ($W_{[LA]}$) was calculated from the assumption that a difference

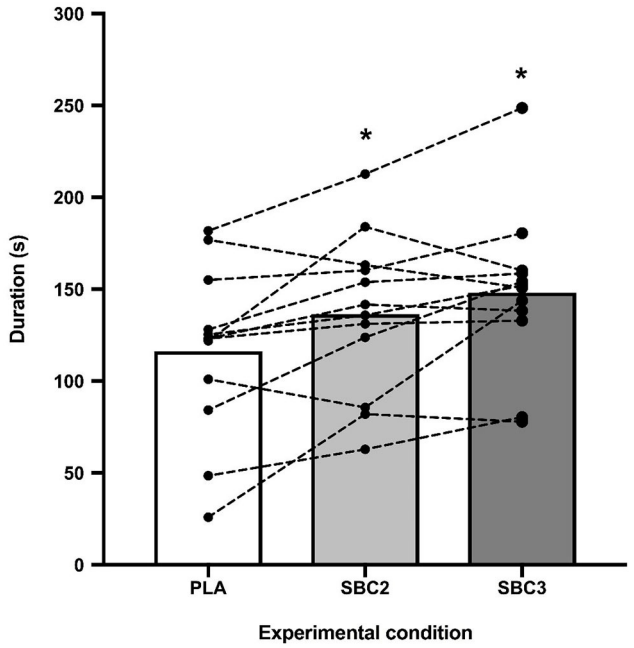

FIGURE 2 | Mean differences and inter-individual variation for TTE cycling performance; SBC2, 0.2 g.kg^{-1} BM $NaHCO_3$; SBC3, 0.3 g.kg^{-1} BM $NaHCO_3$; PLA, sodium chloride (placebo); * sig difference compared to PLA trial ($p < 0.05$).

of 1 mmol.l^{-1} of BLa^- obtained by subtracting baseline [BLa^-] from peak [BLa^-] (i.e., delta [BLa^-]) corresponded to 3 ml.kg^{-1} BM of O_2 (20, 29–32). Therefore, delta [BLa^-] for each of the three 60 s bouts and during TTE cycling (i.e., difference from pre to post) was multiplied by 3 and the participants' body mass to calculate $W_{[LA]}$. The caloric quotient of 20.92 kJ was used to convert between absolute energy demand (in L of O_2) and energy contribution (in kJ) for both energetic systems.

Statistical Analysis

Normality and sphericity were assessed using Shapiro-Wilk and Mauchly tests, before correcting for any violations (Greenhouse Geisser). One-way repeated measures analysis of variance (ANOVA) were conducted for cycling TTE performance and total energy demand and contribution from W_{AER} and $W_{[LA]}$ during exercise protocols. The smallest worthwhile change (SWC) in performance (9.1 s) was calculated as 0.3 x the between-individual SD for cycling TTE during familiarization (33). This was then used as a threshold for interpreting individual differences and in an attempt to identify a true change in exercise performance between the $NaHCO_3$ and the placebo conditions. Two-factor (treatment x time) repeated measures ANOVA's were performed for [BLa^-], RER, W_{AER}, and $W_{[LA]}$ for each of the three 60 s bouts during the HICT. When significant interactions were observed, pairwise comparisons using the bonferroni correction factor were performed. Friedman's two-way ANOVA's were conducted for GI upset. *Post-hoc* Wilcoxon matched-pair signed rank tests were performed when significance was observed, with median, Z score, and significance reported. Fisher's exact test was used to assess the efficacy of the single-blind design. For ANOVA interactions, effect sizes were presented as partial eta-squared (η_p^2) (34). Between treatment effect sizes were calculated by dividing the difference in means by the pooled SD (35), before applying a Hedges g (g) bias correction to account for the small sample size (36). These were interpreted as trivial (<0.20), small (0.20–0.49), moderate (0.50–0.79), or large (≥0.80) (37). Data are presented as mean ± SD and 95% confidence intervals (CI) reported for mean differences. Statistical significance was set at $p < 0.05$ and data were analyzed using SPSS v25 (SPSS Inc., IBM, USA).

