
INDUCED METABOLIC ACIDOSIS BY AMMONIUM CHLORIDE: ACTION MECHANISMS, DOSE AND EFFECTS ON ATHLETIC PERFORMANCE

ACIDOSE METABÓLICA INDUZIDA POR CLORETO DE AMÔNIO: MECANISMOS DE AÇÃO, DOSE UTILIZADA E EFEITOS SOBRE O DESEMPENHO ESPORTIVO

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RESUMO

A relação entre a acidose metabólica e o desempenho esportivo tem sido investigada ao longo dos anos através de manipulações do pH sanguíneo e muscular. Entre as formas de manipulação do pH, o cloreto de amônio (NH₄Cl) é o componente químico mais utilizado quando se pretende induzir um estado de acidose sanguínea previamente ao exercício. Entretanto, investigações acerca da ação desse agente sobre o desempenho esportivo ainda podem ser consideradas escassas, quando foram realizados apenas dois estudos nos últimos 15 anos. Dessa forma, serão abordados na presente revisão os principais aspectos envolvidos na ingestão de NH₄Cl, dando um enfoque aos mecanismos de ação dessa substância, especificações acerca do tipo de dose utilizada e seus efeitos sobre o desempenho esportivo.

Palavras-chave: Cloreto de amônio. Desempenho atlético. Acidose.

ABSTRACT

The relationship between metabolic acidosis and athletic performance has been investigated over the years through manipulation of the blood and muscle pH. Among the pH manipulation manners, the ammonium chloride (NH₄Cl) is the most widely used chemical component when is intentioned to induce a blood acidosis status prior to exercise. However, there is a lack of studies investigating the action of this substance on athletic performance as only two studies were performed in the last 15 years. Thus, it will be addressed in the present review the main aspects involved in NH₄Cl ingestion, giving a focus to the action mechanisms of this substance, specifications about the used dose and their effects on athletic performance.

Keywords: Ammonium chloride. Athletic performance. Acidosis.

Introduction

It has been proposed that in intense efforts above 75 % of maximal oxygen uptake (VO₂max) and/or peak power output (W_{peak}) there is a progressive increase in the intramuscular concentrations of hydrogen [H⁺] ions (eg. decrease in pH) which is associated to an acute muscle fatigue¹. It is believed this decrease in pH (increase of [H⁺]) reduces the action of some enzymes related to anaerobic metabolism, reducing the glycolytic and glycogenolytic rate and, consequently, attenuating the rate of adenosine triphosphate (ATP) production^{2,3}. Additionally, it has been demonstrated that blood lactate concentrations [La] are decreased in acidosis^{2,4,5}. This response may also be attributed to the attenuation of glycolytic activity due to decreases in extracellular and intracellular pH.

Considering the disturbance of the acid-base balance caused by the high-intensity exercise, the extracellular H⁺ buffer capacity has been extensively investigated through pH manipulations^{6,7}. Such manipulations may be performed via ingestion of chemical components, such as ammonium chloride (NH₄Cl). This substance promotes a metabolic acidosis, promoting thus a ergolytic effect during intense efforts.

Thus, the main aspects involved in NH₄Cl ingestion will be addressed in this review, focusing into action mechanisms of this substance, details about the dose used and its effects on sports performance. Due to the lack of studies involving the NH₄Cl ingestion and its effects on sports performance, we considered all the studies found in relation to this topic.

Among these, the performance was evaluated from a simple walk in a self-experiment to continuous intense exercises of constant-load cycling (90 to 110 % of VO_2max) or incremental test performed until exhaustion, 2-min rowing time trial and electrical stimulation or voluntary contractions of specific muscle groups.

Methods

A search was conducted in the PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) databases (no lower date limit; articles published up to November 2015). Initially, we used the following keywords: ‘*ammonium chloride*’, ‘*NH₄Cl*’ (ammonium chloride molecular formula), ‘*ammonium chloride ingestion*’, ‘*acidosis*’, ‘*induced metabolic acidosis*’, ‘*pH*’, ‘*exercise*’, ‘*exercise performance*’ and ‘*high-intensity exercise*’. The search yielded 34 potentially eligible studies. The reference lists of all of the identified articles were fully and carefully checked. We intended to identify articles that met the following criteria: (a) articles demonstrating a link between NH_4Cl ingestion or induced metabolic acidosis with sports performance and (b) research involving humans. A total of 14 studies comparing the effects of acute or chronic NH_4Cl ingestion with a control or placebo condition during exercise (regardless of mode or type of exercise due to lack of studies) were identified and included in the review. The selected studies were published between February 1931 and March 2015.

