Lidocaine alone or combined with Magnesium Sulfate stabilizes hemodynamic parameters during General Anesthesia without prolonging the Neuromuscular Blockade: a randomized, double-blind, controlled trial

Waynice N. Paula-Garcia (wgarcia@fmrp.usp.br)
University of Sao Paulo Faculty of Medicine of Ribeirao Preto: Universidade de Sao Paulo Faculdade de Medicina de Ribeirao Preto https://orcid.org/0000-0003-0020-5295

Gustavo H Oliveira-Paula
University of Sao Paulo Faculty of Medicine of Ribeirao Preto: Universidade de Sao Paulo Faculdade de Medicina de Ribeirao Preto

Hans D de Boer
Martini Hospital: Martini Ziekenhuis

Luís Vicente Garcia
University of Sao Paulo Faculty of Medicine of Ribeirao Preto: Universidade de Sao Paulo Faculdade de Medicina de Ribeirao Preto

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Abstract

Background

Lidocaine and magnesium sulfate have become increasingly utilised

in general anaesthesia. The present study evaluated the effects of these drugs, isolated or combined on the hemodynamic parameters as well as on the cisatracurium-induced neuromuscular blockade (NMB).

Methods

At a University hospital, 64 patients, ASA physical status I and II, undergoing elective surgery with similar pain stimulus, were randomly assigned to four groups. Patients received a bolus of lidocaine and magnesium sulfate before the tracheal intubation and a continuous infusion during the operation respectively: 3 $mg.kg^{-1}$ and 3 $mg.kg^{-1}.h^{-1}$ (Lidocaine -L group), 40 $mg.kg^{-1}$ and 20 $mg.kg^{-1}.h^{-1}$ (Magnesium - M group), equal doses of both drugs (Magnesium plus lidocaine - MLgroup) and, a equivalent volume of isotonic solution (Control - C group). Haemodynamic parameters and neuromuscular blockade features were continuously monitored until spontaneous recovery of the Traino of Four ratio (TOF=0.9).

Results

The Lidocaine group presented a highly significant small hemodynamic fluctuation during the anesthesia induction and maintenance period ($p<0.0001$) with no change at NMB. The magnesium sulfate infusion alone or combined with lidocaine prolonged all the recovery characteristics ($p< 0.0001$). The onset time was not influenced by the studied drugs. The percentage of patients who achieved a TOF ratio of 90% without recovering the first Twich (T1-95%) was higher in the M and ML groups.

Conclusion

Intravenous lidocaine plays a significant role in the hemodynamic stability in patients under general anesthesia without exerting any additional impact on the NMB even combined with magnesium sulfate. Aside from prolonging all NMB recovery characteristics without altering the onset speed, magnesium sulfate enhances the TOF recovery rate without T1 recovery. Our findings may aid clinical decisions involving the use of these drugs by encouraging their association in multimodal anesthesia or other therapeutic purposes.

Trial registration

NCT02483611 (registration date: 06-29- 2015).

Background

Anesthetic additive drugs like lidocaine and magnesium sulfate have become increasingly utilized, alone or in combination, in general anesthesia to meet various objectives, such as: postoperative pain

reduction, reduced and more balanced anesthetic doses, hemodynamic stabilization, and improvement of surgical conditions.[1–9] A combination of lidocaine and magnesium sulfate in a multimodal opioid-sparing- or even opioid-free anesthesia approach may reduce or eliminate the use of opioids in the perioperative period. [10,11] Opioid-sparing or opioid-free anesthesia is a relatively new strategy that is increasingly being used in daily anesthesia practice. Several studies have demonstrated benefits from this approach, including in cancer patients, elderly and obese patients, or those with obstructive sleep apnea.[12] Drugs like lidocaine and magnesium sulfate are frequently used in combination with neuromuscular blocking drugs of which the latter may contribute to residual neuromuscular blockade, and hemodynamic instability during anesthetic procedures. Drugs like lidocaine and magnesium sulfate are frequently used in combination with neuromuscular blocking drugs, of which the latter may contribute to residual neuromuscular blockade and hemodynamic instability during anesthetic procedures. Approximately 40% of patients admitted to the post-anesthesia care unit have residual neuromuscular blockade13, what increases morbidity and mortality, but only 1–3% of patients with residual blockade develop clinically apparent events.[13,14]

Magnesium sulfate infusion administered before anesthesia has been found to increase the speed of onset of a rocuronium, cisatracurium- or vecuronium-induced neuromuscular blockade (NMB) without necessarily enhancing its duration.[15–17] Furthermore, magnesium sulfate infusion re-establishes a clinically relevant degree of muscle paralysis in patients who had recovered from paralysis and causes a significant, prolonged NMB when induced by a single dose of the neuromuscular blocking drug rocuronium.[18,19] One study showed prolonged rocuronium-induced NMB after pre-treatment of magnesium sulfate, however no change in the speed of onset. [20]

Previous studies have shown that local anesthetics, such as lidocaine, interact with neuromuscular blocking drugs.[21–23] Cardoso et al. noted that the combination of lidocaine and rocuronium increased the time to recovery of T1-25%, T1-75%, and T1-95%, but did not prolong the time to final recovery.[24] More recent studies evaluating the clinical effects of lidocaine, in lower dosage, on the neuromuscular blocking drugs cisatracurium and rocuronium have demonstrated no changes in recovery of NMB characteristics or speed of onset.[25–27]

