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A CLOSER LOOK AT MAGNESIUM SUPPLEMENTATION IN NORMOMAGNESEMIC PATIENTS: DOES FORMULATION MAKE A DIFFERENCE?

NORMOMAGNEZEMİLİ HASTALARDA MAGNEZYUM TAKVİYESİNE DAHA YAKINDAN BAKIŞ: FORMÜLASYON FARK YARATIR MI?

Özge Çetinarslan[1*]

[1]T.C. Demiroglu Bilim University, Faculty of Medicine, Department of Cardiology, İstanbul, Türkiye

ABSTRACT

Objective: Magnesium (Mg) modulates vascular tone, cardiac conduction, and autonomic balance. Comparative data on oral formulations in people with normal serum Mg are scarce. We compared haemodynamic, electrophysiologic, and autonomic effects of Mg-oxide versus an organic combination (malate + bisglycinate + citrate) in normomagnesemic adults.

Methods: Single-centre, ambispective cohort (n=181) assigned to Mg-oxide, combination, or control. Paired evaluations after ≥1 month included electrocardiogram, 24-hour Holter, and ambulatory blood pressure monitoring. Outcomes were 24-hour blood pressure (BP) and heart rate (HR), ECG intervals, arrhythmic burden, and time- and frequency-domain heart-rate variability (HRV).

Results: Serum Mg rose with both supplements. Mg-oxide reduced 24-hour systolic BP (-4.2 mmHg) and diastolic BP (-3.5 mmHg), decreased nighttime diastolic BP (-4.4 mmHg), and lowered HR overnight and across 24 hours (each -2.9 bpm). Time-domain HRV improved with Mg-oxide (e.g., RMSSD +22.2 ms), with between-group differences favouring Mg-oxide. The combination produced a frequency-domain shift (LF↓, HF↑, LF/HF↓) without consistent changes in mean BP or HR. On ECG, PR shortened in both supplement arms (~-3.9 ms); QRS (-1.9 ms) and QTc (-7.4 ms) shortened only with the combination. Arrhythmic burden was unchanged. Self-reported sleep satisfaction improved in both supplementation arms; controls were unchanged.

Conclusion: In normomagnesemic adults, Mg-oxide and an organic combination yielded small, formulation-specific physiological effects. Mg-oxide showed improvements in ambulatory BP, HR, and vagal time-domain HRV; the combination produced frequency-domain shifts and slight QTc shortening. With similar short-term safety signals, cost and access may justify Mg-oxide as a pragmatic default; formulation should be tailored to patient goals and context.

Keywords: Autonomic modulation, heart rate variability, magnesium oxide, magnesium supplementation, organic magnesium, sleep satisfaction

ÖZ

Amaç: Magnezyum (Mg) damar tonusunu, kardiyak iletiyi ve otonom dengeyi düzenler. Normal serum Mg düzeyine sahip bireylerde oral formülasyonları karşılaştıran kanıt sınırlıdır. Bu çalışma, normomagnezemik erişkinlerde Mg-oksit ile organik bir kombinasyonun (malat + bisglisinat + sitrat) hemodinamik, elektrofizyolojik ve otonom etkilerini karşılaştırdı.

Yöntem: Tek merkezli, ambispektif kohortta(n=181) katılımcılar Mg-oksit, kombinasyon veya kontrol kollarına atandı. En az 1 ay takviye kullanımı sonrası elektrokardiyogram (EKG), 24 saatlik ritim holter ve ambulatuvar kan basıncı (KB) izlemi yapıldı. Sonlanımlar; 24 saatlik KB ve kalp hızı (KH), EKG aralıkları, aritmik yük ve kalp hızı değişkenliği (HRV) idi.

Bulgular: Serum Mg her iki grupta yükseldi. Mg-oksit, 24 saatlik sistolik ve diyastolik KB'de(-4,2 mmHg ve -3,5 mmHg), gece diyastolik KB'de(-4,4 mmHg) ve hem gece hem 24 saat boyunca KH'da azalma (her biri -2,9 atım/dk) sağladı. Zaman alanı HRV, Mg-oksit ile iyileşti (ör., RMSSD +22,2 ms) ve gruplar arası farklar Mg-oksit lehineydi. Kombinasyon, ortalama KB veya KH'de tutarlı değişiklik olmaksızın frekans alanı kayması üretti (LF↓, HF↑, LF/HF↓). EKG'de PR her iki takviye kolunda kısaldı(~-3,9 ms);QRS (-1,9 ms) ve QTc(-7,4 ms) yalnızca kombinasyonla kısaldı. Aritmik yük değişmedi. Özbildirime dayalı uyku memnuniyeti her iki takviye kolunda arttı.

