ORIGINAL SCIENTIFIC PAPER
ORIGINALNI ZNANSTVENI RAD

Hrvat. Športskomed. Vjesn. 2025; 41:41-49

MAGNESIUM DELAYS RER ELEVATION AND IMPROVES TOLERANCE TO HIGH-INTENSITY RUNNING

MAGNEZIJ ODGAĐA PORAST RESPIRACIJSKOG OMJERA I POBOLJŠAVA TOLERANCIJU TRČANJA PRI VISOKOM INTENZITETU

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Cite as: Banović M, Bobinec R, Vučetić V. Magnesium delays RER Elevation and improves tolerance to high intensity running. Croat Sports Med J. 2026; 41(1):41-9.

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DOI: 10.69589/hsv.41.1.5

ABSTRACT

The respiratory exchange ratio (RER) provides a sensitive marker of metabolic stress during high-intensity exercise. Delayed RER elevation may reflect improved tolerance to rising glycolytic demand and acid–base disturbance. This study examined whether acute intravenous magnesium injection influences the timing of RER transitions during running at vVO_2max and whether these changes correspond with alterations in time to exhaustion in Tlim test.

Sixteen trained runners completed two TLim tests at vVO_2max in a randomized, single-blind crossover design. Before each test, participants received either intravenous magnesium (1 g) or placebo. Breath-by-breath gas exchange was continuously measured. Primary outcomes were times to reach individual maximal RER. Secondary outcomes included time to exhaustion in TLim test, RVO_2max, HRmax.

Magnesium delayed the rise in RER, with athletes reaching individual maximal RER approximately 19.75 s later than in the placebo condition ($p < 0.001$). This was accompanied by a significant increase in time in Tlim test (222.15 ± 45.11 s vs. 207.63 ± 38.69 s; $p < 0.001$). RVO_2 max and HRmax were not different between conditions ($p = 0.57$ and $p = 0.06$). Ventilatory measures showed small, non-significant differences.

Intravenous magnesium injection delays the onset of elevated RER during high-intensity exercise, indicating reduced metabolic disturbance. This effect occurs alongside an increase in time to exhaustion in TLim test but without

SAŽETAK

Respiracijski omjer (RER) predstavlja osjetljiv pokazatelj metaboličkog opterećenja tijekom visokointenzivnog vježbanja. Odgoda porasta RER-a tijekom opterećenja može upućivati na bolju toleranciju metaboličkog stresa. Ovo istraživanje ispitalo je utječe li intravenska primjena magnezija na vrijeme do porasta RER-a tijekom trčanja pri brzini povezanoj s maksimalnim primitkom kisika (vVO_2max) te jesu li ti učinci povezani s vremenom izdržaja u TLim testu.

Provedeno je randomizirano, single-blind, crossover istraživanje u kojem je sudjelovalo šesnaest treniranih trkača koji su izveli dva testa trčanja do iscrpljenja pri vVO_2max. Prije svakog testa ispitanici su primili intravensku injekciju magnezija (1 g) ili placebo. Respiracijski i metabolički parametri praćeni su kontinuirano breath-by-breath metodom. Primarni ishodi bili su vrijeme do postizanja maksimalnog RERa. Sekundarni ishodi uključivali su vrijeme izdržaja u TLim testu, RVO_2max, HRmax.

Primjena magnezija značajno je odgodila porast RER-a, pri čemu su ispitanici postizali maksimalni RER približno 19.75 sekundi kasnije u odnosu na placebo ($p < 0,001$). To je praćeno značajnim produljenjem u vremenu izdržaja u Tlim testu u uvjetu s magnezijem (222.15 ± 45.11 s vs. 207.63 ± 38.69 s; $p < 0.001$). RVO_2max i HRmax nisu se značajno razlikovali između uvjeta ($p = 0.57$ i $p = 0.06$) , dok su ventilacijski pokazatelji pokazivali samo blage, statistički neznačajne razlike.

Intravenska primjena magnezija odgodila je porast RER-a tijekom vježbanja visokog intenziteta, što upućuje

changes in rVO₂max or heart rate, suggesting a peripheral metabolic mechanism rather than altered cardiopulmonary function.

Keywords: *respiratory exchange ratio; RER kinetics; high-intensity exercise; vVO₂max; time to exhaustion; metabolic response*

na smanjenu metaboličku destabilizaciju i bolju toleranciju opterećenja. Ovaj učinak praćen je produljenjem vremena izdržaja, bez promjena u VO_2 ili srčanoj frekvenciji, što upućuje na periferni metabolički mehanizam djelovanja magnezija.