Considering the growing perioperative clinical applications of both lidocaine and magnesium sulfate, the possibility of using these drugs in combination increases. A combination of these drugs may not only be beneficial for surgical patients regarding opioid-sparing effects but may also influence NMB characteristics and promote changes in hemodynamic parameters. Thus, this study's main aim was to evaluate the effects of the lidocaine and magnesium sulfate, isolated or combined, in higher dosage, on the hemodynamic parameters as well as on the cisatracurium-induced neuromuscular blockade (NMB). Considering that studies have shown that lidocaine infusion does not affect NMB, we tested the hypothesis that combined use of lidocaine with magnesium sulfate does not affect cisatracurium-induced NMB compared with magnesium sulfate infusion alone.[25–27]

Methods

In this prospective, randomized, double-blind, controlled trial, sixty-six patients [American Society of Anesthesiologists (ASA) physical status I to II, aged 18 to 60 years] were recruited who were scheduled for surgery (estimated surgical time greater than 90 min, with similar pain stimulus and no need for a neuromuscular block during the surgical procedure). Exclusion criteria were patients with diseases or on medications known to interfere with neuromuscular transmission, hepatic or renal dysfunction, electrolyte abnormalities, allergy to drugs used in the study, body mass index <18 or >29 $kg.m^{-2}$, expected to have difficulties during mask ventilation or intubation, pregnant or breastfeeding.

Using sealed opaque envelopes, numbered sequentially, sixty-four patients were randomly allocated to four parallel treatment groups (figure 1). The seal of the envelope was broken before the induction of general anesthesia by trained study personnel not involved in the data collection. Throughout the perioperative period, care providers, patients, and research team members were blinded to group assignment. The L group received lidocaine 3 $mg.kg^{-1}$ as an IV bolus before the induction of anesthesia and 3 $mg.kg^{-1}.h^{-1}$ IV continuous. infusion during the operation period; the M group received magnesium sulfate 40 $mg.kg^{-1}$ as an IV bolus before the induction of anesthesia and 20 $mg.kg^{-1}h^{-1}$ IV continuous infusion during the operation period. The ML group received equal doses of magnesium sulfate combined with lidocaine at the same conditions during the operation period. The control group received an equivalent volume of isotonic solution.

Patients were monitored using electrocardiography, noninvasive blood pressure measurements, pulse oximetry, capnography (Draeger Medical Systems, Telford, Pennsylvania, USA). Total Intravenous (IV) Anesthesia was standardized for all patients and performed without the use of benzodiazepines, using a propofol target dose (plasma targeting, Injectomat TIVA Agilia, Brazil) of 4 $\mu g \cdot mL^{-1}$ and a remifentanil infusion of 0.5 $mg \cdot kg^{-1} \cdot min^{-1}$. After induction, the propofol infusion target was decreased to 2.5 $\mu g \cdot mL^{-1}$, and infusion of remifentanil was adjusted to 0.1-0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ as needed. If systolic arterial pressure (SAP) or HR increased or decreased by > 30% of baseline for > 60 sec, remifentanil infusion was respectively increased/decreased at 0.05 $\mu g\ kg^{-1}\ min^{-1}$ until achieving the goal value within the range. If necessary, ephedrine´bolus (2.5 to 5 mg) was allowed. Hemodynamic parameters were considered stable when BP and HR were within 20% of baseline values.

After induction of anesthesia and loss of consciousness, the neuromuscular function was assessed by monitoring the adductor pollicis muscle via acceleromyography with a TOF-Watch SX device (Organon Ireland Ltd., a subsidiary of Merck & Co., Inc., Swords, Co., Dublin, Ireland) according to the neuromuscular research consensus. [28]

The monitoring system was positioned on the side opposite to the blood pressure cuff and IV line. Pediatric surface electrodes (Red Dot®, 3M Health Care, Neuss, Germany) were placed on cleaned skin over the ulnar nerve on the volar side of the wrist. The transducer's position was secured by placing the thumb in a hand adapter and fixed a temperature sensor at the distal end of the forearm. TOF tracing was

stabilized by administering 1 min of TOF repetitive stimulation, followed by 5 s of 50-Hz tetanus stimulation, and then another period of repetitive TOF stimulation for 3-4 min. CAL 2 mode determined the supramaximal threshold and to calibrate the transducer of the accelerometer. After calibrating the device and stabilization, the mean of three TOF's values was recorded in each patient and used as a reference. Then, the TOF recovery value was considered the measured equivalent of 90% of this predefined value. The same procedure was performed for the T1 measurements. Then, bolus doses of solutions were administered to assigned groups over 5 min. Subsequently, a total of 0.15 $mg.kg^{-1}$ cisatracurium over 5 seconds (time point zero) was administered, which was followed by tracheal intubation when the TOF ratio reached zero. Patients were monitored until they achieved spontaneous recovery from NMB (TOF ratio=0.9). Values of T1, T2, T3, T4, and TOF ratio, as well as skin temperature, were recorded. No additional cisatracurium injections were permitted. After measuring onset time, stimulation mode was changed to TOF (2 Hz, stimulus duration of 200 μs, square wave, 15 s intervals). Finally, adequate normalization of the TOF recovery results according to the baseline values was provided to detect residual paralysis reliably.

All neuromuscular monitoring data were transferred in real-time and stored on a laptop using the TOF-Watch SX monitor computer program (version 2.5.INT; Organon Ltd., Dublin, Ireland).