Sonuç: Normomagnezemik erişkinlerde Mg-oksit ve organik kombinasyon küçük, formülasyona özgü fizyolojik etkiler gösterdi. Mg-oksit ambulatuvar KB, KH ve vagal zaman alanı HRV'de iyileşmeler sağladı; kombinasyon ise frekans alanı kaymaları ve hafif QRS ve QTc kısalması oluşturdu. Benzer kısa dönem güvenlik sinyalleriyle, maliyet ve erişim Mg-oksiti pragmatik bir varsayılan kılabilir; formülasyon seçimi hasta hedefleri ve bağlama göre bireyselleştirilmelidir.

Anahtar Kelimeler: Otonom modülasyon, kalp hızı değişkenliği, magnezyum oksit, magnezyum takviyesi, organik magnezyum, uyku memnuniyeti

***Corresponding author/İletişim kurulacak yazar:** Özge Çetinarslan; T.C. Demiroglu Bilim University, Medicine Faculty, Department of Cardiology,İstanbul, Türkiye.
Phone/Telefon: +90 (216) 537 012 41 42, **e-mail/e-posta:** ozgec.arslan@gmail.com
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Introduction

Magnesium (Mg) plays a vital role in cardiovascular health by influencing blood pressure, cardiac rhythm, vascular tone, and neuromuscular transmission.[1] While Mg supplementation has been associated with improvements in blood pressure and arrhythmic parameters, the comparative efficacy of different oral formulations remains underexplored.[2] In particular, the most commonly used oral form, magnesium oxide (Mg-oxide), has rarely been directly compared with newer organic combinations such as magnesium malate, bisglycinate, and citrate.[3]

Although prior studies have examined Mg's effects on heart rate or blood pressure, few have comprehensively evaluated a broader set of cardiovascular parameters, including atrial and ventricular ectopy, QRS duration, heart rate variability (HRV) indices, and ambulatory blood pressure profiles.[4]

Another gap concerns the impact of supplementation in normomagnesemic individuals; many investigations have focused primarily on Mg-deficient populations.[5] Against this backdrop, we aimed to compare three groups: patients using Mg-oxide alone, patients taking a combination of Mg malate + bisglycinate + citrate, and a control group not using any Mg supplement. By evaluating heart rate, arrhythmic burden, time- and frequency-domain HRV, and ambulatory blood pressure parameters across these groups, we sought to clarify the relative benefits of each supplementation strategy and address existing knowledge gaps. Our goal is to inform evidence-based clinical decisions and public health recommendations regarding optimal Mg supplementation for cardiovascular health.[6]

Methods

Study Design and Setting

This single-center, ambispective observational cohort comprised a retrospective chart-review window (the preceding six months) followed by a prospective follow-up visit at which electrocardiogram (ECG), 24-hour ryhthm holter, and ambulatory blood pressure monitoring (ABPM) were repeated after ≥1 month of supplementation. No investigational product was administered; participants were already using commercially available magnesium (Mg) supplements as part of routine care. Patients were classified into three groups according to Mg intake: Mg-oxide, combination formulation (Mg-malate+Mg-bisglycinate+Mg-citrate), or control (no Mg supplementation).

Participants and Eligibility Criteria

Formulation choice had been made by treating physicians prior to study inception. Group allocation was retrospective. Eligible participants in the supplementation groups had taken the assigned product for ≥1 month (maximum 8 months) and agreed to repeat ECG, 24-hour holter, and ABPM for paired comparisons.

Inclusion criteria

1. Age ≥18years.
2. Documented Mg supplementation for ≥1month (for Mg groups) or no supplementation (control).
3. Availability of pre-supplementation ECG, 24-hour rhythmm holter, and ABPM records.
4. Baseline serum magnesium within the laboratory reference interval (normomagnesemia).
5. Written informed consent for repeat evaluation.

Exclusion criteria

1. Mg supplementation <1month (for Mg supplementation groups).
2. Incomplete baseline data (missing ECG, Holter, or ABPM).
3. Refusal of follow-up testing.
4. Initiation, discontinuation, or dose modification of any cardiovascular or autonomically active medicationbetween the two assessments.
5. Presence of a permanent pacemaker or other cardiac implantable electronic device.
6. New diagnosis of cardiovascular disease within the last 6 months (e.g., coronary artery disease, clinically relevant arrhythmia, heart failure, or hypertension).
7. Chronic kidney disease [estimated glomerular filtration rate (eGFR) <60mL/min/1.73m²], chronic heart failure, active malignancy, diabetes mellitus, or dyslipidemia.
8. Active systemic infection between assessments.
9. Marked change in physical activity or exercise routine between pre- and post-evaluation.

Exposure (Supplementation Groups)

Participants were stratified as follows: Mg-oxide group; combination group receiving a blend of Mg-malate, Mg-bisglycinate, and Mg-citrate; and control group with no Mg supplementation. Doses and brands reflected routine clinical practice: Mg-oxide; 1 sachet once daily with food, delivering 365 mg elemental Mg/day and combination supplement (magnesium malate + bisglycinate + citrate); 200 mg elemental Mg per tablet; once daily with food.