NH₄Cl and mechanisms of action

Among the possible causes of metabolic acidosis, including deficiency in acid excretion, loss of base and overproduction of metabolic acids, this may be caused by the ingestion of substances such as acetazolamide, hydrogen chloride (HCl) and NH_4Cl ^{6,8,9}. The NH_4Cl administration has been the most used to investigate the effects of previous metabolic acidosis during exercise^{2,6,7}. However, investigations about the action of this substance on sports performance can still be considered scarce and intensified in the last 15 years^{7,10}.

The first time NH_4Cl was related to metabolic acidosis occurred in 1921, when Haldane¹¹ suggested that after NH_4Cl ingestion it would have rapidly passed into the bloodstream and then into the liver, the ammonia (NH_3) portion being converted into urea and the remaining portion of HCl would be the cause of metabolic acidosis, reducing the alkaline reserve of blood and other tissues.

Although NH_4Cl can not in fact be considered an acid because it is a salt consisting of a weak base (NH_4OH) and a strong acid (HCl), the administration of that substance promotes metabolic acidosis because its degradation increases the $[\text{H}^+]$ in the blood^{6,10}. The HCl (a strong acid) remaining from the degradation of NH_4Cl is easily ionizable in solution (H^+Cl^-) because it is considered a strong acid and its H^+ cation promotes metabolic acidosis. Under these conditions, H^+ reacts with the body fluid buffer bases, including HCO_3^- , in order to attenuate metabolic acidosis^{9,12}. Thus, a decrease in the HCO_3^- concentrations $[\text{HCO}_3^-]$ and pH, in addition to an increase in chloride ion levels, is expected after the NH_4Cl administration^{6,10,12}.

During rest, the decrease in blood $[\text{HCO}_3^-]$ and pH after NH_4Cl ingestion alters the behavior of some respiratory parameters, as increased H^+ buffering by HCO_3^- increases VCO_2 ^{13,14}, thus promoting an increase in ventilation and respiratory rate, in order to eliminate CO_2 formed and maintain the arterial partial pressure of carbon dioxide (PaCO_2 or PCO_2) relatively stable^{9,15,16}. As a consequence, both PCO_2 and partial pressure of end-tidal carbon dioxide (PetCO_2) decrease after this ventilatory adjustment^{4,15}.

The decrease in pH after induced acidosis by NH_4Cl ingestion alters the intracellular/extracellular H^+ gradient across the sarcolemma, which reduces the H^+/La^- monocarboxylate transporter activity and, consequently, decreases the H^+ efflux from the muscle to the blood during exercise^{2,6}. This reduction in the H^+ efflux to the blood leads to its accumulation intracellularly and may inhibit muscle glycogenolytic and glycolytic flux during exercise because of the inhibition of glycogen phosphorylase and/or phosphofructokinase, respectively^{2,17}. Under these conditions (low intracellular pH), increased ventilation during exercise could aid reduce this retention of H^+ ions in the intracellular environment, increasing its efflux into the blood and, as a consequence, reestablishing the glycogenolytic and glycolytic activity to maintain the ATP production¹⁵.

Furthermore, it has been previously reported that acidosis seems to negatively affect the rate of oxidative phosphorylation^{6,18}. However, the mechanisms by which acidosis can impair aerobic metabolism are not fully elucidated. Among the possible mechanisms, a decrease in carbohydrate-derived substrate delivery to the tricarboxylic acid cycle has been suggested as it has been shown that a high $[\text{H}^+]$ inhibits the activity of the phosphofructokinase enzyme, decreasing the pyruvate formation and, thus delaying the rate of oxidative phosphorylation^{6,18}. Acidosis also appears to reduce mitochondrial sensitivity for oxidative phosphorylation^{6,18}. Therefore, these studies may indicate that a decrease in pH, either promoted by exercise or NH_4Cl ingestion, appears to inhibit mitochondrial oxidative capacity and respiration¹⁸⁻²⁰.

