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Alkalinizers: Influence of Blood Acid-Base Status on Performance

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1. INTRODUCTION

The ingestion of a dose of 0.3 g/kg sodium bicarbonate or sodium citrate 2-3 h prior to high intensity exercise causes induced alkalosis and generally enhances performance. This is probably due to a greater efflux of hydrogen ions from the pH gradient across the muscle membrane. Diminished high intensity performance has been associated with consumption of high fat high protein meals, probably due to reduced intracellular buffering. This review examines the evidence for these findings.

2. PHYSIOLOGICAL BACKGROUND

Muscle fibres derive their energy for high intensity exercise from phosphagen stores and from anaerobic glycogenolysis. Increased glycogenolytic activity leads to an accumulation of lactic acid and a concomitant rise in hydrogen ion (H^+) concentration in muscle and blood. The elevation of H^+ and associated decrease in intracellular pH may cause an inhibition both of glycogenolysis and muscle contractility, thereby hindering performance. A buffer of significant importance in humans is the bicarbonate (HCO_3^-) buffer, present both intracellularly and in blood. Elevating the bicarbonate concentration in blood has been shown to result in an accelerated efflux of lactate ions (La^-) and H^+ from both intact human muscle, and isolated rat and frog muscle. Since the major transport mechanism of La^- is intimately linked to H^+ efflux via a lactate/proton co-transport mechanism, enhancing the concentration of blood bicarbonate following the ingestion of a salt of either bicarbonate or citrate should lead to a greater efflux of H^+ from muscle, and so maintain cellular pH. For this reason alkalinizers such as sodium bicarbonate and sodium citrate have been used as potential ergogenic aids prior to single or multiple bouts of intense exercise. Results from studies performed over the last 60 years have produced equivocal findings, which may be due to differences in timing and dosage of the alkalinizer, and/or the duration and intensity of exercise undertaken.

Blood HCO_3^- concentrations can also be influenced by dietary status. Studies over the last decade have highlighted the fact that a high carbohydrate, low fat diet leads to increases in blood HCO_3^-, base excess and blood pH, whereas a high fat, low carbohydrate or a high fat,

high protein diet leads to a reduction in blood HCO_3^-, base excess and blood pH. Furthermore, the high carbohydrate, low fat diet appears to enhance intense exercise compared to the high fat, low carbohydrate diet.

This review will briefly examine the rationale for the use of alkalinizers before reporting on some of the studies where bicarbonate and citrate ingestion have been undertaken, and also where dietary manipulation has been used for the expressed purpose of altering the acid-base status of the blood.

3. RATIONALE FOR THE USE OF ALKALINIZERS

Exercise of short duration and high intensity recruits predominantly fast glycolytic (FG) fibres in the active muscles [1]. These fibres draw upon anaerobic glycogenolysis for the synthesis of the majority of ATP necessary for muscle contraction [2]. A high rate of anaerobic glycogenolysis results in the formation and accumulation of lactic acid in muscle arising from:-

i) a lack of oxygen in the active muscle fibres,
ii) an increase in the rate of pyruvate formation such that this exceeds the rate it can be removed by oxidative processes, and
iii) the recruitment of predominantly FG fibres rich in the muscle isoform of lactate dehydrogenase (M-LDH) which favours formation of lactate from pyruvate.

At the physiological pH range of muscle and blood, 99.8% of the lactic acid produced exists in its ionised form [3], and therefore there is a concomitant increase in $[H^+]$ in muscle. The increase in $[H^+]$ will cause a decrease in muscle pH unless the H^+ is either buffered or removed. A small proportion of undissociated lactic acid diffuses freely through the sarcolemma, with the majority being actively transported using specific carrier-mediated systems. Proton efflux systems include a Na^+/H^+ exchange system, an HCO_3^-/Cl^- dependent exchange system, and a lactate/proton co-transport system [4]. Both the lactate/proton co-transport system and diffusion of undissociated lactic acid remove H^+ and lactate from the cells, and are of particular importance for pH regulation during and after muscle activity [5].

Accumulation of lactic acid in muscle has been related to a decline in maximal force generation [6] and the decrease in muscle pH considered as a significant fatiguing factor. This is supported by many experimental findings [7]. During maximal exercise the pH in muscle can decline from a resting value of 7.0 to values in the range of 6.5 to 6.3 [8]. This increase in H^+ accumulation not only affects metabolism and metabolic reactions directly [9], but also can disturb the intracellular ionic milieu, resulting in different proportions of free and bound forms of ionic species such as Mg^{2+} [10]. In addition, H^+ may compete directly with Ca^{2+} for access to the Ca^{2+} binding sites on troponin C [11].