Data Collection and Measurements

Anthropometric and clinical variables included age, sex, height, weight, body mass index (BMI), waist circumference (WC), smoking status, average daily traffic exposure (hours), and self-reported sleep satisfaction. ECG/Holter-derived metrics comprised PR interval, QRS duration, and corrected QT (QTc), which was calculated using Bazett's correction (QT/√RR).[7] Heart rate (HR; daytime, nighttime, 24-hour; minimum/maximum/mean) and HRV parameters-SDNN, SDANN, RMSSD, pNN50, HRV triangular index (HRV-TI), and frequency-domain indices LF, HF, and LF/HF ratio-were derived and named in accordance with Task Force standards.[8] ABPM outputs included daytime, nighttime, and 24-hour systolic, diastolic, and mean blood pressure;

interpretation (day/night windows and thresholds) followed the European Society of Hypertension/European Society of Cardiology (ESH/ESC) hypertension guideline.[9] Renal function was assessed using the CKD-EPI creatinine equation (2009) to estimate eGFR.[10] Sleep satisfaction was captured at both time points with a three-level, investigator-defined item (non-validated; no licensed instrument required).

Outcomes

Primary endpoints were 24-hour systolic blood pressure/diastolic blood pressure (SBP/DBP), 24-hour mean HR, and time-domain HRV (RMSSD, pNN50). Secondary endpoints included additional ABPM parameters (daytime/nighttime SBP/DBP/mean), frequency-domain HRV (LF, HF, LF/HF), ECG intervals (PR, QRS, QTc), and arrhythmic burden (atrial and ventricular premature contractions, bigeminy, couplets).

Ethics

The study protocol was approved by the Acıbadem Mehmet Ali Aydınlar University and Acıbadem Healthcare Institutions Medical Research Ethics Committee (ATADEK; approval no. ATADEK 2025/02). All procedures adhered to relevant regulations and the Declaration of Helsinki. Written informed consent was obtained from all participants prior to data collection.

Statistical Analysis

Continuous variables are reported as mean±SD or median [IQR] as appropriate; categorical variables as counts (percentages). Distributional assumptions were assessed using Shapiro-Wilk and Kolmogorov-Smirnov tests. Within-group pre/post changes were analyzed using paired t-tests or Wilcoxon signed-rank tests. Between-groupcomparisons of change scores used one-way ANOVA (with Bonferroni post-hoc) or Kruskal-Wallis (with Dunnpost-hoc). Categorical variables were compared using the chi-square test; McNemar test was applied for paired proportions. To mitigate confounding from non-random allocation, we implemented inverse-probability weighting (IPW) based on a multinomial logistic model for group assignment including age, sex, baseline BP/HR, BMI, smoking, and relevant comorbidities; stabilized weights were truncated at the 1st/99th percentiles. Multivariable models of primary outcomes were additionally adjusted for age, sex, baseline BP/HR, and comorbidities; this adjustment did not materially change effect estimates. Two-sided $\alpha=0.05$ was used; very small p-values are reported as $p<0.001$. No a priori sample-size calculation was performed; analyses used an available-case approach without imputation. Statistical analyses were conducted in SPSS v27 (IBM Corp.).

Results

Baseline Characteristics

A total of 181 participants were analyzed (Mg-oxide: n=62; Mg-combination: n=61; Control: n=58). Groups were comparable at baseline for age, sex, anthropometrics (weight, height, BMI, WC), smoking status, medication use (β-blocker, ACEi/ARB, CCB), and average daily traffic exposure time. Baseline renal function was preserved overall (mean eGFR 96.7±21.1mL/min/1.73m²) with no clinically relevant between-group differences. Table 1 summarizes baseline characteristics.

Table 1. Basal characteristics of study group

Parameters	Mg-oxide Group (n:62)	Mg Combination Group (n:61)	Control Group (n:58)	Inter-group p value
Age, years (mean + SD)	51.5 ± 17.2	44.4 ± 17.4	49.8 ± 19.2	0.056
Sex, female, n (%)	38 (63.3)	41 (68.3)	42 (70)	0.721
Weight, kg (mean + SD)	71.4 ± 14.4	77.6 ± 17.6	75.3 ± 17.6	0.164
Height, cm (mean + SD)	164.5 ± 8.1	167.5 ± 7.2	165.4 ± 7.3	0.093
BMI, kg/m² (mean + SD)	26.1 ± 4.2	27.5 ± 5.8	27.4 ± 5.8	0.310
WC, cm (mean + SD)	91.6 ± 15.3	92.5 ± 16.1	93.0 ± 16.6	0.901
eGFR	93.2 ± 18.8	102.1 ± 20.5	94.7 ± 23.1	0.053
Smoking, n (%)	35 (58.3)	45 (75.0)	46 (76.7)	0.053
Daily traffic hours (mean + SD)	0.9 ± 1.2	1.4 ± 1.5	1.3 ± 1.2	0.092
β-blocker use, n (%)	5 (8.1)	6 (9.8)	5 (8.6)	0.939
ACEi/ARB use, n (%)	9 (14.5)	9 (14.8)	8 (13.8)	0.988
CCB use, n (%)	6 (9.7)	6 (9.8)	6 (10.3)	0.992