Doses used

The first study relating the NH_4Cl use to a state of metabolic acidosis was a self-experiment, in which Haldane¹¹ in 1921 conducted the experiment on its own. In that study, Haldane ingested large amounts (5 to 55 g) of NH_4Cl on six different occasions. In two of these experiments the duration was one week each. During their experiments, Haldane¹¹ reported that about 13% of ingested NH_4Cl was excreted as acid, and NH_3 thus was excreted as urea. In addition, there was a high respiratory rate during rest. Haldane also reported that walking at three miles per hour (mph ~ 5 km/h) resulted in a severe increase in respiratory rate and cycling was impossible. The author of the manuscript reported, therefore, that NH_4Cl ingestion caused a marked and prolonged acidosis and symptoms of this status included an increase in acid and NH_3 excretion. Since then, several studies have used NH_4Cl when it is desired to promote and investigate the aspects related to metabolic acidosis.

The study of metabolic acidosis induced by NH_4Cl ingestion generally used chronic NH_4Cl ingestion protocols^{11,21,22}. However, with the advancement of science and technology, in addition to increasing interest in the search for a better understanding of the processes related to acidosis during exercise without leading to gastrointestinal discomfort⁴, this condition started to be manipulated through the acute NH_4Cl ingestion^{4,7,10}. In one study from a series of five studies conducted by a Canadian group at McMaster University, Jones et al.⁴ reported that the use of an acute dose of $0.3 \text{ g}\cdot\text{kg}^{-1}$ body mass (BM) of NH_4Cl , ingested over the 180 min, would avoid gastrointestinal discomfort related to higher doses of this salt. Since then, most studies intended to promote a metabolic acidosis state prior to the exercise started using this administration protocol^{4,5,7}. This dose has been shown to be effective in negatively affect the extracellular medium, increasing blood levels of H^+ and reducing the blood $[\text{HCO}_3^-]$ and base excess, as a consequence^{5,23,24}.

However, considering the dose of $0.3 \text{ g}\cdot\text{kg}^{-1}$ of NH_4Cl BM can also lead to strong sensations of gastrointestinal discomfort¹⁰, efforts have been made in order to find an optimal dose to significantly alter acid-base status without promoting or at least decreasing the side effects promoted by the typical protocol of NH_4Cl ingestion¹⁰. In their study, Siegler et al.¹⁰

submitted eight healthy volunteers to intake of $0.2 \text{ g}\cdot\text{kg}^{-1}$ BM of NH_4Cl in three equal doses at 90, 60 and 30 min before exercise. After ingestion, this protocol resulted in a significant reduction in pH, $[\text{HCO}_3^-]$ and excess base. However, the authors did not report whether this dose reduced the sensations of gastrointestinal discomfort associated with higher doses of NH_4Cl , making it difficult to interpret the efficacy of the used NH_4Cl ingestion protocol. In addition, the performance (failure to exhaustion in said study) during successive plantar flexion was not altered after metabolic acidosis.

Performance after NH_4Cl ingestion

The first study, in fact, after the initial study by Haldane¹¹ to report the effects of NH_4Cl administration on performance was performed by Denning et al. 10 years later²². In their experiment, Denning et al.²² submitted a healthy man to a condition considered normal ("control") and later to a situation of acidosis (NH_4Cl) and alkalosis (sodium bicarbonate, NaHCO_3). Metabolic acidosis was induced by the ingestion of 15 g of NH_4Cl for two consecutive days. In all three conditions the man performed a race at an intensity of 9.3 km/h to exhaustion. In metabolic acidosis condition the man was not able to run for more than 15 min and blood sample data revealed a low concentration of lactic acid. On the other hand, during the other conditions he was able to run between 18-20 min and presented higher concentrations of lactic acid, in addition to less "pain" at the end of the task. The authors have suggested that the capacity to neutralize lactic acid is reduced when exercise is started in a state of acidosis and this response would be associated with a reduction in the amount of HCO_3^- available.