The following variables were measured:

1. Speed of onset – time in seconds required to reduce T1 response to 5% of initial contraction force.
2. Clinical duration (Dur25%) – elapsed time in minutes for T1 response to recover 25% of its initial value.
3. Recovery index – elapsed time in minutes between the recovery of the T1 response from 25% of its initial value (Dur25%) to 75% of its initial value (Dur75%).
4. Pharmacological duration – elapsed time in minutes for the T1 response to recover 95% of its initial value (Dur95%).
5. Spontaneous recovery – time in minutes to the recovery of T4/T1 to 90% of its initial value.

Body temperature, respiratory (end-tidal CO2) and hemodynamic parameters (systolic, diastolic, mean blood pressure and heart rate) were recorded and annotated at various times: M1- when the patient arrived in the operating room; M2- immediately before induction of anesthesia; M3- before the infusion of the tested solutions (saline, magnesium sulfate or magnesium sulfate associated with lidocaine); M4- five minutes after M3 (end of the infusion loading dose of test solutions); M5 immediately before intubation; M6- one minute after tracheal intubation and M7 every fifteen minutes until the end of the study. Heating elements were used to maintain their skin and central temperatures above 32 and 36 °C, respectively. All unexpected events that occurred during the study were recorded as adverse effects.

The Shapiro-Wilk test was used to assess normality. The clinical and demographic characteristics are expressed as the means ± SD or medians (IQR [range]) and were compared by analysis of variance, the Kruskal-Wallis test, or the chi-square test, where appropriate. Given that studies have suggested that the

area under the curve (AUC) can provide a more accurate analysis of the hemodynamic data [29, 30], this approach was used to compare the hemodynamic responses among the study groups. The pharmacodynamic variables (i.e., speed of onset, clinical duration, recovery rate, and total duration) were represented as box-and-whisker plots showing the range, quartiles, and median. The AUCs of the changes in mean arterial pressure (MAP) and HR were expressed as mean ± SD (normally distributed data). The pharmacodynamic variables were compared among the groups via the Kruskal-Wallis test, followed by Dunn's multiple comparison test. The AUCs of the changes in mean arterial pressure (MAP) and HR were compared among the groups by the one-way ANOVA followed by Tukey multiple comparison test. Both multiple comparison tests were used to control the type I error at 5%. The percentage of patients who achieved a TOF ratio of 90% without reaching 95% recovery of the first twitch (T1) response was compared among the groups by the chi-square test. A p-value <0.05 was considered statistically significant for all outcome variables.

For the sample size calculation, we considered a previous study showing that magnesium sulfate prolongs rocuronium-induced NMB.[16] Having chosen a significance level of 5% and a power of 80%, we used the spontaneous recovery means of that previous study (73.2 ± 22 min with MgSO4 and 57.8 ± 14.2 min with saline) to calculate the number of participants required to detect a similar effect.[31] The calculation revealed that N=14 patients were needed per group. As we included N=15-16 per group, we had 85% power to detect the same differences as planned a priori.

Results

Between 2015 and 2018, 64 patients were recruited and randomized in this study. Patient characteristics are shown in Table 1. Most patients were ASA1, who underwent rhinoplasty and reductive mastopexy. There was no significant difference in the baseline variables between the groups. After data collection, one patient was excluded from the control group because her surgical procedure was completed in less than 90 min (figure 1).

Hemodynamic parameters among study groups, evaluated by the AUCs for changes in MAP and HR at the six times points during anesthesia induction, are shown in figure 2 (A-D). The lidocaine group presented a significant small fluctuation on MAP and HR measures during anesthesia induction (Total AUC ± SE: L Group- 18.11 ± 12.17 and 6.49 ± 7.01 respectively; compared to the other groups: C group- 59.34 ± 11.87 and 20.56 ± 20.34 respectively; M group-53.41 ± 9.85 and 25.79 ± 11.92; ML Group-52.88 ± 8.97 and 16.49 ± 14.05; p<0,0001. During the maintenance phase of anesthesia, the study groups presented similar behavior: Total AUC ± SE: L Group- 932,6 ± 307,6 and 144.3 ± 106.3 respectively; compared to the other groups: C group-1609 ± 281.5 and 548.50 ± 296.1 respectively; M group- 1375 ± 248.7.85 and 387.7 ± 195.0; ML Group-1453 ± 268.4 and 295 ± 192; p<0,0001.

Concerning to the NMB characteristics, lidocaine infusion did not exert any effect. However, an infusion of magnesium sulfate, associated, but not lidocaine, prolonged all NMB recovery features (p<0.0001,

table 2, figure 4), without changing the speed of onset of cisatracurium (C group: 147.8±29,75; L group: 134,9±29,62; M group: 146,9±45,27; ML group: 142,8±42,80, p=0,7624, figure 3).

Interestingly, the percentage of patients who achieved a TOF ratio of 90% without reaching T1-95% was higher in the M and ML groups than in the C and L groups (50.0%, 56.2% and 20.0%, 25.0% respectively). There were no adverse events reported in this study.

Discussion

This prospective, randomized, double-blind, controlled study evaluated the effects of intravenous lidocaine combined with magnesium sulfate (bolus and continuous infusions) in general anesthesia. The main findings of the study showed that: (a) Intravenous lidocaine plays a significant role for the hemodynamic stability in patients under general anesthesia, without exerting any additional impact on the NMB even combined with magnesium sulfate; (b) Magnesium sulfate prolonged the time of recovery in all pharmacodynamic parameters studied (i.e., clinical duration, recovery index, total duration, and spontaneous recovery); (c) There were no differences in the speed of onset among groups; (d) Patients in the magnesium sulfate groups had higher rates of TOF recovery without T1 recovery than those in the control and L group.