Mg: Magnesium, SD: Standard deviation, BMI: Body mass index, WC: Waist circumference, ACEi: Angiotensin coverting enzyme inhibitors, ARB: Aldoterone receptor blockers, CCB: Calcium channel blockers

Serum Biomarkers

Serum magnesium increased within all groups (both supplementation arms and controls; all p<0.001), with a slightly higher post-supplementation level in the combination group; however, between-group differences in change (Δ) were not significant (p=0.716). Serum creatinine decreased modestly within groups (p<0.01) without a between-group difference in Δ (p=0.101) (Supplementary Table1).

Ambulatory Blood Pressure

At baseline, ABPM values were similar across groups. After supplementation, the Mg-oxide group showed reductions in 24-hour SBP (mean Δ −4.2±12.4mmHg, p=0.003), 24-hour DBP (Δ −3.45±8.33mmHg, p=0.003), and nighttime DBP (Δ −4.38±12.91mmHg, p=0.014), whereas changes were not significant in the combination or control groups. Between-group analyses of Δ favored Mg-oxide for 24-hour SBP and DBP (global p values significant; see Table *2*), indicating a greater overall BP reduction with Mg-oxide. Baseline HR parameters were comparable between groups. Post-supplementation, Mg-oxide exhibited lower nighttime mean HR (Δ −2.88±8.28beats/min, p=0.049) and lower 24-hour mean HR (Δ −2.89±7.17beats/min, p=0.007); the combination and control groups showed no meaningful change. Between-group tests of Δ were significant for nighttime mean HR and 24-hour mean HR (see Table 3), again favoring Mg-oxide.

Table 2. Comparison of systolic and diastolic blood pressure parameters before and after magnesium supplementation in three study groups

Parameters, mmHg	Mg-oxide Group (n:62) Mean ± SD	Mg Combination Group (n:61) Mean ± SD	Control Group (n:58) Mean ± SD	Inter-group p value
Pre-Mg daily SBP	126.5 ± 14.5	127.8 ± 17.2	125.4 ± 17.0	0.769
Post-Mg daily SBP	122.5 ± 16.7	128.0 ± 14.1	124.9 ± 17.1	0.208
Difference in daily SBP	-3.99 ± 20.14	-0.21 ± 8.40	-0.50 ± 0.10	0.071
Intra-group difference p-value	0.265	0.696	0.980	—
Pre-Mg nighttime SBP	117.4 ± 13.6	118.4 ± 15.6	116.6 ± 15.7	0.851
Post-Mg nighttime SBP	112.5 ± 16.4	119.0 ± 16.0	116.7 ± 15.7	0.127
Difference in nighttime SBP	-4.8 ± 19.1	0.7 ± 10.9	+0.10 ± 0.00	0.354
Intra-group difference p-value	0.094	0.094	0.970	—
Pre-Mg 24-hour SBP	125.4 ± 14.7	125.2 ± 16.2	124.5 ± 16.7	0.905
Post-Mg 24-hour SBP	121.3 ± 12.1	125.5 ± 14.3	124.4 ± 16.6	0.263
Difference in 24-hour SBP	-4.2 ± 12.4	0.3 ± 8.1	0.10 ± 0.10	<0.001
Intra-group difference p-value	0.003	0.785	0.935	—
Pre-Mg daily DBP	74.9 ± 12.0	75.7 ± 8.1	75.0 ± 8.1	0.911
Post-Mg daily DBP	72.3 ± 11.2	75.8 ± 7.5	75.2 ± 7.9	0.051
Difference in daily DBP	-2.66 ± 13.51	0.04 ± 6.91	0.20 ± 0.20	0.418
Intra-group difference p-value	0.219	0.906	0.987	—
Pre-Mg nighttime DBP	66.4 ± 13.5	64.9 ± 8.9	64.2 ± 9.0	0.510
Post-Mg nighttime DBP	66.4 ± 11.0	66.4 ± 10.8	64.4 ± 9.1	0.160
Difference in nighttime DBP	-4.38 ± 12.91	1.48 ± 8.09	0.20 ± 0.10	0.045
Intra-group difference p-value	0.014	0.289	0.978	—
Pre-Mg 24-hour DBP	74.0 ± 12.7	72.8 ± 7.6	73.4 ± 9.0	0.894
Post-Mg 24-hour DBP	70.5 ± 10.7	73.2 ± 7.3	72.9 ± 9.2	0.145
Difference in 24-hour DBP	-3.45 ± 8.33	0.34 ± 6.14	-0.50 ± 0.20	0.002
Intra-group difference p-value	0.003	0.785	0.899	—

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; Mg: Magnesium; SD: Standard deviation; Pre-Mg: Before magnesium supplementation; Post-Mg: After magnesium supplementation