Ključne riječi: *respiracijski omjer; kinetika RER-a; vježbanje visokog intenziteta; vVO₂max; vrijeme izdržaja; metabolički odgovor*

INTRODUCTION

Magnesium is an essential mineral fundamentally involved in human metabolism, neuromuscular activity, and cardiopulmonary regulation, making it particularly relevant for understanding performance in high-intensity exercise[11,10,26,4]. As a cofactor for more than 300 enzymatic reactions[11,10], magnesium supports ATP synthesis[16], mitochondrial oxidative phosphorylation[23], ion transport, membrane stability[26,24], and the proper function of key enzymes in glycolysis and oxidative metabolism[12]. Because high-intensity exercise places substantial demands on bioenergetics and neuromuscular control[20], even subtle variations in magnesium availability may influence performance, fatigue resistance, and metabolic resilience[4,32].

Athletic populations are frequently interested in magnesium supplementation due to its reported effects on muscle relaxation, reduced cramping, improved excitation-contraction coupling, and enhanced mitochondrial efficiency[30,13,22,16]. However, scientific findings have been mixed. Some studies report improvements in endurance, muscle strength, and recovery[29,17,32], while others find neutral effects, particularly in well-trained athletes who are not magnesium-deficient[28,18]. One major cause of inconsistent findings is that most research has examined magnesium during moderate or incremental exercise, not during high-intensity exercise, where metabolic instability is greatest and magnesium-dependent processes may be more limiting[20].

Previous studies examining oral magnesium supplementation have used a wide range of dosages and intervention durations, contributing to the variability of reported outcomes. Trials evaluating effects on exercise performance have typically administered daily doses ranging from 250 to 500 mg of elemental magnesium over periods of 1 to 8 weeks, with longer interventions generally aiming to correct marginal deficiencies rather than elicit acute ergogenic effects[32,13]. For example, early work demonstrated improvements in aerobic capacity and muscle function following several weeks of supplementation in physically active individuals[5], while similar multi-week protocols reported mixed or null findings in well-trained athletes who were likely magnesium-replete at baseline[28]. More recent investigations have distinguished between acute and chronic supplementation, with acute oral intake showing inconsistent or minimal effects on performance, whereas repeated daily dosing over several weeks has been associated with improved strength, reduced fatigue, or enhanced metabolic efficiency in some athletic populations[14,27]. Reviews addressing the physiological roles of magnesium emphasize that supplementation strategies must consider baseline magnesium status, total daily dose, and duration of intake, as benefits are more likely when supplementation is sustained over time or when addressing marginal deficiency[4,19,25,13]. These discrepancies underscore the need to investigate magnesium under conditions where metabolic demand is extremely high and where acute changes in ionic and enzymatic regulation may have immediate physiological consequences, such as during high-intensity exercise.

One of key variables for examining metabolic responses during exercise is the respiratory exchange ratio (RER), defined as the ratio between carbon dioxide production (VCO_2) and oxygen consumption (VO_2). RER provides insight into substrate use and acid–base balance. During low-to-moderate exercise, it reflects the proportion of fat versus carbohydrate oxidation[31]. However, at high intensities, RER rises above 1.00 due to the onset of anaerobic glycolysis, lactate production, and bicarbonate buffering of accumulating hydrogen ions[31,1,6]. Because of this sensitivity to metabolic drift and acid–base disturbance, RER is a powerful non-invasive indicator of metabolic stability during high-intensity exercise.

In trained athletes, a time-to-limitation test (TLim) performed at velocity associated with VO_2max (vVO_2max) is considered one of the most demanding physiological assessments. Unlike incremental tests, which quantify peak aerobic capacity, TLim assesses high-intensity performance, reflecting the athlete's ability to sustain a critical workload. This domain is characterized by rapid increases in glycolytic flux, lactate accumulation, neuromuscular fatigue, and impaired intracellular homeostasis[2,3,20,6]. Any intervention that delays these processes, such as magnesium supplementation, may improve results of TLim test.

Acute intravenous magnesium injection is a good way to examine magnesium's physiological role because it bypasses

gastrointestinal absorption limitations and rapidly elevates serum magnesium[7,15]. Although serum magnesium does not perfectly reflect intracellular levels, increased extracellular magnesium can influence neuromuscular excitability, mitochondrial enzyme function, sodium-potassium ATPase activity, and calcium handling[11,23,8]. Magnesium's role as a natural calcium antagonist is especially important: by moderating calcium influx, magnesium may contribute to reducing neuromuscular fatigue, delaying recruitment of type II fibers, and help maintain muscle efficiency during high-intensity exertion[22,11,].