In contrast, in 1948 Asmussen et al.²¹ suggested that induced metabolic acidosis by NH_4Cl has no effect on cycling performance and lactate concentration. In this experiment, two volunteers performed different modes of cycling: one volunteer performed a constant load test (2,000 mkg per min) and the other volunteer was instructed to perform an amount of work as fast as possible (9,860 mkg). Both tests were performed after the approximate intake of 15 g of NH_4Cl on the day before the test and approximately 5 g of the salt at the beginning of the experimental test. Although the authors were not able to clearly explain their results, it should be recognized that the lack of resources of the time did not contribute to a better understanding of their data. The NH_4Cl administration protocol itself used by Asmussen et al.²¹ may not have generated a sufficient state of metabolic acidosis to alter performance since the authors of that study used a protocol in which the volunteers ingested a maximum of 20 g NH_4Cl , different from Haldane¹¹ and Denning et al.²², who used up to 55 and 30 g of this substance, respectively.

Although performance was not the main focus of this study, the first to report the effects of an acute NH_4Cl ingestion protocol on performance were Sutton et al.²⁵. In this study, the acute intake of $0.3 \text{ g}\cdot\text{kg}^{-1}$ of NH_4Cl resulted in an acute metabolic acidosis, impairing the time to exhaustion (acidosis: 2.37 ± 0.56 min; placebo: $3.69 \pm 1, 14$ min) in a cycling constant-load test (33 and 66 % VO_2max for 20 min at each intensity, followed by exercise at 90 % VO_2max until exhaustion) when compared to placebo condition. However, these results was not commented by authors as this was not the main aim of the study, as mentioned previously.

The following year, a study by the same group provided further details about the acute administration of NH_4Cl and its effects on performance⁴. Using the same ingestion protocol ($0.3 \text{ g}\cdot\text{kg}^{-1}$ of NH_4Cl or CaCO_3) and an exercise protocol similar to that used by Sutton et al.²⁵ (33 and 66 % VO_2max for 20 min at each intensity, followed by exercise at 95 % VO_2max until exhaustion), Jones et al.⁴ found that performance in intense exercise was also reduced after induced metabolic acidosis by acute NH_4Cl ingestion (160 ± 22 s) in relation to placebo

condition (270 ± 13 s). Jones et al.⁴ attributed their results to a decrease in glycolytic activity due to an intramuscular increase in $[H^+]$ associated with an increase in blood $[H^+]$ after salt ingestion. Low plasma $[La]$ in acidosis was also associated with a higher consumption of this ion by the liver and other tissues rather than a reduction in their production. Although it was not reported by the authors if volunteers had any type of gastrointestinal discomfort, they justified that the use of an acute dose and that amount was the maximum that healthy volunteers were able to sustain without gastrointestinal discomfort in previous studies.

In order to further investigate the mechanisms by which metabolic acidosis impairs exercise tolerance, the same group replicated the experiment conducted by Jones et al.⁴, but this time more invasively using the muscle biopsy technique²⁶. As in previous studies in the group^{4,25}, performance was impaired after NH_4Cl ingestion (acidosis: 3.13 ± 0.97 min, 4.56 ± 1.31 min). Furthermore, based on the results of the actions of some glycolysis-intermediating enzymes, reduction in muscle $[La]$ and lower rate of muscle glycogen depletion in acidosis condition, Sutton et al.²⁶ suggested that both glycolysis and glycogenolysis are inhibited by metabolic acidosis.