Table 3. Comparison of heart rate parameters before and after magnesium supplementation in three study groups

Parameters, beats/minute	Mg-oxide Group (n:62) Mean ± SD	Mg Combination Group (n:61) Mean ± SD	Control Group (n:58) Mean ± SD	Inter-group p value
Pre-Mg daily mean HR	80.3 ± 12.6	85.7 ± 12.6	82.5 ± 12.1	0.143
Post-Mg daily mean HR	78.8 ± 8.3	86.0 ± 11.6	82.3 ± 12.0	0.050
Difference in daily mean HR	-1.54 ± 9.61	0.23 ± 10.51	0.20 ± 0.10	0.109
Intra-group difference p-value	0.170	0.356	0.987	—
Pre-Mg nighttime mean HR	67.0 ± 7.7	67.3 ± 9.9	65.4± 8.8	0.455
Post-Mg nighttime mean HR	64.1 ± 7.5	69.1 ± 8.5	65.1 ± 8.9	0.003
Difference in nighttime mean HR	-2.88 ± 8.28	1.84 ± 0.06	0.30 ± 0.10	0.006
Intra-group difference p-value	0.049	0.039	0.988	—
Pre-Mg 24-hour mean HR	76.1 ± 9.7	79.6 ± 9.7	77.6 ± 9.8	0.039
Post-Mg 24-hour mean HR	73.2 ± 9.3	79.9 ± 10.7	77.3 ± 9.4	0.001
Difference in 24-hour mean HR	-2.89 ± 7.17	0.23 ± 6.09	0.30 ± 0.40	0.014
Intra-group difference p-value	0.007	0.560	0.997	—

Mg: Magnesium; SD: Standard deviation; Pre-Mg: Before magnesium supplementation; Post-Mg: After magnesium supplementation

ECG Intervals and Arrhythmic Burden

PR interval shortened in both supplementation arms (each Δ −3.9ms; p≈0.01) with no change in controls. QRS duration decreased slightly only in the combination group (Δ −1.9±5.6ms, p=0.024). QTc decreased significantly in the combination group (Δ −7.4±26.1ms, p=0.049), while the Mg-oxide group showed no significant QTc change. Arrhythmic burden (APC, VPC, bigeminy, couplets) did not change materially within or between groups (Supplementary Table 2).

Heart Rate Variability

At baseline, SDNN, SDANN, HRV-TI, NN50, pNN50, and RMSSD did not differ between groups. Following supplementation, the Mg-oxide group demonstrated improvements in time-domain vagal indices RMSSD (Δ +22.2±51.6ms, p<0.001), pNN50 (Δ +2.9±8.1%, p=0.006), and NN50 (Δ +4.1×10³, p=0.032). Between-group comparisons of Δ favored Mg-oxide over combination for RMSSD, pNN50, and NN50 (all p<0.01). In contrast, the combination group showed a frequency-domain shift-LF decreased (Δ −9.1±20.6, p<0.001), HFincreased (Δ +4.6±13.8, p=0.015), and LF/HF decreased (Δ −1.3±4.0, p=0.007) without consistent gains in time-domain indices or mean HR. Controls were unchanged (Table 4).

Sleep Satisfaction

Self-reported sleep satisfaction by a three-level questionnaire improved in both supplementation groups (to 78.3% in Mg-oxide and 83.3% in combination; both p<0.001), while the control group showed no significant change (p=0.754) (Table 5).

Discussion

Principal Findings

In this ambispective cohort of normomagnesemic adults, magnesium oxide (Mg-oxide) yielded broader haemodynamic and autonomic benefits than an organic combination (malate+bisglycinate+citrate). Mg-oxide was associated with reductions in 24-hour SBP/DBP and lower nighttime and 24-hour mean HR, whereas the combination did not produce consistent changes in these endpoints. Time-domain vagal HRV indices (RMSSD, pNN50, NN50) improved with Mg-oxide, while the combination showed a selective frequency-domain shift (↓LF/HF with ↑HF) that did not translate into parallel gains in time-domain HRV or mean HR. QTc shortened modestly only in the combination group, and arrhythmic burden did not change materially in any group. Self-reported sleep satisfaction increased in both supplementation arms, but the underlying item was non-validated. Together, these findings do not support a clinical advantage of the combination over Mg-oxide in normomagnesemic individuals.