The concept of multimodal general anesthesia has recently extended the idea of balanced anesthesia, including some other additional drugs like lidocaine, magnesium sulfate, β–blockers, and α2-agonists that target different neuroanatomical circuits and multiple neurophysiologic mechanisms.[32] The pharmacologic explanation of the multimodal general anesthesia approach is based on the firmly established observation that when anesthetic drugs of different mechanisms are combined, they typically interact synergistically.[33] Lidocaine and magnesium sulfate indirectly block sympathetic effects and are well established in opioid-sparing multimodal analgesic strategies.[34] Interaction between parenteral magnesium and nondepolarizing neuromuscular blocking drugs has been previously described. Facilitating a neuromuscular blockade with magnesium involves the following mechanisms: decreased pre-junctional release of acetylcholine via inhibition of voltage-dependent calcium channels; reduced sensitivity of endplate to acetylcholine; and attenuating the direct excitability of muscle fibers, presumably by altering electrical threshold of muscle membrane.[35] Typically, magnesium sulfate is administered as a bolus dose of 30–50 $mg.kg^{-1}$, followed by a maintenance dose of 6–20 $mg.kg^{-1}.h^{-1}$.[36] Previous studies have shown similar results as described in this study concerning the prolongation of NMB by magnesium using a similar dosage. [16, 37, 38]

Contradictory findings have been reported concerning whether the NMB latency period (speed of onset) is reduced or not by magnesium sulfate pre-treatment. Preadministration of magnesium sulfate (30–50 mg kg^{-1}) infused over 10 minutes has been shown to prolong recovery and reduce the onset time of rocuronium and vecuronium. [37, 39] However, a short period of infusion before administering a neuromuscular blocking drug left onset time unchanged. Also, pre-treatment with magnesium sulfate

(60 mg kg^{-1}) infused over 1-minute prolonged recovery but did not reduce the onset time of rocuronium- and pancuronium-induced neuromuscular blockade. These findings possibly reflect differences in neuromuscular blocking drugs' pharmacodynamic properties, and the prolonged infusion time before administering the neuromuscular blocking drug seemed to improve the drug's action.

Our findings corroborate those of Kussman and James. [20, 40] Analogous to Kussman's suggestion about rocuronium's pharmacodynamics, one possible explanation for the constant speed of cisatracurium onset observed in our study is that we used a short time's period for magnesium sulfate infusion. Indeed, a 5-min infusion period immediately before muscle relaxant administration provides insufficient time for the magnesium sulfate to reach terminal motor nerves at a high enough concentration to interfere with cisatracurium initiation. Some reports have even shown no enhancement of NMB by magnesium sulfate, using magnesium sulfate only as a pre-treatment dosage.[15, 17]

Interestingly, many patients in magnesium sulfate infusion groups reached 90% of their initial TOF response without T1 recovering to 95% of its original value. According to Kopman et al. [41], after spontaneous recovery of the TOF ratio to 80% or higher, the T1 response often returns to 150% or higher relative to control value. In contrast, Staals et al. [42] reported findings that were similar to ours. After they achieved the reversal of rocuronium-induced NMB with sugammadex, the authors observed that a full recovery of the TOF ratio was reached while T1 remained depressed. The real meaning of this finding is unknown and probably does not have significant clinical repercussions. Although these authors suggested that using TOF value as a single measure may not be enough to prevent a residual blockade under those particular conditions, other studies observed that magnesium sulfate did not significantly affect the time of reversal of rocuronium-induced neuromuscular blockade by sugammadex.[43]

In our study, the prevalence of individuals in groups M and ML, who recovered their TOF ratio to 90% without recovering of T1, suggests magnesium sulfate's interference. However, further studies are needed to confirm and better understand this effect.

Perioperative IV administration of lidocaine varies among studies based on the dose of lidocaine bolus (100 mg or 1–5 mg kg^{-1}), infusion during maintenance (1–6 mg kg^{-1} h^{-1} or 2–4 mg min^{-1}) and duration of infusion.[44, 45] However, the use of doses and lidocaine as high as 5 mg.kg.h^{-1} infused for 6 hours is reported without adverse effects.[46] Typically, lidocaine dose used in studies assessing its impact on NMB [25–27] has been between 1.5 and 2 mg.kg^{-1} (bolus) and 2 mg.kg^{-1}.h^{-1} (maintenance) and results similar to ours were obtained in these studies. Although lidocaine is widely used and is especially useful as an adjuvant during general anesthesia for its analgesic and opioid-sparing effects, few studies have systematically assessed the incidence of adverse effects or optimal dose.[44] We have considered using high doses to evaluate possible hemodynamic changes. Some studies have shown some interactions between local anesthetics and neuromuscular blocking drugs.[21–24] However, more recently, studies evaluating the clinical effects of lidocaine on neuromuscular blocking actions of cisatracurium and rocuronium have demonstrated no changes in NMB recovery characteristics or speed of onset periods.[25–

[27] Corroborating these observations, in the present study, lidocaine infusion, even in higher doses, did not result in any additional effects of magnesium sulfate alone on NMB and effectively prevented MAP and HR fluctuations during anesthesia induction and maintenance. Importantly, this hemodynamic stability is particularly relevant in specific conditions, such as in intracranial aneurysm management.[45]

Surgical patients need to be fully awake at the recovery ward postoperative, with acceptable pain, without respiratory depression, especially for morbid obesity or obstructive sleep apnea.[12] It is also known that opioids present side effects including postoperative nausea and vomiting, shivering, ileus, and urine retention[47] and can achieve both short-lasting analgesia and long-lasting hyperalgesia due to their upregulation of compensatory pronociceptive pathways.[48] In addition, opioids may have detrimental immunological effects and may affect surgical outcomes or a variety of disease processes, including bacterial and viral infections and cancer.[49, 50] The impact of opioid-mediated immune effects can be particularly dangerous in certain vulnerable populations, such as elderly or immunocompromised patients.