The contention that intracellular acidosis may cause fatigue has been challenged, and it has been proposed that there are at least two components to fatigue [12]. One, is due to the direct effect of intracellular acidosis, and a major component not dependent on intracellular acidosis but sensitive to the external pH has also been suggested. If the external environment of muscle cells becomes more alkalotic, then there are possibilities that the rate of efflux of H^+ and lactate ions will be enhanced, thereby maintaining the pH of the cell closer to neutral. In vitro

studies using isolated frog muscle bathed in solutions containing HCO_3^- have shown this to be the case [13], as have studies using bicarbonate ingestion on intact human muscles during incremental exercise [14]. More recently, a cell membrane lactate transporter has been identified where La^- and H^+ efflux both follow a favourable pH gradient i.e. the rate of transport is directly related to the extracellular pH [15]. The use of alkalinizers could therefore improve high intensity exercise by providing an alkalotic environment external to the working muscle cells, resulting in a faster rate of efflux of the La^- and H^+ produced via anaerobic glycogenolysis. The faster rate of efflux of H^+ would maintain the pH within the cell for some period and so offset the fatiguing effects of H^+.

4. STUDIES USING BICARBONATE INGESTION

The first *in vivo* studies using sodium bicarbonate ingestion were performed 60 years ago in the Harvard Fatigue Laboratory [16,17], in which the authors provided evidence of improved performance and attributed this to the lactic acid being buffered by the alkalotic treatment. Following these early studies, little research was reported in this field until the late 1970's/early 1980's when three almost identical studies showed significant effects of bicarbonate ingestion on cycling to exhaustion at 90-95% VO_2max [18-20]. The dose given to the subjects in these studies was 0.3 g/kg body mass, subsequently shown to be an ideal load [21]. However, two studies performed a few years later showed that no significant improvements in power accrued following bicarbonate ingestion whilst undergoing a 30 s Wingate test on a cycle ergometer [22,23]. It could be proposed, on the basis of the findings from the latter five studies mentioned [18-23], that the duration of exercise needs to be accounted for if an ergogenic effect of bicarbonate is to be observed. A 30 s test would be too short to allow for sufficient accumulation of lactic acid and subsequent efflux of H^+ from muscle for bicarbonate to manifest its ergogenic effects. On the other hand, events lasting for approximately 5 min [18-20] are likely to be influenced by a significant lactic acid production and accumulation, and thereby the rate of H^+ efflux.

Support for the notion that the time period for exercise is important for any ergogenic effect of bicarbonate ingestion can be gleaned from studies where the time to exhaustion or time to achieve a given distance is analysed. Table 1 highlights some studies which have produced significant findings in favour of bicarbonate loading as well as those in which no improved responses were evident [18-38]. It is clear that intense exercise of short duration (i.e. < 60 s) is unlikely to benefit from bicarbonate ingestion, whereas performance of intense exercise of duration > 60 s may benefit. What is also apparent from these studies is that the dose of bicarbonate ingested may also influence findings i.e. a high dose (0.4 g/kg) resulted in enhanced performance of exercise lasting 60 s [34,37] which was not apparent from other studies using a lower dose [24]. Confirmation of this has come from a meta-analysis of 35 studies involving bicarbonate ingestion [39], in which the authors concluded that performance trials with a large anaerobic component, large doses of sodium bicarbonate, or repetitive work bouts were more likely to show significant ergogenic effects. Two recent studies in which the same author used a systematic approach to determine the effect of dose of bicarbonate ingested [21] and duration of exercise [40] have reinforced the contention that a dose of 0.3 g/kg body mass and a duration of at least 60 s of intense exercise are necessary for any ergogenic effect to be realised.

The degree of alkalosis induced by the ingestion of varying quantities of bicarbonate could influence the rate of $H^+$and La^- efflux, although there is difficulty in establishing a dose-response relationship from the various reports. This is due to factors such as lack of declaring blood pH, blood HCO_3, and base excess from pre-ingestion to pre-exercise, variations in the time from ingestion to exercise (1-3 hours), variations in the time course of ingesting the bicarbonate (all at once to 3 hours), and variations in the volume of fluid ingested. It is clear that taking a dose of 0.3 g/kg of sodium bicarbonate is likely to increase blood HCO_3 by 3-10 mM and increase pH by 0.03-0.1 units. The volume of fluid taken over the ingestion period may influence the degree of alkalosis as may the form of placebo ingested. A larger volume of fluid increases the degree of alkalosis and reduces gastro-intestinal side effects[41], whilst the ingestion of sodium chloride as a placebo has been shown to enhance acidosis[41], thereby magnifying the differences between placebo and experimental treatments.