In the only study investigating the effects of chronic NH_4Cl ingestion on sports performance in humans since the experiments performed between the 20s and 40s^{11,21,22}, Bulbulian et al.²⁷ randomly assigned 11 healthy but untrained men and women into a placebo ($N = 5$) and experimental ($N = 6$) groups. Participants in the placebo group ingested $6 \text{ g}\cdot\text{day}^{-1}$ of $CaCO_3$ while the members of the experimental group ingested $12 \text{ g}\cdot\text{day}^{-1}$ ($0.13 - 0.21 \text{ g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$) of NH_4Cl . In both groups, a maximum incremental test (25 W every 2 min) and submaximal (40 % W_{max}) of cycling were applied before and after 10 consecutive days of substance ingestion. The performance in the incremental test was not altered after chronic NH_4Cl ingestion (pre-ingestion: 11.4 ± 2.9 min, post ingestion: 11.5 ± 2.6 min) in relation to placebo group (pre-ingestion: 13.3 ± 4 min; post ingestion: 13.7 ± 4.1 min). On the other hand, although performance was not significantly altered, plasma $[La]$ was significantly reduced following chronically induced acidosis during the submaximal test. The authors reported that similar pH values between the groups suggest complete renal compensation accompanied by alkaline reserve depletion, although $[HCO_3^-]$ have not been measured. The results of Bulbulian et al.²⁷ are somewhat surprising as previous studies using a chronic ingestion protocol with a lower amount of NH_4Cl (at most 55 g) compared to that used in the present study (~ 120 g) reported an alteration of the acid-base status with subsequent impairment in sport performance^{11,22}. In this case, it is worth mentioning that the authors themselves acknowledged that their findings should be interpreted with extreme caution.

In the fourth study performed by the Canada group²⁴, the performance of six healthy men was not altered in a 30-s cycling test in which they were required to exercise their maximum strength after acute intake of $0.3 \text{ g}\cdot\text{kg}^{-1}$ BM of placebo ($CaCO_3$) or NH_4Cl . These results do not corroborate with the findings of the first three studies performed by such group^{4,25,26}. In this study, mean power (acidosis: 957 ± 88 W, placebo: 972 ± 92 W) and total work performed (acidosis: 20.4 ± 3.5 kJ, placebo: 21.5 ± 3.4 kJ) were not altered by the manipulation. The main difference between the study of McCartney et al.²⁴ and the others previously mentioned seems to be in the exercise duration, which in the present study was 30 s while in the other three studies in the series the total duration of the test was around 45 min. As muscle pH is unchanged by ingestion of NH_4Cl during rest but is progressively and significantly reduced during prolonged exercise performed under these conditions, the short duration of exercise may not have been enough to alter muscle pH to the point to negatively affecting performance. This seems to be supported by the fact that $[La]$ during exercise was unchanged after manipulation.

In the last study of the five series, the influence of the acute ingestion of 0.3 g·kg⁻¹ BM of NH₄Cl on the performance of six healthy men was analyzed by Kowalchuk et al.²³ through a step incremental cycling test (100 kpm·min⁻¹) to exhaustion. The tests were performed using a randomized design. The time to exhaustion and peak power output were significantly impaired by induced metabolic acidosis (18.1 ± 2.4 min and 1,717 ± 95 kpm·min⁻¹) when compared to placebo intake (19.5 ± 3 min and 1,867 ± 120 kpm·min⁻¹). The authors attributed the elevation in ventilation to stimulation of chemoreceptors because of the high [H⁺]. Reduced plasma [La] was associated to an inhibition of glycolytic activity or an increase in lactate metabolism, as according to the authors, plasma [La] represents a balance between the production and the efflux of this ion, in addition of its consumption by the tissues that metabolize it.

Although a clear influence of induced metabolic acidosis on glycolysis and lactate metabolism (production and muscle efflux) was progressively presented by this group of researchers throughout the series of five studies, the main factor influencing the intramuscular environment in terms of [H⁺] (eg. pH), glycolytic activity, lactate production and efflux during exercise, after NH₄Cl ingestion, had not yet been fully demonstrated by the experimental models of this period. In addition, no study of the series analyzed intramuscular pH during rest and exercise after NH₄Cl ingestion, avoiding a better interpretation and understanding of the processes occurring in the intramuscular environment during rest and exercise in humans and under such condition.