RESULTS

Performance was greater for SBC2 (136.4 ± 43.5 s) and SBC3 (158.7 ± 63.3 s) compared to PLA (116.2 ± 46.6 s) (**Figure 2**). These increases were significant for SBC2 (+20.2 s; CI: 0.4, 39.9; $p = 0.045$; $g = 0.77$) and SBC3 (+31.9 s; CI: 10.8, 53.1; $p = 0.004$; $g = 1.13$). A total of 8 out of 12 participants improved their performance above the SWC following SBC2, whilst 11 participants (out of 12) improved above this threshold following SBC3 (**Figure 3**). There was an 11.7 s mean difference in favor of SBC3 vs. SBC2, but this increase was not significant ($p = 0.303$; $g = 0.48$). Nonetheless, seven of the participants (out of 12) improved their performance above the SWC for SBC3 vs. SBC2, whilst this was only in favor of SBC2 for a single participant.

Grouped mean ± SD data for [BLa^-] and RER are presented in **Table 1**. No significant differences were displayed during the HICT protocol ($p > 0.05$). Post-TTE [BLa^-] was elevated for SBC2 (+2.35 mmol.l^{-1}; CI: 0.06, 4.64; $p = 0.04$; $g = 0.77$) and SBC3 (+3.13 mmol.l^{-1}; CI: 1.44, 4.82; $p = 0.001$; $g = 1.40$) compared to PLA. There was a small effect size for SBC3 vs. SBC2 (+0.78 mmol.l^{-1}; $p = 0.34$; $g = 0.46$). Peak RER was also increased for SBC2 (+0.09 AU; CI: 0.03, 0.15; $p = 0.005$; $g = 1.14$) and SBC3 (+0.11 AU; CI: 0.03, 0.19; $p = 0.011$; $g = 0.98$) compared to PLA.

Total energy demand and contribution of the oxidative and glycolytic energetic systems during the HICT are presented in **Table 2**. No significant differences were displayed for energy demand or contribution from W_{AER} or $W_{[LA]}$ ($p > 0.05$), although $W_{[LA]}$ contribution was moderately increased for SBC2 (+3.71 kJ; $p = 0.09$; $g = 0.66$) and SBC3 (+7.12 kJ; $p = 0.14$; $g = 0.60$) compared to PLA (23.40 ± 8.93 kJ). There was a small effect size for $W_{[LA]}$ contribution when comparing SBC3 vs. SBC2 (+3.41 kJ; $p = 0.99$; $g = 0.27$). Energy contribution from W_{AER} was greater during the second 60 s bout for PLA vs. SBC2 (+4.16 kJ; CI: 0.50, 7.81; $p = 0.03$; $g = 0.86$). No significant differences were observed for energy contribution from W_{AER} or $W_{[LA]}$ during TTE cycling ($p > 0.05$; **Figures 4A,B**), although $W_{[LA]}$ was moderately increased for SBC2 (+7.77 kJ; $p = 0.10$; $g = 0.65$) and SBC3 (+7.95 kJ; $p = 0.07$; $g = 0.70$) compared

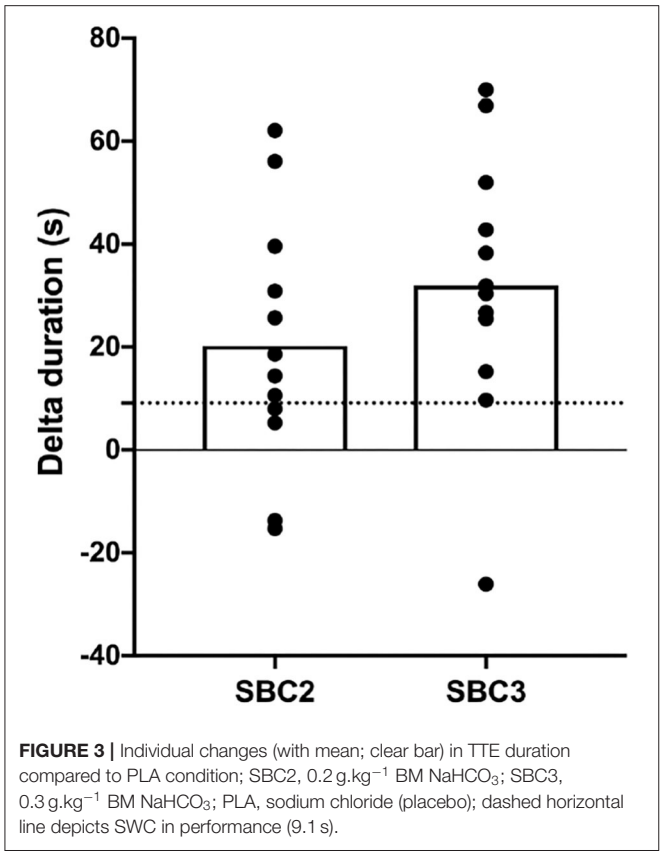

FIGURE 3 | Individual changes (with mean; clear bar) in TTE duration compared to PLA condition; SBC2, 0.2 g.kg^{-1} BM $NaHCO_3$; SBC3, 0.3 g.kg^{-1} BM $NaHCO_3$; PLA, sodium chloride (placebo); dashed horizontal line depicts SWC in performance (9.1 s).