Comparison with Prior Evidence

Clinical enthusiasm for magnesium in rhythm control partly derives from acute-care settings, where intravenous Mg has reduced ventricular and supraventricular arrhythmias in meta-analysis and pragmatic studies (e.g., acute-onset AF). These data, however, cannot be assumed to generalize to chronic oral supplementation in patients with normal baseline Mg. Our results align with that nuance: despite small ECG interval shifts (PR shortening in both groups, QTc shortening only with the combination), we observed no reduction in arrhythmic burden and no superiority of the combination over Mg-oxide on core clinical surrogates (24-h BP/HR). This challenges the common perception that chelated/organic blends are inherently more effective than Mg-oxide.[11]

The divergence between time-domain and frequency-domain HRV-i.e., Mg-oxide improved RMSSD/pNN50 while the combination lowered LF/HF without parallel time-domain gains-may reflect measurement sensitivity and timescaledifferences: frequency-domain shifts can mark short-term

sympathovagal balance, whereas time-domain metrics often correlate with short-term vagal modulation in daily life. The small QTc shortening with the combination and PRshortening in both arms were of limited magnitude and uncertain clinical relevance in this normomagnesemic population. Collectively, the pattern favors Mg-oxide for global haemodynamic and vagal effects, with the combination showing selective spectral changes rather than broader physiologic improvement.[12-14]

Table 4. Comparison of the pre- and post-supplementation values of time-domain heart rate variability (HRV) parametersin three groups: magnesium oxide (Mg-oxide), magnesium combination (malate, bisglycinate, citrate), and control

Parameters	Mg-oxide Group (n:62) Mean ± SD	Mg Combination Group (n:61) Mean ± SD	Control Group (n:58) Mean ± SD	Inter-group p value
Pre-Mg SDNN	147.0 ± 38.0	154.3 ± 42.2	156.5 ± 42.8	0.513
Post-Mg SDNN	155.7 ± 39.9	147.8 ± 39.8	154.7 ± 42.1	0.325
Difference in SDNN	8.7 ± 33.3	-6.6 ± 29.3	-1.8 ± 0.60	0.77
Intra-group difference p-value	0.182	0.094	0.870	—
Pre-Mg SDANN	123.5 ± 36.9	133.2 ± 41.0	131.8 ± 40.3	0.288
Post-Mg SDANN	122.5 ± 33.0	122.1 ± 41.4	130.9 ± 40.3	0.397
Difference in SDANN	-1.0 ± 27.6	-11.2 ± 34.2	-0.90 ± 0.00	0.003
Intra-group difference p-value	0.433	0.039	0.976	—
Pre-Mg HRV-TI	30.0 ± 8.7	31.0 ± 8.6	31.7 ± 9.3	0.466
Post-Mg HRV-TI	33.0 ± 10.2	31.6 ± 8.6	31.7 ± 9.2	0.509
Difference in HRV-TI	2.98 ± 9.66	0.62 ± 7.48	0.00 ± 0.10	0.155
Intra-group difference p-value	0.075	0.667	0.990	—
Pre-Mg NN50 (x10^3)	10.3 ± 10.6	14.1 ± 10.7	14.8 ± 13.1	0.050
Post-Mg NN50 (x10^3)	14.5 ± 18.9	12.5 ± 10.3	14.3 ± 12.8	0.318
Difference in NN50 (x10^3)	4.1 ± 14.3	-1.6 ± 5.4	-0.50 ± 0.30	<0.001
Intra-group difference p-value	0.032	0.027	0.912	—
Pre-Mg pNN50 (%)	10.5 ± 10.6	14.2 ± 11.8	15.4 ± 14.0	0.06
Post-Mg pNN50 (%)	13.4 ± 14.4	13.1 ± 11.8	16.0 ± 14.0	0.520
Difference in pNN50 (%)	2.9 ± 8.1	-1.1 ± 5.3	0.60 ± 0.00	<0.001
Intra-group difference p-value	0.006	0.071	0.923	—
Pre-Mg RMSSD	77.6 ± 44.0	70.6 ± 31.2	77.6 ± 44.7	0.988
Post-Mg RMSSD	99.8 ± 65.8	79.0 ± 44.5	75.6 ± 46.8	0.084
Difference in RMSSD	22.2 ± 51.6	8.4 ± 37.2	-2.00 ± 2.10	0.003
Intra-group difference p-value	<0.001	0.207	0.798	—
Pre-Mg LF	66.4 ± 16.6	62.8 ± 18.7	68.0 ± 15.1	0.391
Post-Mg LF	61.4 ± 17.2	53.7 ± 19.3	68.1 ± 15.0	<0.001
Difference in LF	-5.0 ± 20.8	-9.1 ± 20.6	0.10 ± 0.10	0.002
Intra-group difference p-value	0.209	<0.001	0.989	—
Pre-Mg HF	23.2 ± 11.3	28.2 ± 14.2	23.7 ± 11.3	0.151
Post-Mg HF	26.3 ± 11.3	32.9 ± 13.0	24.3 ± 11.0	<0.001
Difference in HF	3.2 ± 14.2	4.6 ± 13.8	0.60 ± 0.30	0.011
Intra-group difference p-value	0.196	0.015	0.870	—
Pre-Mg LF/HF	6.6 ± 12.9	3.8 ± 4.3	6.0 ± 12.6	0.106
Post-Mg LF/HF	3.2 ± 2.8	2.5 ± 2.6	5.7 ± 11.6	<0.001
Difference in LF/HF	-3.3 ± 13.6	-1.3 ± 4.0	-0.30 ± 1.00	0.005
Intra-group difference p-value	0.175	0.007	0.768	—