Despite this strong mechanistic rationale, few studies have evaluated how acute magnesium administration influences metabolic responses during high-intensity exercise. Most published research investigates chronic oral supplementation, often in populations with marginal magnesium deficiency, limiting its relevance for competitive athletes. Moreover, almost no studies have examined magnesium's effect on RER kinetics, even though RER provides one of the clearest windows into substrate switching, glycolytic stress, ventilatory compensation, and acid–base balance during severe-intensity work.

Therefore, the purpose of this study was to evaluate the acute effects of intravenous magnesium injection on metabolic and physiological responses, especially RER kinetics and time to exhaustion, during a TLim test at vVO_2max in trained runners. We hypothesized that magnesium might affect sports performance in TLim test.

METHODS

We conducted a prospective, randomized, single-blind crossover design study to examine the acute effects of intravenous magnesium injection on physiological and metabolic responses during high-intensity treadmill running. The study was conducted in accordance with the Declaration of Helsinki, and ethical approval was obtained from the Faculty of Kinesiology, University of Zagreb, Croatia. Participants were 16 trained competitive athletes, runners, who were free of cardiovascular, pulmonary, metabolic, and neuromuscular disorders. Written informed consent was obtained from all athletes or their guardians.

Pre-participation medical screening included medical history, physical examination, resting 12-lead ECG, serum magnesium assessment, and kidney function evaluation. All participants demonstrated serum magnesium concentrations within physiologically normal range, indicating that none were hypomagnesemic before testing. Athletes were instructed to avoid caffeine, alcohol, and vigorous training throughout the testing period and to maintain similar nutritional routines on all testing days. The intravenous injection volume used (10 mL) complied fully with World Anti-Doping Agency (WADA) regulations and therefore did not constitute doping.

Each athlete attended the diagnostic center on three occasions: the first visit involved assessment of vVO_2max using the KF1 protocol, and the second and third visits consisted of the two randomized time-to-limitation (Tlim) trials performed under magnesium and placebo conditions. To determine maximal aerobic capacity and obtain running velocity at VO_2max (vVO_2max), each athlete completed a graded spiroergometric test using the standardized KF1 treadmill protocol. The test began with a 1-minute standing baseline, followed by incremental speed increases of 0.5 $km \cdot h^{-1}$ every 30 seconds at a constant 1.5% incline until volitional exhaustion. VO_2max attainment was verified when at least two of the following criteria were met: attainment of a VO_2 plateau despite increasing speed, respiratory exchange ratio (RER) > 1.10, heart rate within 10 beats of predicted HRmax, post-exercise blood lactate > 8 $mmol \cdot L^{-1}$, and subjective exhaustion.

After determining vVO_2max, athletes completed two Tlim tests at this velocity, separated by a 3-day washout period. Unlike the KF1 protocol, which is a progressive incremental test, the Tlim test begins immediately at the running speed corresponding to vVO_2max. The participant runs at this constant speed for as long as possible, and the outcome is expressed as the time to exhaustion at vVO_2max. Prior to each Tlim test, participants performed a standardized warm-up. They then received either intravenous magnesium sulfate (1 g magnesium diluted to 10 mL of total volume in saline) or placebo injection (10 mL saline only). Both solutions were clear and indistinguishable. A computer-generated randomization sequence determined treatment order. Participants were blinded to their condition, and the investigator responsible for supervising the treadmill testing was not involved in subsequent data analysis.

Respiratory and metabolic variables were continuously recorded using a portable breath-by-breath metabolic system (MetaMax 3B-R2; Cortex Biophysik GmbH, Leipzig, Germany). The device was calibrated before each session using certified reference gases for two-point gas analyzer calibration and a 3-L syringe for flow calibration. This ensured valid and reliable measurement of ventilatory and metabolic parameters. Measured variables included VO_2, VCO_2, RER, ventilation (VE), tidal volume, breathing frequency, and heart rate. Data were averaged in 10-second intervals to preserve sensitivity to rapid metabolic changes, and the wireless data-transfer system allowed unrestricted movement during treadmill running.

RER kinetics were quantified using individual RER values and time to reach individual maximal RER.

Time to exhaustion during TLim was recorded. A qualified physician was present during all testing sessions to ensure safety and to perform intravenous injections.

Statistical analyses were performed using Statistica 13.3 (TIBCO Software Inc., Palo Alto, CA, USA). Descriptive statistics were calculated to summarize central tendency and dispersion. The Shapiro–Wilk test was used to evaluate the normality of all variables. Differences between the magnesium and placebo conditions were examined using paired Student's t-tests for normally distributed data or the

Wilcoxon signed-rank test when normality assumptions were not met. Statistical significance was set at $p < 0.05$. Effect sizes (Cohen's dz) were calculated to assess the magnitude of the observed effects.