TABLE 1 | Physiological variables ([BLa$^-$] and RER) obtained during the HICT and TTE cycling.

		90%	95%	100%	TTE
[BLa$^-$] (mmol.l^{-1})	SBC2	4.71 ± 1.38	6.91 ± 1.52	8.73 ± 1.80	14.09 ± 3.95*
	SBC3	4.30 ± 1.43	6.86 ± 1.66	9.35 ± 3.68	14.87 ± 3.01*
	PLA	4.26 ± 1.43	6.79 ± 2.06	8.13 ± 2.46	11.74 ± 3.47
RER (AU)	SBC2	1.08 ± 0.06	1.07 ± 0.04	1.08 ± 0.03	1.25 ± 0.06*
	SBC3	1.11 ± 0.05	1.09 ± 0.06	1.09 ± 0.06	1.26 ± 0.10*
	PLA	1.08 ± 0.07	1.07 ± 0.06	1.05 ± 0.04	1.15 ± 0.06

Data are mean ± SD; HICT, high-intensity, interval cycling test (60 s bouts at 90, 95, and 100% maximal aerobic power); TTE, time to exhaustion; SBC2, 0.2 g.kg^{-1} BM $NaHCO_3$; SBC3, 0.3 g.kg^{-1} BM $NaHCO_3$; PLA, sodium chloride (placebo).
** sig difference compared to PLA ($p < 0.05$).*

to PLA (15.62 ± 9.27 kJ). No difference was reported for $W_{[LA]}$ when comparing SBC3 vs. SBC2 (+0.18 kJ; $p = 1.00$; $g = 0.01$).

Treatments were successfully single-blinded and taste-matched (Fisher's exact test, $p = 0.28$). One subject identified all three beverages, eight only correctly perceived one of the three beverages, and the remaining three were unsure on all treatments. Eight participants reported their severest symptom after either SBC2 (4/12) or SBC3 (4/12), although some reported no difference between treatments (3/12), whereas one experienced

TABLE 2 | Total energy demand and contribution of the oxidative and glycolytic systems during the HICT.

		SBC2	SBC3	PLA
Energy demand (L of O_2)	W_{AER}	5.1 ± 0.9	5.1 ± 0.8	5.3 ± 0.8
	$W_{[LA]}$	1.3 ± 0.4	1.5 ± 0.8	1.1 ± 0.4
Energy contribution (kJ)	W_{AER}	105.8 ± 18.9	106.4 ± 17.0	110.1 ± 17.2
	$W_{[LA]}$	27.1 ± 8.5	30.5 ± 17.4	23.4 ± 8.9

Data are mean ± SD; HICT, high-intensity, interval cycling test (60 s bouts at 90, 95, and 100% maximal aerobic power); W_{AER}, oxidative phosphorylation contribution; $W_{[LA]}$, glycolytic contribution; SBC2, 0.2 g.kg^{-1} BM $NaHCO_3$; SBC3, 0.3 g.kg^{-1} BM $NaHCO_3$; PLA, sodium chloride (placebo).

the severest symptom following PLA (**Table 3**). No intervention or time interaction was observed at 30- or 60-min post-ingestion for any GI symptom ($p > 0.05$), or at post-exercise for vomiting, flatulence, GF, BUR, or diarrhea ($p > 0.05$). Nonetheless, symptom severity was increased post-exercise following SBC3 compared to PLA for nausea (10.0 vs. 1.0 mm; $Z = -2.197$; $p = 0.028$) and belching (8.0 vs. 1.0 mm; $Z = -2.371$; $p = 0.018$), but not for SBC2 compared to PLA ($p > 0.05$). Increases in the severity of nausea post-exercise was also observed following SBC3 compared to SBC2 ($Z = 2.366$; $p = 0.018$; **Figure 5A**), but not belching ($Z = 1.352$; $p = 0.176$; **Figure 5B**). There was no difference between aggregate GI upset between SBC2 and SBC3 at any time point (all $p > 0.05$).