HRV: Heart Rate Variability; SDNN: Standard Deviation of NN intervals; SDANN: Standard Deviation of the Average NN interval;HRV-TI: HRV Triangular Index; NN50: Number of successive NN interval differences >50 ms; pNN50: Percentage of NN50; RMSSD: Root Mean Square of Successive Differences; LF: Low frequency; HF: High frequency; Mg: Magnesium; SD: Standard Deviation

Table 5. Self-reported sleeping satisfaction levels before and after Mg supplementation in three groups: magnesium oxide (Mg-oxide), magnesium combination (malate, bisglycinate, citrate), and control

Sleeping Satisfaction	Mg-oxide Group (n:62) n (%)	Mg Combination Group (n:61) n (%)	Control Group (n:58) n (%)	Inter-group p value
Pre-Mg				
Satisfied	23 (37.0)	28 (45.9)	18 (30.0)	
Indecisive	15 (24.1)	18 (29.5)	30 (51.7)	0.166
Dissatisfied	24 (38.7)	15 (24.5)	10 (17.24)	
Post-Mg				
Satisfied	48 (77.4)	50 (81.9)	16 (27.5)	
Indecisive	7 (11.4)	4 (6.5)	32 (55.1)	<0.001
Dissatisfied	7 (11.4)	7 (11.4)	10 (17.2)	
Intra-group Difference p-value	<0.001	<0.001	0.754	—

Mg: Magnesium

Clinical Implications

For normomagnesemic adults seeking cardiovascular modulation (BP/HR and short-term vagal tone), our data suggest Mg-oxide as a pragmatic first-line option. It delivered the most consistent reductions in 24-hour BP and mean HR and improved time-domain HRV-all with a reimbursed, low-cost formulation. Although the combination achieved a slightly higher self-reported sleep satisfaction rate, nighttime HR actually decreased only with Mg-oxide and increased in the combination group; thus, we caution against inferring sleep-related physiologic superiority from a non-validated three-level questionnaire alone. Clinicians should prioritize objective ABPM/HRV outcomes and patient-specific goals when choosing a formulation.

Safety and Tolerability

Both formulations were generally well tolerated; no clinically relevant between-group differences emerged in renal indices or adverse arrhythmic outcomes. Serum Mg rose in both arms, and serum creatinine declined modestly without between-group differences in change, supporting the biologic activity and short-term renal safety of either approach in individuals with preserved kidney function. These observations align with the broader literature emphasizing cautious use of Mg when renal excretion is impaired.[15-18]

Conclusions

In normomagnesemic adults, both magnesium oxide and an organic combination (malate + bisglycinate + citrate) were associated with modest and formulation-specific physiological changes. Magnesium oxide showed small but consistent improvements in 24-hour blood pressure and mean heart rate alongside gains in time-domain vagal HRV indices (e.g., RMSSD, pNN50), whereas the combination produced a selective frequency-domain shift (↓LF/HF with ↑HF) and a small QTc shortening, without parallel changes in ambulatory BP or mean HR. Arrhythmic burden did not meaningfully change in any group, and self-reported sleep satisfaction improved in both supplementation arms. Given the modest effect sizes and similar short-term safety signals, cost and access considerations can justify magnesium oxide as a cost-effective default; however, formulation choice should ultimately be individualized to patient goals and context.

Limitations

This study has several constraints that warrant caution when interpreting the findings. First, group allocation was non-random; although we applied multivariable adjustment, residual confounding is possible. Second, sleep satisfaction and autonomic tone were assessed with a non-validated three-point question rather than polysomnography or formal autonomic testing. Third, supplementation relied on over-the-counter products and self-reported adherence. Finally, the single-centre design and modest sample of normomagnesemic adults limit generalisability to hypomagnesemic populations, other ethnic groups and longer-term outcomes. Larger, multi-centre randomised trials are needed to confirm these findings.

Ethical Approval

The study protocol was approved by the Acıbadem Mehmet Ali Aydınlar University and Acıbadem Healthcare Institutions Medical Research Ethics Committee (ATADEK; approval no. ATADEK 2025/02). All procedures adhered to relevant regulations and the Declaration of Helsinki. Written informed consent was obtained from all participants prior to data collection.

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contributions

The author conceived the study, collected and analyzed the data, interpreted the results, and wrote the manuscript.