RESULTS

Sixteen trained competitive runners (10 females, 6 males; age 18.81 ± 3.39 years) participated in the study. Mean height was 177.29 ± 10.39 cm and mean body mass was 64.16 ± 11.53 kg. All athletes demonstrated normal pulmonary function (FVC 4.87 ± 1.03 L) and high aerobic capacity (rVO₂max 53.25 ± 4.38 ml·kg⁻¹·min⁻¹, assessed via the KF1 protocol). Measured serum magnesium levels were 0.81 ± 0.04 mmol/L, all within normal range.

Acute intravenous magnesium administration produced several meaningful effects on performance and metabolic responses during TLim test.

The most prominent finding was a significant improvement in time to exhaustion in TLim test. Participants sustained running at vVO₂max for 229.69 ± 43.47 s following magnesium administration compared with 215.06 ± 36.07 s after placebo, yielding a mean improvement of 14.63 s (p 0.00). Individual response profiles revealed that nearly all athletes (all athletes except one individual) improved in magnesium condition.

Table 1. Descriptive statistics
Tablica 1. Deskriptivna statistika

Variable	N	Mean	Min	Max	Range	Std.Dev.
Age (y)	16	18,81	16,00	28,00	12,00	3,39
Height (cm)	16	177,29	161,50	196,30	34,80	10,39
Weight(kg)	16	64,16	49,90	90,10	40,20	11,53
Mg (mmol/L)	16	0.81	0.75	0.90	0.15	0.04
FVC (L)	16	4,87	3,68	7,58	3,90	1,03
rVO2max-KF1(ml/kg/min)	16	53,25	45,83	61,46	15,63	4,38
tTLim-mag (s)	16	229,69	143,00	308,00	165,00	43,47
tTLim-non (s)	16	215,06	139,00	262,00	123,00	36,07
tRER-TLim-mag (s)	16	128,75	84,00	183,00	99,00	31,07
tRER-TLim-non (s)	16	109,00	70,00	161,00	91,00	26,87
RVO2max-TLim-mag (ml/kg/min)	16	53,10	42,74	63,17	20,43	5,23
RVO2max-TLim-non (ml/kg/min)	16	53,46	44,53	63,66	19,13	4,57
HRmax-TLim-mag (bpm)	16	183,13	168,00	200,00	32,00	9,43
HRmax-TLim-non (bpm)	16	185,00	170,00	202,00	32,00	9,61
VO2max-TLim-mag (L/min)	16	3,42	2,63	5,09	2,46	0,75
VO2max-TLim-non (L/min)	16	3,44	2,59	5,13	2,54	0,73

Legend: Mg-initial serum magnesium level; FVC-forced vital capacity; RVO2max-KF1-relative maximal oxygen uptake in KF1 protocol; tTLim-mag-time to exhaustion in TLim test with magnesium; tTLim-non- time to exhaustion in TLim test with placebo; tRER-TLim-mag- time to reach maximal RER in TLim test with magnesium; tRER-TLim-non- time to reach maximal RER in TLim test with placebo; RVO2max-TLim-mag- relative maximal oxygen uptake in TLim test with magnesium; RVO2max-TLim-non- relative maximal oxygen uptake in TLim test with placebo; HRmax-TLim-mag- maximal heart rate in TLim test with magnesium; HRmax-TLim-non-maximal heart rate in TLim test with placebo; VO2max-TLim-mag-maximal oxygen uptake in TLim test with magnesium; VO2max-TLim-non-maximal oxygen uptake in TLim test with placebo

Legenda: Mg-početna razina magnezija u serumu; FVC-forsirani vitalni kapacitet; RVO2max-KF1-relativni maksimalni primitak kisika u KF1 protokolu; tTLim-vrijeme izdržaja u TLim testu s magnezijem; tTLim-non- vrijeme izdržaja u TLim testu s placebom; tRER-TLim-mag- vrijeme do postizanja maksimalnog respiracijskog omjera u TLim testu s magnezijem; tRER-TLim-non- vrijeme do postizanja maksimalnog respiracijskog omjera u TLim testu s placebom; RVO2max-TLim-mag- relativni maksimalni primitak kisika u TLim testu s magnezijem; RVO2max-TLim-non- relativni maksimalni primitak kisika u TLim testu s placebom; HRmax-TLim-mag- maksimalna srčana frekvencija u TLim testu s magnezijem; HRmax-TLim-non-maksimalna srčana frekvencija u TLim testu s placebom; VO2max-TLim-mag-maksimalni primitak kisika u TLim testu s magnezijem; VO2max-TLim-non-maksimalni primitak kisika u TLim testu s placebom

Table 2. Time to exhaustion in TLim test comparisson between magnesium and placebo trials in seconds

Tablica 2. Usporedba vremena izdržaja u TLim testu između uvjeta s magnezijem i uvjeta s placebom u sekundama