Choosing drugs without hyperalgesia or damaging immune effects may be an essential consideration in anesthesia. Therefore, opioid-free or opioid-reduced anesthesia procedures are justified and have gained popularity.[51, 52] Given these new situational demands for anesthesia and pain control protocols, evidence that the lidocaine can provide hemodynamic stability during anesthesia and its addition to magnesium sulfate does not add any side effect is valuable. These findings may encourage the lidocaine infusion alone or combined with magnesium sulfate in clinical practice for various therapeutic purposes, including opioid-free/ sparring anesthesia with or without neuromuscular blockers. The mechanisms and the precise dosage regimen for the hemodynamic stability provided by lidocaine warrants further research.

Our study has some limitations. The actual plasma concentrations of cisatracurium were not measured. However, we choose this nondepolarizing neuromuscular blocking agent because its duration of action has low inter-individual variability.[53] Moreover, its clearance from plasma results from a nonenzymatic degradation whose rate is primarily affected by pH and temperature.[54] The arterial blood gases were not measured, but we excluded surgical procedures potentially resulting in metabolic acidosis and, also, the mean nasopharyngeal temperatures and end-tidal CO_2 partial pressures were in the normal range and, did not differ between groups.

Conclusions

Intravenous lidocaine plays a significant role in the hemodynamic stability in adults patients under general anesthesia without exerting any additional impact on the NMB even combined with magnesium sulfate. Aside from prolonging all NMB recovery characteristics without altering the onset speed, magnesium sulfate enhances the TOF recovery rate without T1 recovery. Our findings may aid clinical decisions involving the use of these drugs by encouraging their association in multimodal anesthesia or other therapeutic purposes.

Abbreviations

ASA American Society of Anesthesiology

AUC Area under curve

CI Confidence interval

CO_2 Carbon dioxide

HR Heart Rate

IQR Interquartile range

IV Intravenous

MAP Mean Arterial Pressure

NMB Neuromuscular blockade

SD Standard deviation

SE Standard error

TOF Train of Four

T1 first twich

T2 second twich

T3 third twitch

T4 fourth twich

Declarations

Competing interest

Hans D. de Boer has received research grants from Merck and is treasurer of the ERAS Society. The authors declare that they have no other competing interests.

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available as permission from participants to publicity share the dataset has not been obtained.

Ethics approval and consent to participate

This study has been approved by the Institutional Ethics Committee of the Hospital das Clínicas of the Faculty of Medicine of Ribeirao Preto, University of Sao Paulo, Brazil (protocol number: 5362/2013). The protocol adhered to the applicable Equator guidelines and was published by ClinicalTrials.gov ID (number NCT02483611)-registration date: 06-29- 2015. https://clinicaltrials.gov/ct2/show/NCT02483611. Written informed consent was obtained from each participant prior to data collection or study intervention.

Consent for publication

Not Applicable

Funding

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Authors' contributions

WNPaula-Garcia and LVGarcia designed and conducted the study, analyzed the data, and writed the manuscript. GHOliveira-Paula and HDdeBoer analyzed the data and writed the manuscript. All authors have read and approved the manuscript.

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Tables

Table 1: Clinical and demographic characteristics of the patients.

	C (n=15)	L (n=16)	M (n=16)	ML (n=16)	*p* value
Age (years)	36±11,84	34,65±9,45	34,88±11,95	32,88±9,06	NS
Gender(F/M)	7/8	8/8	8/8	8/8	NS
ASA PS I/II	14/1	14/2	14/2	13/3	NS
BMI (Kg/ m^2)	24.07 ± 3.79	24.95 ± 3.44	25.74 ± 3.46	23.24 ± 2.63	NS

ASA PS: American Society of Anesthesiologists physical status; **BMI:** body mass index; C: control group; **L:** lidocaine group; **M:** magnesium sulfate group; **ML:** magnesium sulfate plus lidocaína group. Values are the mean ± S.D. **NS**: not significant

Table 2: Neuromuscular Blockage Recovery characteristics

	CD	RI	TD	SR
C	64.88 (57.05–70.23 [40.50-92.90])	14.73 (14.25–16.00 [11.00-24.25])	81.79±13.50	90.0±12.78
L	69.74 (63.54–79.63 [50.90-106.70])	16.71 (11.14–19.38 [7.75-34.00])	89.12±12.69	101,2±11.68
M	82.68 (76.83–91.19 [72.62-99.27])	24.00 (16.38–30.00 [12.00-37.75])	112.50±12.63	120.2±10.88
ML	85.70 (82.55–88.05 [71.78-115.8]	20.50 (18.56–26.88 [12.20-45.25])	108.30±10.52	125.5±15.31
p	p<0.0001	p<0.0001	p<0.0001	p<0.0001

CD: clinical duration; **RI:** recovery index; **TD**: total duration; **SR**: Spontaneous recovery; **p**: p value; **C:** control group; **L:** lidocaine group; **M:** magnesium sulfate group; **ML:** magnesium sulfate plus lidocaína group. Values are medians (IQR [range]) the mean or means ± SD.