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Supplementary Table 1. Comparison of pre- and post-supplementation serum magnesium and creatinine levels

Parameters	Mg-oxide Group (n:62) Mean ± SD	Mg Combination Group (n:61) Mean ± SD	Control Group (n:58) Mean ± SD	Inter-group p value
Pre-supplementation Mg level	1.97 ± 0.2	2.00 ± 0.1	1.98 ± 0.1	0.057
Post- supplementation Mg level	2.02 ± 0.11	2.07 ± 0.05	2.03 ± 0.07	<0.001
Difference in Mg level	0.05 ± 0.07	0.07 ± 0.07	0.05 ± 0.07	0.716
Intra-group difference p-value	<0.001	<0.001	<0.001	—
Pre-supplementation creatinine level	0.81 ± 0.17	0.77 ± 0.18	0.81 ± 0.21	0.530
Post- supplementation creatinine level	0.76 ± 0.17	0.75 ± 0.18	0.77 ± 0.21	0.987
Difference in creatinine level	-0.05 ± 0.05	-0.02 ± 0.05	-0.04 ± 0.05	0.101
Intra-group difference p-value	<0.001	0.002	<0.001	—
Pre-supplementation eGFR	93.2 ± 18.8	102.1 ± 20.5	94.7 ± 23.1	0.053
Post- supplementation eGFR	98.3 ± 19.3	104.2 ± 21.4	98.5 ± 24.5	0.244
Difference in eGFR	5.1 ± 6.4	2.1 ± 5.5	3.8 ± 5.9	0.019
Intra-group difference p-value	< 0.001	0.005	< 0.001	—

Mg: Magnesium; eGFR: Estimated glomerular filtration rate

Supplementary Table 2. Comparison of ECG and arrhythmia parameters before and after magnesium supplementation in three groups

Parameters	Mg-oxide Group (n:62) Mean ± SD	Mg Combination Group (n:61) Mean ± SD	Control Group (n:58) Mean ± SD	Inter-group p value
Pre-Mg PR duration, ms	151.5 ± 23.5	146.8 ± 22.2	145.8 ± 26.0	0.310
Post-Mg PR duration, ms	147.6 ± 25.7	142.9 ± 17.2	144.4 ± 26.0	0.701
Difference in PR duration, ms	-3.9 ± 12.0	-3.9 ± 11.7	-1.40 ± 0.00	0.020
Intra-group difference p-value	0.018	0.011	0.788	—
Pre-Mg QRS duration, ms	81.4 ± 11.6	83.2 ± 10.3	82.5 ± 8.8	0.500
Post-Mg QRS duration, ms	83.7 ± 9.5	81.3 ± 10.0	82.4 ± 8.7	0.229
Difference in QRS duration, ms	2.2 ± 9.0	-1.9 ± 5.6	0.10 ± 0.10	0.106
Intra-group difference p-value	0.336	0.024	0.911	—
Pre-Mg QTc duration, ms	423.2 ± 23.0	416.3 ± 20.2	413.3 ± 26.8	0.210
Post-Mg QTc duration, ms	426.9 ± 20.2	408.8 ± 22.7	412.9 ± 26.7	<0.001
Difference in QTc duration, ms	3.7 ± 20.0	-7.4 ± 26.1	-0.40 ± 0.00	0.04
Intra-group difference p-value	0.316	0.049	0.878	—
Pre-Mg APC, n	163.3 ± 235.9	332.1 ± 1031.7	356.4 ± 1031.2	0.651
Post-Mg APC, n	153.8 ± 277.2	90.0 ± 149.1	350.0 ± 1030.0	0.750
Difference in APC, n	-9.6 ± 252.1	-242 ± 1015.3	-6.40 ± 1.20	0.114
Intra-group difference p-value	0.078	0.142	0.670	—
Pre-Mg VPC, n	786.6 ± 2419.1	558.4 ± 2142.4	1139.2 ± 3114.8	0.032
Post-Mg VPC, n	1094 ± 3644.8	469.1 ± 2027.5	1130.0 ± 3110.0	0.137
Difference in VPC, n	307.5 ± 1291.9	-89.3 ± 2374.1	-9.20 ± 4.80	0.344
Intra-group difference p-value	0.458	0.218	0.677	—
Pre-Mg Bigemini Count, n	7.8 ± 31.1	59.6 ± 230.8	64.8 ± 231.1	0.807
Post-Mg Bigemini Count, n	8.7 ± 35.0	15.6 ± 83.2	64.9 ± 230.0	0.987
Difference in Bigemini Count, n	0.8 ± 4.4	-44.0 ± 167.3	0.10 ± 1.10	0.720
Intra-group difference p-value	0.113	0.260	0.567	—
Pre-Mg Couplet Count, n	4.40 ± 23.34	0.30 ± 1.14	0.37 ± 1.18	0.806
Post-Mg Couplet Count, n	4.77 ± 23.32	1.23 ± 6.51	0.38 ± 1.18	0.408
Difference in Couplet Count, n	0.37 ± 1.41	0.93 ± 5.46	0.01 ± 0.00	0.362
Intra-group difference p-value	0.065	0.776	0.870	—

ECG: Electrocardiogram; Mg: Magnesium; ms: Milliseconds; APC: Atrial Premature Contractions; VPC: Ventricular Premature Contractions; QTc: Corrected QT interval; SD: Standard Deviation; PR: PR interval; QRS: QRS complex duration