Variable	TLim-mag	TLim-non	t	p
tTLim (s)	229,69 ± 43,47	215,06 ± 36,07	4,15	0,00

Legend: tTLim- time to exhaustion in TLim test; TLim-mag- Tlim test with magnesium; TLim-non- Tlim test with placebo; t- t-value in t-test; p- p value in t-test

Legenda: tTLim- vrijeme izdržaja u TLim testu; TLim-mag- Tlim test s magnezijem; TLim-non- TLim test s placebom; t- t-vrijednost u t-testu; p- p vrijednost u t-testu

Magnesium also produced a significant effect on metabolic stability, as reflected by RER kinetics. Time to reach individual maximal RER, a sensitive indicator of the shift toward anaerobic metabolism, was delayed in the magnesium condition. Athletes reached their individual maximal RER later during the magnesium trial (128.75 ± 31.07 s) than during placebo trial (109.00 ± 26.87 s), resulting in a mean delay of 19.75 s ($p < 0.001$).

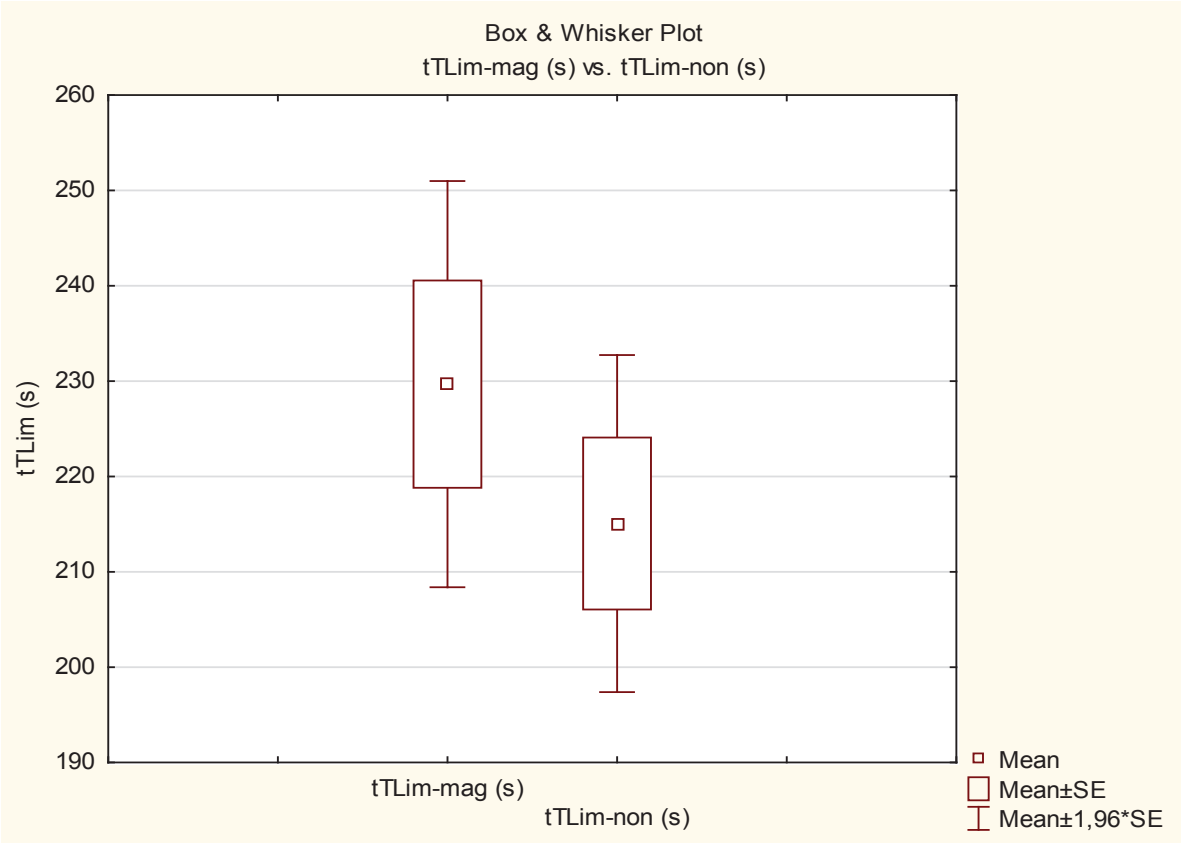
Table 3. Time to reach maximal RER in TLim test comparisson between magnesium and placebo trials in seconds

Tablica 3. Usporedba vremena do dostizanja maksimalnog RERa u TLim testu između uvjeta s magnezijem i uvjeta s placebom

Variable	TLim-mag	TLim-non	t	p
tRER-TLim (s)	128,75 ± 31,07	109,00 ± 26,87	4,43	0,00

Legend: tRER-TLim- time to reach maximal RER in TLim test; TLim-mag- TLim test with magnesium; TLim-non- TLim test with placebo; t- t value of t-test; p- p value of t-test.