Figures

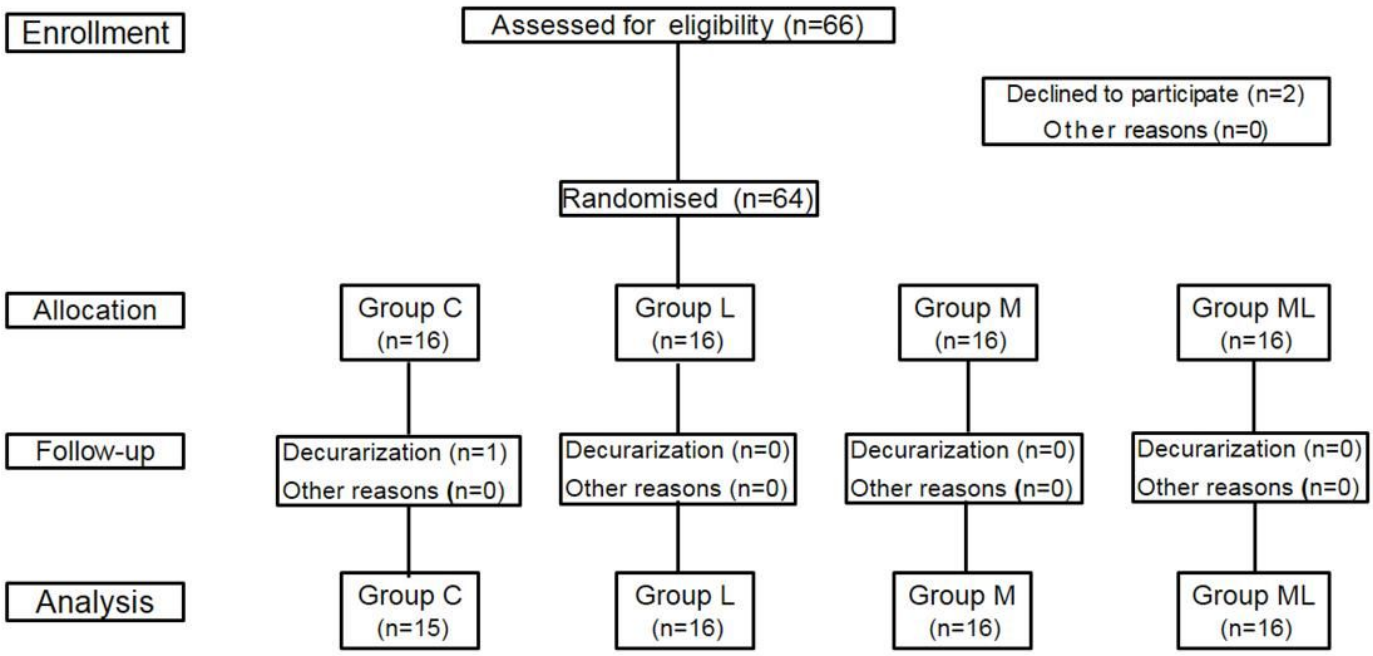

Figure 1

CONSORT flow diagram of participants allocation. C: control group; M: magnesium sulfate group; ML: magnesium sulfate combined with lidocaine group.