Table 1
Summary of the effect of bicarbonate ingestion in relation to approximate duration of the test and to the dose ingested (first author only is listed in the reference column).

Studies where significant effect shown			Studies where no effect shown		
Reference	Duration (s)	Dose (g/kg)	Reference	Duration (s)	Dose (g/kg)
Sutton[18]	360	0.3	Kinderman[24]	60	0.2
Jones[19]	400	0.3	Inbar[22]	30	0.15
Sutton[20]	300	0.3	McCartney[23]	30	0.3
Wilkes[25]	120	0.3	Katz[26]	100	0.2
Costill[27]	160	0.2	Parry-Billings[29]	30	0.3
Wijnen[28]	120	0.3	Brien[31]	120	0.3
MacLaren[30]	330	0.25	Gaitanos[32]	10x6	0.3
MacLaren[14]	250	0.2			
McKenzie[33]	120	0.3			
Goldfinch[34]	60	0.4			
George[35]	1800	0.2			
Lavender[37]	10x10	0.3			
McNaughton[38]	60	0.4			
Bird[39]	250	0.3			

5. STUDIES USING CITRATE INGESTION

Comparatively few studies have been reported on the use of citrate ingestion with a view to enhancing blood buffering capacity. Perhaps the first study to determine the influence of sodium citrate *per se* on exercise was performed at Liverpool [29], and this was followed by at least two more recent investigations [42,43]. Earlier investigations had employed ingestion of fruit juices high in potassium citrate as the alkalotic agent [44-47]. Significant improvements were observed in swimming [44,47] but not in cross-country or treadmill

running [45,46]. The three more recent studies presented equivocal findings with no significant effects being evident on repeated cycle sprint exercise [29] or on a single bout of cycling at 95% VO_2max [42], although significant improvements for 'all-out' cycling over 60 s were observed when doses of 0.3-0.5 g/kg were ingested [43]. Citrate occurs in many foods and so could provide a natural means of promoting alkalosis. An increase in citrate intake does result in significant increases in blood HCO_3, base excess, and pH [29,42,43], probably by stimulating the liver to excrete bicarbonate. One advantage of ingesting citrate rather than bicarbonate is that gastro-intestinal distress is reduced; additionally in one study [29] a trend towards a more enhanced performance was observed with citrate than with bicarbonate.

6. STUDIES USING DIETARY PRACTICES

The effects of dietary practices on extracellular alkalosis have been examined in a series of reports from researchers at the University Medical School in Aberdeen [48-52]. These studies revealed that a diet in which the carbohydrate consumed was less than 10% of the total energy resulted in metabolic acidosis, whereas a diet in which the carbohydrate consumed was 65-75% of the total energy resulted in metabolic alkalosis. In two of the studies [48,50], performance was assessed as time to exhaustion at an intensity corresponding to 100% VO_2max; the low carbohydrate intake significantly impaired performance whereas a high carbohydrate diet failed to improve performance significantly compared with a normal dietary intake. The dietary components responsible for the observed metabolic acidosis were the elevations in free fatty acid, 3-hydroxybutyrate and plasma protein concentrations following a high fat, high protein diet. Thus, alterations in blood buffer base and increases in the circulation of both organic strong ions and non-volatile weak acids caused by the diet, influenced acid-base balance and so affected time to exhaustion during high intensity exercise. In a subsequent study [52] the authors concluded that the metabolic acidosis induced by a high fat, high protein diet caused a reduction in muscle buffering capacity rather than enhanced the efflux of H^+. It therefore appears that carbohydrate status was not the crucial factor in these studies since performance was not affected by a high carbohydrate diet; rather, a high fat high protein diet resulted in metabolic acidosis and impaired performance.

We investigated the effects of dietary status and bicarbonate loading [53] on cycle ergometry to exhaustion at an exercise intensity corresponding to 110% VO_2max. A low carbohydrate, high fat diet for 3 days depressed performance which could be partially alleviated by the ingestion of sodium bicarbonate; a high carbohydrate, bicarbonate loaded condition significantly improved performance.