Legenda: tRER-TLim- vrijeme do postizanja maksimalnog respiracijskog omjera u TLim testu; TLim-mag- TLim test s magnezijem; TLim-non- TLim test s placebom; t- t vrijednost t-testa; p- p vrijednost t-testa.

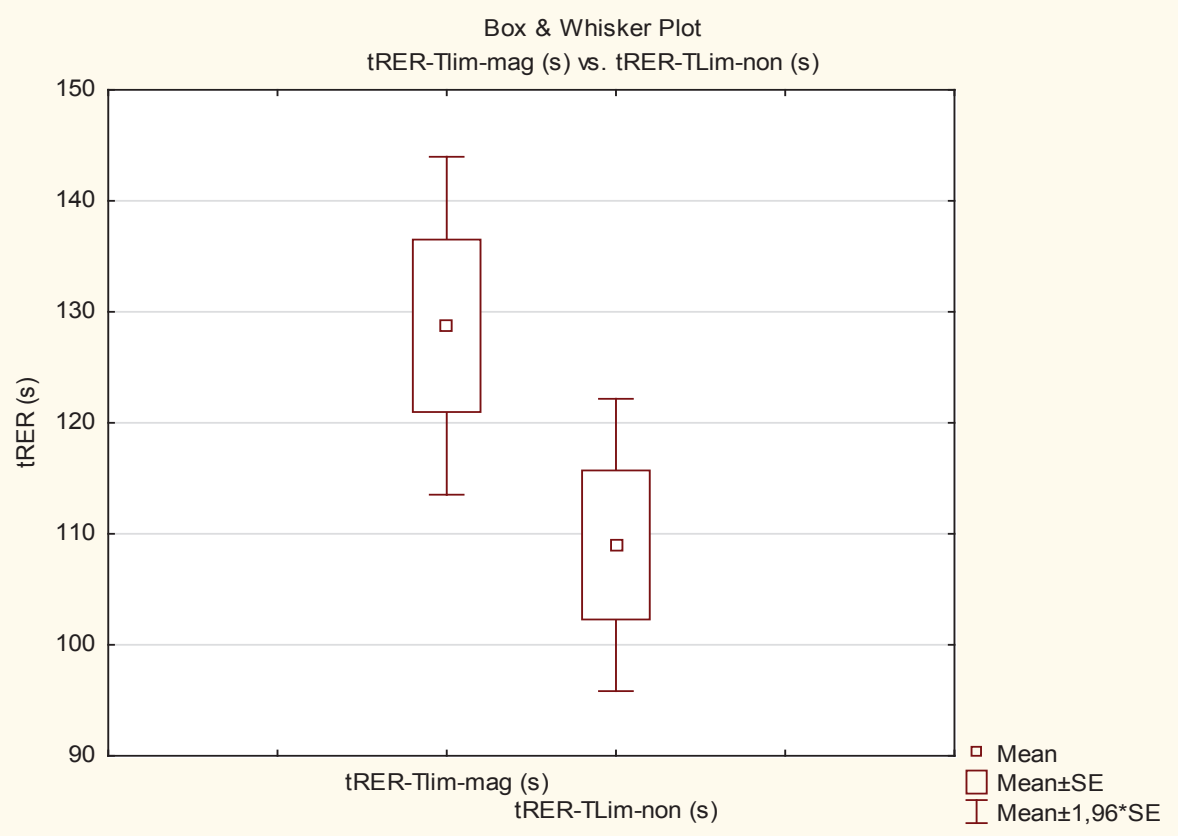


Legend: tTLim- time to exhaustion in TLim test; TLim-mag- Tlim test with magnesium; TLim-non- Tlim test with placebo

Legenda: tTLim- vrijeme izdržaja u TLim testu; TLim-mag- Tlim test s magnezijem; TLim-non- TLim test s placebom

Figure 1. Time to exhaustion in TLim test comparisson between magnesium and placebo trials in seconds

Slika 1. Usporedba vremena izdržaja u TLim testu između uvjeta s magnezijem i uvjeta s placebom u sekundama



Legend: tRER- time to reach maximal RER in TLim test; TLim-mag- TLim test with magnesium; TLim-non- TLim test with placebo
Legenda: tRER- vrijeme do postizanja maksimalnog respiracijskog omjera u TLim testu; TLim-mag- TLim test s magnezijem; TLim-non- TLim test s placebom

Figure 2. Time to reach maximal RER in TLim test comparisson between magnesium and placebo trials in seconds
Slika 2. Usporedba vremena do dostizanja maksimalnog RERa između uvjeta s magnezijem (Mg) i uvjeta s placebom (non) u sekundama

Despite these significant differences in time to exhaustion and metabolic responses, magnesium did not alter oxygen uptake. Mean RVO_2max during Tlim was 53.10 ± 5.23 $ml \cdot kg^{-1} \cdot min^{-1}$ in the magnesium condition and 53.46 ± 4.57 $ml \cdot kg^{-1} \cdot min^{-1}$ with placebo (p = 0.57).