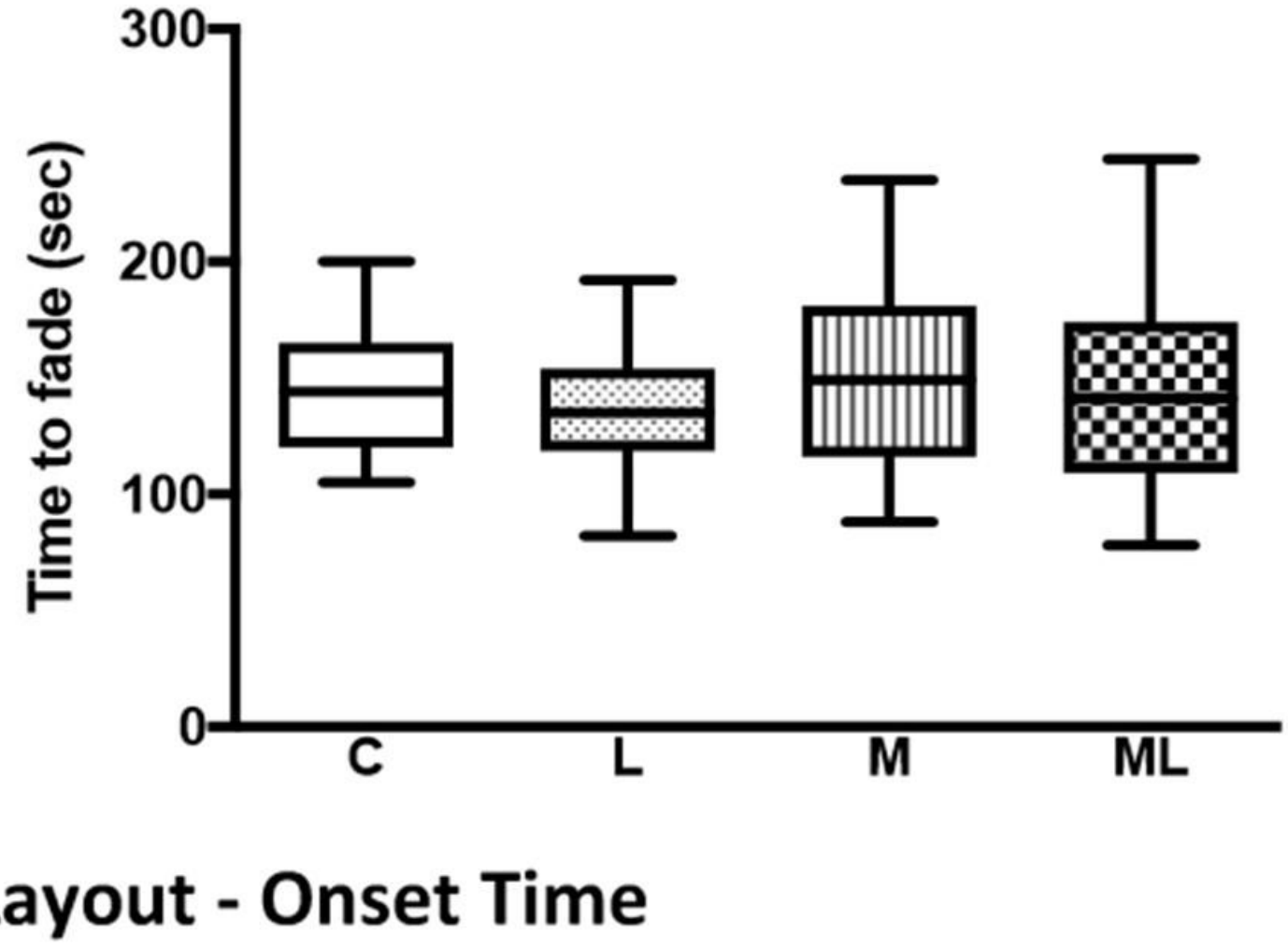

Figure 2

Area under the curve (AUC) of hemodynamic parameters. (A) AUC of the mean arterial pressure (MAP) in the induction period. (B) AUC of the MAP during the maintenance period. (C) AUC of heart rate (HR) in the induction period. (D) AUC of HR during the maintenance period. C: control group; M: magnesium sulfate group; ML: magnesium sulfate combined with lidocaine group. The box-and-whisker plots show the range and quartiles. The boxes extend from the 25th percentile to the 75th percentile, with a line at the median. The whiskers show the highest and lowest values; * p=0.0033 versus the C and M groups.