DISCUSSION

This study is the first to explore the dose-response effects of $NaHCO_3$ ingestion when administered at a standardized time point on estimated energy system contribution and performance during intermittent cycling exercise. Both 0.2 and 0.3 g.kg^{-1} BM $NaHCO_3$ improved cycling TTE and estimated glycolytic contribution during HICT, therefore both doses can be employed as an ergogenic strategy. Only minimal dose-dependent differences in GI upset were observed, although the smaller dose mitigated severity of post-exercise nausea and belching. The key finding of this study therefore is that 0.2 g.kg^{-1} BM of $NaHCO_3$ can increase estimated glycolytic system contribution and be ergogenic for intermittent exercise performance.

Improvements in cycling TTE were observed for SBC2 and SBC3, with the moderate-to-large effect sizes reflective of previous findings employing a similar TTE protocol (26). The present study adds to previous work (17, 38), however, that ergogenic benefits can also be observed with a lower dose of $NaHCO_3$. Importantly, however, more participants improved over the SWC for SBC3 vs. SBC2, and a small effect size between treatments was observed in favor of SBC3 at the group level. This contradicts findings by McKenzie et al. (38) that displayed a 4 s difference in TTE for 0.15 and 0.3 g.kg^{-1} BM

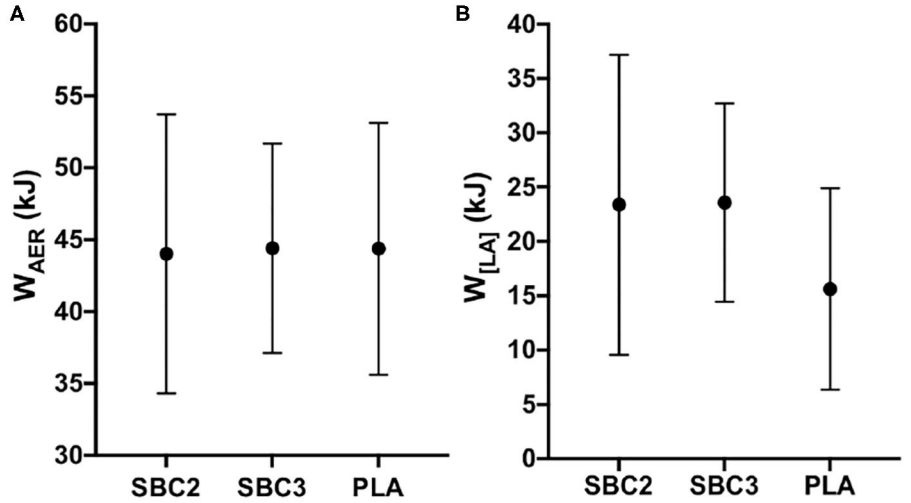

FIGURE 4 | (A,B) Mean ± SD for W_{AER} **(A)** and $W_{[LA]}$ **(B)** contribution during TTE cycling; SBC2, 0.2 g.kg^{-1} BM $NaHCO_3$; SBC3, 0.3 g.kg^{-1} BM $NaHCO_3$; PLA, sodium chloride (placebo).

$NaHCO_3$, and Gough et al. (12) where only a 0.1% variation in 4-km cycling time trial performance was present for 0.2 and 0.3 g.kg^{-1} BM doses. This discrepancy could be explained by differences in administration approach (standardized time point vs. time-to-peak), or the high-degree of inter-individual variation present in acid base balance following $NaHCO_3$ ingestion. Nonetheless, based on seven participants improving their performance following SBC3 vs. SBC2 (based on SWC), it is likely the athlete will secure the largest benefit from this higher dose. These dose-dependent differences in performance could also be attributed to the timing of exercise protocols. The cycling TTE protocol commenced ∼75 min after $NaHCO_3$ ingestion accounting for both the warm-up and HICT, however it is expected that [HCO_3–] will continue to rise until ∼80 min post-ingestion for SBC3, by which point [HCO_3–] will have started to decline for SBC2 in most individuals (12, 14). Nonetheless, athletes unable to pre-determine their time-to-peak HCO_3– can still employ either dosing strategy of the present study to obtain performance benefits during high-intensity cycling exercise.