Table 4. Relative VO2max in TLim test comparisson between magnesium and placebo trial
Tablica 4. Usporedba relativnog primitka kisika u TLim testu između uvjeta s magnezijem i uvjeta s placebom

Variable	TLim-mag	TLim-non	t	p
RVO2max-TLim (ml/kg/min)	53.10 ± 5.23	53.46 ± 4.57	-0,58	0,57

Legend: RVO2max-TLim- relative maximal oxygen uptake in TLim test; TLim-mag – TLim test with magnesium; ; TLim-non- TLim test with placebo; t- t value of t-test; p- p value of t-test.
Legenda: RVO2max-TLim- relativni maksimlni primitak kisika u TLim testu; TLim-mag – TLim test s magnezijem; ; TLim-non- TLim test s placebom; t- t vrijednost u t-testu; p- p vrijednost u t-testu

Similarly, no significant differences emerged in maximal heart rate. HRmax was 183.13 ± 9.43 bpm with magnesium and 185.00 ± 9.61 bpm with placebo (p = 0.06).

Table 5. Maximal heart rate in TLim test comparisson between magnesium and placebo trial
Tablica 5. Usporedba maksimalne frekvencije srca u TLim testu između uvjeta s magnezijem i uvjeta s placebom

Variable	TLim-mag	TLim-non	t	p
HRmax-Tlim (bpm)	183.13 ± 9.43	185.00 ± 9.61	-2,03	0,06

Legend: HRmax-TLim- maximal heart rate in TLim test; TLim-mag – TLim test with magnesium; ; TLim-non- TLim test with placebo; t- t value of t-test; p- p value of t-test.
Legenda: HRmax-TLim- maksimalna srčana frekvencija u TLim testu; TLim-mag – TLim test s magnezijem; ; TLim-non- TLim test s placebom; t- t vrijednost u t-testu; p- p vrijednost u t-testu

DISCUSSION

This study examined the acute effects of intravenous magnesium sulfate injection on metabolic and physiological responses during high-intensity treadmill running in Tlim test performed at the velocity associated with maximal oxygen uptake (vVO_2max). The primary findings were clear: magnesium significantly prolonged time to exhaustion in TLim test and delayed the rise in respiratory exchange ratio (RER), indicating enhanced metabolic stability during severe-intensity exercise. Importantly, these ergogenic effects occurred without significant changes in oxygen uptake (VO_2max) or maximal heart rate (HRmax), suggesting that magnesium influences peripheral metabolic and/or neuromuscular pathways rather than cardiopulmonary function.

Magnesium's relevance to exercise performance arises from its extensive involvement in essential metabolic processes. As a cofactor in more than 300 enzymatic reactions, including ATP synthesis, oxidative phosphorylation, glycolysis, and protein formation, magnesium plays a critical role in sustaining high rates of energy turnover during intense exercise[10,11,12,16,]. It helps stabilize ATP, regulate ion channels, modulate cellular excitability, and facilitate mitochondrial enzyme activity[16,11,23]. These functions become particularly important during high-intensity exercise, when metabolic demand rapidly exceeds the capacity of oxidative pathways and the body relies on glycolysis, phosphocreatine hydrolysis, rapid ATP turnover, and efficient acid–base regulation.

The prolonged time to exhaustion in TLim test in the magnesium condition demonstrates improved fatigue tolerance. Tlim at vVO_2max is a sensitive measure of physiological resilience under high-intensity conditions, capturing the point where neuromuscular fatigue, metabolic acidosis, and ion imbalance converge to force exercise termination[2,20,6]. By delaying exhaustion, magnesium appears to support metabolic pathways that counteract intracellular disruptions typically associated with high-intensity exercise, such as rising hydrogen ion concentration, impaired calcium handling, and compromised ATP availability.

One of the most striking findings was the delayed elevation of RER. During low- to moderate-intensity exercise, RER reflects the balance between fat and carbohydrate oxidation. During high-intensity exercise, however, RER is driven by bicarbonate buffering of hydrogen ions, lactate production, and increased CO_2 generation [1,31]. A rapid rise in RER is therefore a hallmark of metabolic instability. The delay in RER elevation observed in the magnesium trial suggests improved tolerance to metabolic stress, or more specifically, a slower shift toward anaerobic metabolism.