Accordingly, Hultman et al.²⁸ attempted to clarify whether a state of induced metabolic acidosis by NH₄Cl would affect intracellular pH and force during electrical stimulation of the quadriceps muscle. For this, the quadriceps of one leg of five healthy men and women was electrically stimulated for 75 s. Muscle biopsies were performed immediately before and after stimulation. The volunteers then ingested 0.3 g kg⁻¹ BM of NH₄Cl over a period of 3 h. After this period (3 h), the same protocol of electrical stimulation and muscle biopsy were repeated using the other leg of the volunteers. Acidification with NH₄Cl produced a significant decline in blood pH and HCO₃⁻, but muscle pH was not altered at rest. However, after 75 s of stimulation the muscle pH was significantly reduced compared to control condition. Force production was significantly reduced after metabolic acidosis (~ 55.4 %) when compared to placebo (~ 44.6 %). Although using an electrical stimulation protocol, the finding of a decreased muscle pH after NH₄Cl ingestion confirms the idea that intramuscular [H⁺] is affected during muscle contraction by high extracellular [H⁺] after NH₄Cl ingestion. However, Hultman et al.²⁸ assumed that, as H⁺ production is limited to intracellular space, the decrease in intramuscular pH during electrical stimulation occurred predominantly due to intracellular changes. In addition, it has been suggested that part of this response may have been due to a higher consumption of H⁺ from the extracellular medium by the muscle, reducing the buffering capacity. However, it is currently known that this does not appear to be the mechanism responsible for the decrease in intramuscular pH during exercise performed after a state of induced metabolic acidosis, but this is due to a reduction in the efflux of H⁺ from the muscle to the blood, leading to its accumulation intracellularly^{2,17}.

In a study conducted by Brien and McKenzie²⁹ was tested the effects of artificially induced acidosis on the performance of six well-trained rowers. Using a randomized, double-blind design, rowers ingested 0.3 g·kg⁻¹ of NH₄Cl (acidosis) or lactulose (control) for a period of 2 h, starting 3 h before the test and ending the intake 1 h before of the test. The athletes then performed a six-minute rowing test, in which the first four minutes were performed at 80 % of maximal effort (unspecified) followed by two minutes of maximal effort. However, the work performed (38.3 ± 4.7 vs. 42 ± 2 kJ) and power (318.8 ± 39.2 vs. 350 ± 16.7 W) during peak period were not altered by induced metabolic acidosis compared to control condition,

respectively. The authors' main argument for unchanged performance after NH_4Cl acidosis was based on the physical fitness level of their sample (well trained rowers). This rationale is based on the idea that athletes have a greater capacity for buffering the H^+ associated with maximal exercise, allowing them to sustain the maximum effort for an extended period of time before a loss in sports performance. It is worth noting that the relatively small sample size ($N = 6$) may also have contributed to these findings, as the statistical power was also reduced.

From the 1990s to the present, the number of studies using NH_4Cl as a substance responsible for inducing a state of metabolic acidosis and verifying the effects of such a condition on sports performance has declined considerably^{5,7,10,30}. In the first of these studies, the performance of 18 men (uninformed health status) in a cycling test performed until the identification of fatigue threshold intensity (identified by EMG) was assessed by Housh et al.³⁰ after intake of $0,3 \text{ g}\cdot\text{kg}^{-1}$ BM of NH_4Cl (acidosis) or NaHCO_3 (alkalosis) over three hours. A placebo or control condition was not used in this study. No significant differences were found between the conditions for working capacity at the fatigue threshold (acidosis: $231 \pm 43 \text{ W}$, alkalosis: $216 \pm 49 \text{ W}$). The discussion of the single result of the aforementioned study makes difficult as no blood or respiratory variables have been analyzed. Furthermore, failure to use a placebo or control condition is a strong limitation of study design as it is not possible to establish a comparison between a relatively normal acid-base condition and after dietary manipulation in the extracellular environment (induced metabolic acidosis or alkalosis). It is interesting to note that the authors reported that several volunteers complained of gastrointestinal discomfort after NH_4Cl ingestion, which should further increase caution regarding the interpretation of the result in that study.

In 1993, Jacobs et al.⁵ investigated whether changes in blood pH would affect sports performance. Eight men, performing regular strength training, performed 50 maximal knee extensions ($\sim 60 \text{ s}$), isokinetically, three hours after ingesting $0.3 \text{ g}\cdot\text{kg}^{-1}$ BM of NH_4Cl (acidosis) or CaCO_3 (placebo). Peak torque was not significantly different between conditions (acidosis: $218 \pm 42 \text{ N m}$, placebo: $222 \pm 28 \text{ N m}$). Jacobs et al.⁵ attributed their results to the choice of test, suggesting that high intensity but submaximal exertion tests are more appropriate to verify the effects of induced metabolic acidosis by NH_4Cl . In this study, participants were required to exercise maximum force during knee extensions. Based on the short duration of exercise ($\sim 60 \text{ s}$) and data from the blood [La], which was not different between conditions in the first two minutes of recovery, it could also be suggested that manipulation was not effective in altering negatively the intramuscular pH and consequently to promote inhibitory effects on glycolytic activity at that time.