Moderate, albeit non-significant, increases were observed for $W_{[LA]}$ during the HICT without altering energy demand or contribution from W_{AER}, which is in agreement to findings from recent studies (20, 21, 31). Despite not achieving statistical significance, these increases were considered substantial for both SBC2 (+15.8%) and SBC3 (+30.3%) when compared to PLA, with the relatively small absolute changes in $W_{[LA]}$ attributed to the controlled total mechanical work during the HICT (20). The most novel finding, however, was that there may be a dose-response effect of $NaHCO_3$ ingestion on changes in energy system contributions, with a small effect size present for $W_{[LA]}$ in favor of SBC3. Considering that enhanced HCO_3– buffering capacity is responsible for elevating glycolytic contribution, one explanation for these dose-dependent results could relate to the total amount of H^+ that can be neutralized. Assuming that total blood volume is ∼5 L and that [HCO_3–] was as small as ∼1.0 mmol.l^{-1} higher for SBC3 vs. SBC2, then the higher dose could have allowed the neutralization of an extra ∼5 mmoles of H^+ (based on the 1:1 stoichiometry of HCO_3– and H^+ reaction), in theory eliciting a greater up-regulation of glycolytic contribution (20). It is important to note, however, that as the current methodology only indirectly assesses glycolytic flux (i.e., from changes in [BLa^-]), these increases in $W_{[LA]}$ contribution may overestimate glycolytic activation, instead reflecting greater lactate efflux from working muscles (5). Nonetheless, previous research

TABLE 3 | The severest gastrointestinal (GI) symptoms for participants during each experimental trial.

Participant	SBC2	SBC3	PLA
1	**BUR (90.0)****	Vomiting (80.0)**	GF (39.0)
2	**BUR (19.0)**	GF (17.0)	GF (14.0)
3	**Belching (20.0)**	GF (18.0)	Belching (5.0)
4	**GF (24.0)**	**GF (24.0)**	Belching (23.0)
5	Nausea (31.0)	**AD (33.0)**	Nausea (23.0)
6	**GF (59.0)**	**GF (59.0)**	Belching (39.0)
7	**GF (12.0)**	GF (10.0)	Nil (0.0)
8	GF (39.0)	AD (31.0)	**GF (69.0)**
9	GF (10.0)	**Flatulence (49.0)**	Belching (21.0)
10	Flatulence (21.0)	**AD (71.0)**	AD (13.0)
11	**Nil (0.0)**	**Nil (0.0)**	**Nil (0.0)**
12	GF (17.0)	**GF (72.0)**	GF (66.0)

*Symptom scores (out of 100 mm) are displayed in parenthesis; SBC2, 0.2 g.kg^{-1} BM $NaHCO_3$; SBC3, 0.3 g.kg^{-1} BM $NaHCO_3$; PLA, sodium chloride (placebo); BUR, bowel urgency rating; GF, gut fullness; AD, abdominal discomfort; **Reported 5–10 min after laboratory visit; highest symptom severity for each participant highlighted in bold.*

has corroborated the findings of the present study following $NaHCO_3$ ingestion (23), therefore it seems plausible that both dosing strategies partially up-regulate glycolytic activation during high-intensity cycling.

The ingestion of $NaHCO_3$ resulted in mild-to-moderate GI symptoms, although both doses were well-tolerated, which agrees with previous research (14). Minimal dose-dependent differences were observed for GI upset, though the reduced post-exercise nausea and belching for SBC2 agrees with Gough et al. (12) where belching was exacerbated for the higher dose. The reduced severity of GI upset from this study could be attributed to the body mass of the participants in the present study (mean = 68 ± 6 kg) compared to those that have reported greater severity of GI upset in healthy males (15) and trained rugby players (10) (90 ± 6 and 95 ± 13 kg). Relative dosing protocols were derived during early laboratory studies to normalize post-exercise base deficit (39), and therefore fail to account for physiological differences such as body mass and the total absolute $NaHCO_3$ dose. Athletes with high body mass administer a greater absolute $NaHCO_3$ dose despite minimal differences in gut absorption rates, particularly for the first 60 min post-ingestion (14), which most likely exacerbates GI upset. There might be an upper threshold for absolute $NaHCO_3$ doses, with doses above this exacerbating GI upset. At present, 0.2 $g.kg^{-1}$ BM $NaHCO_3$ is a suitable strategy for mitigating GI upset; however, future research could examine the effect of absolute dosage on symptom severity and exercise performance.