Several biological mechanisms could explain this effect. Firstly, magnesium enhances mitochondrial efficiency by supporting enzyme complexes in the electron transport chain, which may stabilize oxidative ATP production longer before glycolysis becomes dominant[16,23]. Secondly, magnesium acts as a natural calcium antagonist, preventing excessive intracellular calcium accumulation[22,11], and this delays fatigue. Thirdly, magnesium is involved in acid–base control, influencing ATP hydrolysis and buffering reactions[16]. Improved acid–base stability could delay the onset of bicarbonate buffering, thereby slowing CO_2 accumulation and RER elevation.

The lack of change in VO_2max during the TLim test underscores that magnesium did not influence oxygen transport or utilization. This is important because it suggests magnesium's effects did not emerge by modulating cardiorespiratory function in this trial. If VO_2 had increased, it might have indicated improved aerobic capacity or enhanced oxygen delivery. The absence of such changes supports the interpretation that magnesium's ergogenic effects are metabolic rather than cardiopulmonary. Similarly, unchanged HRmax indicates magnesium does not significantly influence autonomic cardiovascular regulation at peak effort.

The findings also fit within current models of fatigue and performance in high-intensity exercise. The VO_2 slow component, which is an upward drift in oxygen consumption over time, is attributed to reduced muscle efficiency, elevated recruitment of fast-twitch fibers, and metabolic instability[21,20]. If magnesium attenuates the mechanisms driving the slow component, such as impaired mitochondrial efficiency or calcium dysregulation, this may explain the observed improvements in Tlim and RER kinetics. While the VO_2 slow component was not directly measured in this study, the metabolic behavior captured by RER strongly suggests reduced metabolic drift.

Contextualizing these results with prior literature, the study aligns more closely with research showing positive effects of magnesium on muscle function, endurance, and metabolic regulation[5,17], rather than studies reporting null effects[28,18]. Many null findings may stem from different intensities or types of exercise. Magnesium's ergogenic effects may be most pronounced during high-intensity exercise, where the metabolic systems it regulates are under maximal stress. Moreover, intravenous administration provides rapid, reliable elevation of serum magnesium, avoiding variability related to gastrointestinal absorption seen with oral supplementation.

Overall, the combined results indicate that magnesium significantly improves tolerance to high-intensity exercise primarily through metabolic stabilization, as evidenced by delayed RER elevation and prolonged time to exhaustion. The absence of changes in VO_2 or HRmax suggests that magnesium's ergogenic influence stems from peripheral metabolic or neuromuscular mechanisms rather than central cardiopulmonary adaptations.

Practical implications of this study are notable for athletes involved in sports requiring repeated or sustained high-intensity efforts. Even relatively small increases in

time to exhaustion can influence competitive outcomes. For instance, small improvements in performance at vVO_2max may alter tactical opportunities in middle-distance running or team sports[2,9].

Given that the 10 mL intravenous dose used is fully compliant with World Anti-Doping Agency guidelines, acute magnesium supplementation could theoretically be used in elite settings under medical supervision. The question is, is it a justified use. However, intravenous administration is impractical for regular use, and the long-term safety of repeated IV magnesium injections has not been thoroughly evaluated in athletes. Future research should examine whether optimized oral or transdermal protocols could replicate the acute metabolic benefits seen here. Exploring chronic supplementation could reveal whether magnesium enhances training adaptations.

This study's limitations include its relatively small sample size and the absence of intracellular magnesium measurements. Serum magnesium often remains normal even when intracellular stores are reduced, and intracellular levels may fluctuate dramatically during exercise. pH values were not collected during trials, limiting direct insight into acid–base regulation. Additionally, electromyographic data could have clarified magnesium's effects on muscle activation. Finally, the study population were trained runners; findings may differ in cyclists, swimmers, or team-sport athletes.

Despite these limitations, the results demonstrate that acute intravenous magnesium injection enhances tolerance to high-intensity exercise by stabilizing metabolic responses and delaying fatigue-related physiological transitions. Magnesium's influence appears strongest where metabolic strain is greatest, suggesting that its optimal application may be in scenarios requiring sustained, high-intensity performance.

CONCLUSION

Intravenous magnesium injection delayed RER elevation during high-intensity running and increased time to exhaustion, without altering VO_2max or heart rate. These findings indicate that magnesium enhances exercise tolerance through peripheral metabolic mechanisms by delaying fatigue-related physiological transitions. Further research should determine whether similar effects occur with oral supplementation and across different exercise modalities.

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