Twelve years have passed since the study by Jacobs et al.⁵ to the next study, conducted by Robergs et al.⁷, in which sports performance was assessed after pH manipulations intended to promote an "artificially" acidic blood environment. In this study, 12 competitive cyclists performed a cycling test at an intensity corresponding to 110 % of VO_2max after NH_4Cl (acidosis) ingestion at a rate of $0.3 \text{ g}\cdot\text{kg}^{-1}$ or CaCO_3 (placebo, not reported). The substances were ingested 60 minutes before the experimental tests. Blood pH was significantly reduced after NH_4Cl ingestion when compared to CaCO_3 intake. The time of exhaustion was also significantly lower in the acidosis condition than in placebo (uninformed values). Although performance data for induced acidosis have not been commented on, their findings deserve attention. As for Brien and McKenzie²⁹, Robergs et al.⁷ also used competitive athletes. However, the findings of these studies in relation to performance are contradictory. This may have occurred because the number of participants used by Brien and McKenzie²⁹ ($N = 6$) was half the sample used by Robergs et al.⁷.

The last study involving acute NH_4Cl ingestion and performance in some type of physical exercise was recently published by Siegler et al.¹⁰. In their study, Siegler et al.¹⁰ submitted eight healthy men to an exercise protocol in which they were required to perform nine plantar flexion (3 s of contraction followed by 3 s of relaxation) at 55 % of maximal voluntary contraction (CVM) for one minute. At the end of each minute the volunteers performed a CVM. The protocol lasted until the task failed. Participants ingested $0.2 \text{ g}\cdot\text{kg}^{-1}$ BM of NH_4Cl (acidosis) or $0.3 \text{ g}\cdot\text{kg}^{-1}$ BM of CaCO_3 (placebo), starting 90 min and ending 30 min before exercise. The authors reported that reduction in NH_4Cl dose was due to intolerance of participants at higher doses of NH_4Cl . However, Siegler et al.¹⁰ did not report throughout the manuscript whether participants complained about the new ingestion protocol. Furthermore, task failure time (acidosis: 531 ± 166 s, placebo: 592 ± 163 s) and force during MVC (acidosis: 930 ± 151 N, placebo: 894 ± 121 N) were not impaired by induced metabolic acidosis. Siegler et al.¹⁰ have pointed out that although acidosis has reduced muscle shortening velocity, the degree to which the pH affects the contraction rate is also dependent on other factors, such as the ionic distribution of K^+ , Na^+ and Cl^- , and this may have contributed to this lack of difference between the conditions. In addition, the authors suggested that acidosis induced through NH_4Cl during a state of uncontrolled compensatory hyperventilation may not have been enough to reduce intracellular pH, which could therefore alter performance.

Conclusion

From the results of the studies described in detail in the present review, the acute administration of reduced doses of NH_4Cl seems to be effective in promoting a state of metabolic acidosis, in addition to considerably reducing the symptoms of gastrointestinal discomfort related to larger doses. Furthermore, regardless of the amount and form of ingestion, the acute administration of NH_4Cl induces a state of metabolic acidosis and impairs performance in continuous short- and long-term exercise. This performance impairment appears to be related to a reduction in muscle blood efflux, which further decreases intramuscular pH during exercise and, as a consequence, inhibits glycolysis and glycogenolysis. On the other hand, metabolic acidosis induced before exercise by NH_4Cl ingestion does not seem to alter performance in relatively short-duration exercise (between 30 and 120 s) and of varied intensity, in addition to exercise protocols involving only one specific muscle group. In addition to the need for additional research involving NH_4Cl ingestion and sports performance due the lack of studies on this issue, performance after NH_4Cl manipulation should be tested in different types of exercise, because of the 15 studies here described, 10 of these studies used cycling as an exercise protocol.

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