7. CONCLUSIONS

It is clear that the ingestion of bicarbonate and citrate results in the augmentation of blood HCO_3 and an alkalotic extracellular environment. There is no evidence that a simple relationship exists between the degree of induced alkalosis and improvements in high intensity exercise, although in general the greater the ingestion of alkalinizer the more likely will an ergogenic effect be exhibited. As to the duration of exercise, the greater the level of metabolic acidosis from lactic acid production that is achieved during exercise, the greater the ergogenic

effect. The key factor associated with the ergogenic effect of alkalinizers appears to be the creation of a pH gradient across the muscle cell and the enhancement of La^- and H^+ efflux. Studies in which diet is manipulated to induce metabolic acidosis by reducing the carbohydrate intake or increasing the fat and protein intake have resulted in impaired performance, probably due to a reduction in intracellular buffer capacity.

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Discussion: Alkalinizers: Influence of Blood Acid-Base Status on Performance

J.P. Clarys:
Most of the things that you have been talking about were short-term situations. Do you know what the effects are of long-term uses of sodium bicarbonate?

D.P.M. MacLaren:
That is a question that could be asked with regard to ergogenic aids in general. To my knowledge there have not been any studies which have used sodium bicarbonate ingestion over a prolonged period of time such as in a 'training study'. As to the possible health effects of long term use, we do not know what they are.

F. Brouns:
How long is the effect of bicarbonate maintained after ingestion and, are there any differences between males and females in the effects observed?

D.P.M. MacLaren:
The answer to both questions is: I do not know. In our studies, the alkalinizer was ingested between 2 hours and 3 hours prior to exercise. So we really have not investigated anything which was taken, say, 6 or 12 hours before, but I guess that the clearance of bicarbonate by the kidney must be within the period of 12-24 hours. With regard to female athletes, I must admit we have never used female athletes in these particular studies and I think the studies that are reported in literature have generally not used females athletes either.

J.B. Leiper:
It is quite easy to induce a mild acidosis using dietary manipulation, however, in the studies that we have carried out in Aberdeen, we found it very difficult to produce a chronic alkalosis, even in vegetarians, by solely dietary means. Can you suggest any mechanism whereby we could chronically induce an alkalosis, rather than using a repeated intake of something such as sodium bicarbonate within the few hours before exercise?

D.P.M. MacLaren:
No, I do not really think so. Not without probably causing some gastrointestinal discomfort. But again, if you turn the question around slightly, it is worth mentioning that in a recent study from your laboratory (Ball *et al.*, 1996), a 24-hour dietary-induced acidosis followed by sodium bicarbonate ingestion prior to exercise still impaired performance. The results from this study suggest that it might not be the changes in the acid-base status that is important within muscle, but the glycogen content of muscle. In one of our recent studies (MacLaren *et al.*, 1996), using 13 subjects a low carbohydrate diet followed by ingestion of bicarbonate resulted in blood bicarbonate values back to normal, we still found a significant impairment in performance.

J.B. Leiper:

That is the point I wanted to make. By increasing the carbohydrate intake you are affecting muscle glycogen content and that seems to be the main problem. It is difficult to alter blood pH by dietary manipulation without influencing muscle glycogen content.

D.P.M. MacLaren:

But quite clearly, in our studies we have shown that a combination of a high carbohydrate intake for three days, followed by sodium bicarbonate ingestion 2.5-3 hours before, results in significant improvements in performance.

F. Brouns:

You could induce alkalosis by high calcium carbonate ingestion, but as far as I know, it can have potential side-effects if done over a prolonged period of time, causing milk alkali syndrome.

S. Erill:

I wonder whether sleep medicine could offer an answer, in the sense that positive pressure ventilation is used to treat some of the sleep apneas and manipulating the apparatus, perhaps one could induce some kind of chronic, nightly respiratory alkalosis.

T.D. Fahey:

Infusion of bicarbonate has been used to try to shift the oxyhemoglobin dissociation curve in climbers. Are you aware of anybody that has done infused bicarbonate studies? You could avoid the GI problems this way.

D.P.M. MacLaren:

I must admit I have not. All the studies that I have examined have been concerned with ingestion rather than infusion. In one study that we reported we examined athletes who ran to exhaustion at their V_{OBLA} (20 to 30 minutes) and showed significant improvements (George and MacLaren, 1988). It was suggested that we might have actually shifted the oxyhaemoglobin curve to the left. But if that were to happen at the muscle level, then less oxygen should have been given up to the muscle.