There are methodological limitations in the present study that future research should address. Firstly, the single-blind design of this study is a limitation that is important to note. Important methodological choices were adopted, however, to mitigate any potential impact of this design. This included the standardized verbal encouragement during exercise, and the use of a supplement belief questionnaire, as per previous research (12). The findings from the latter methodological decision suggested that the supplement was blinded from the participants and therefore the single-blind design has no impact on the efficacy of $NaHCO_3$ ingestion. Moreover, our inability to quantify changes in absolute demand and contribution from the ATP-PCr energetic system is a limitation. This was due to the relatively short recovery period (90 s) between each bout of the HICT that did not allow a clear EPOC curve to form and therefore, it was decided that the ATP-PCr energy contribution calculations should be excluded from our analysis. Lastly, it was not possible to measure changes in [HCO_3–] following $NaHCO_3$ ingestion in the present study. Evidence suggests, however, that the HCO_3– response is similar for 0.2 and 0.3 $g.kg^{-1}$ BM $NaHCO_3$ doses within ∼60 min, therefore participants were likely at a similar level of alkalosis irrespective of dose (12, 14). This timing of $NaHCO_3$ ingestion employed in this study was selected to assess of the potential ergogenic effects for athletes unable to adopt an individualized time-to-peak HCO_3– approach, or access a blood gas analyser. Based on the observed ergogenic benefits for both doses vs. PLA, it should further enhance the practical application of $NaHCO_3$ supplementation to the athlete with limited funding.

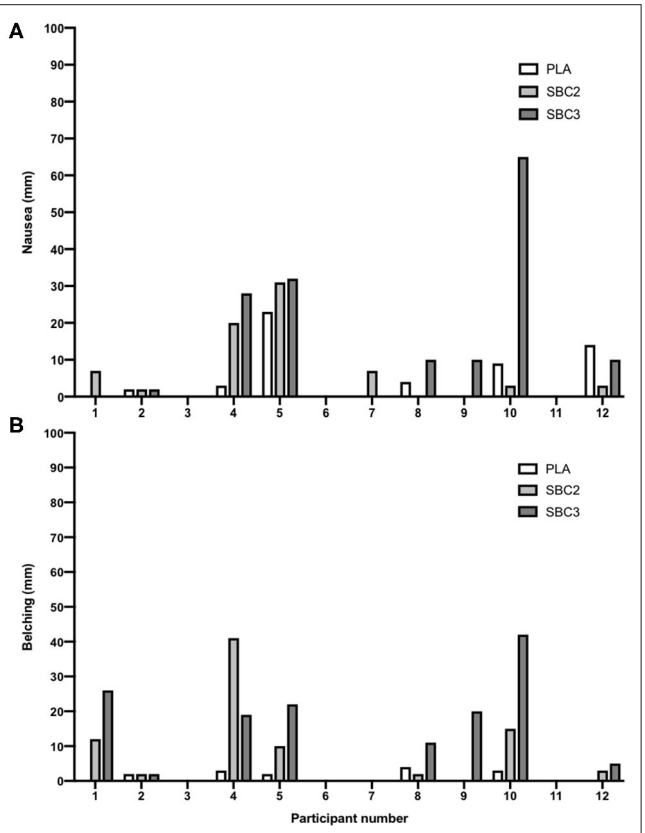

FIGURE 5 | (A,B) Inter-individual variations in post-exercise nausea and belching; self-reported symptoms via visual analog scales (out of 100 mm); SBC2, 0.2 $g.kg^{-1}$ BM $NaHCO_3$; SBC3, 0.3 $g.kg^{-1}$ BM $NaHCO_3$; PLA, sodium chloride (placebo).

CONCLUSION

Ingestion of 0.2 and 0.3 $g.kg^{-1}$ BM elevated glycolytic contribution to high intensity exercise and are ergogenic strategies to improve exercise performance. It is likely that athletes will gain increased benefit from SBC3, despite the occurrence of higher GI upset. Nonetheless, some athletes may still opt for the lower dose if this displays greater tolerability, whilst still securing an ergogenic benefit. The present study also shows that the contemporary time to peak alkalosis strategy might not be required when ingested 60 min prior to exercise, however direct comparisons between these two methods of ingestion are required.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Essex. The patients/participants

provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

KR, WG, and LG designed the study. WG completed the data collection, whilst WG and LG completed the majority of the manuscript, MF, SS, and KR also contributed. All authors reviewed the paper and provided feedback. LG and WG completed the preparation of the manuscript.

ACKNOWLEDGMENTS

We would like to thank all the participants for their time and efforts in this study. All authors have no conflict of interests to declare.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.