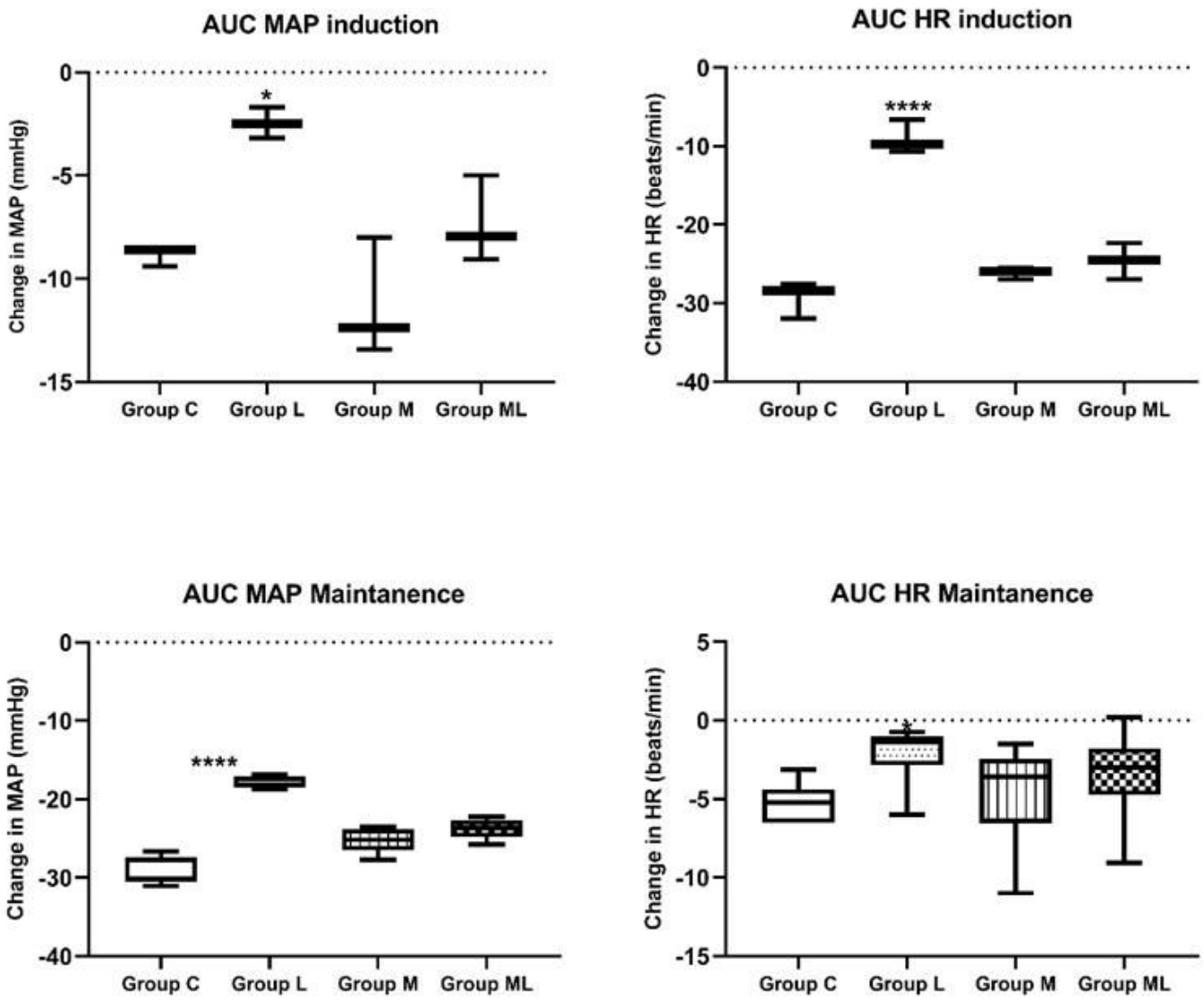

Figure 3

Speed of onset. C: control group; M: magnesium sulfate group; ML: magnesium sulfate combined with lidocaine group. The box-and-whisker plots show the range and quartiles. The boxes extend from the 25th percentile to the 75th percentile, with a line at the median. The whiskers show the highest and lowest values; $p>0.05$ versus the M and ML groups.

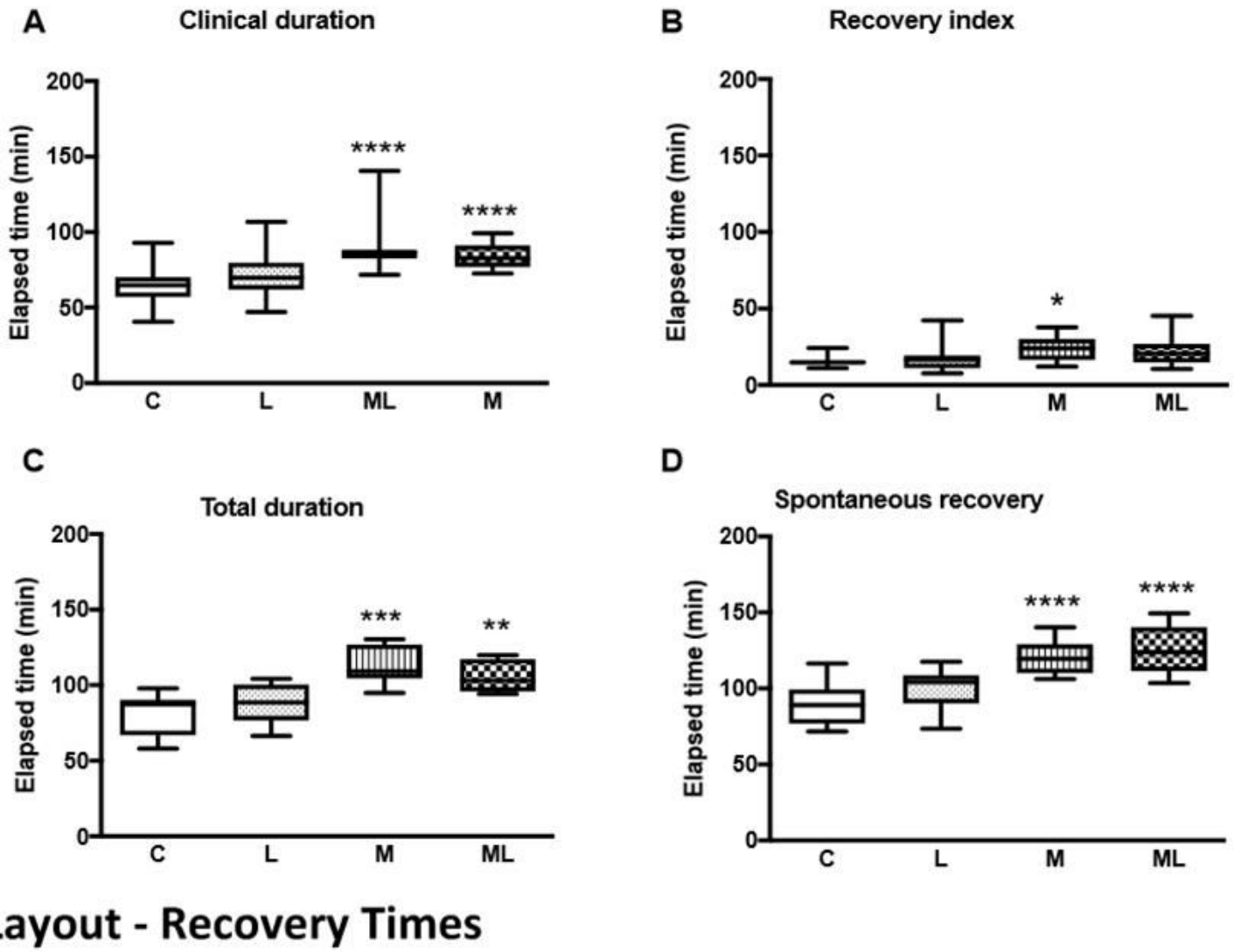

Figure 4

Recovery characteristics. (A) Clinical duration. (B) Recovery index. (C) Total duration. (D) Spontaneous recovery. C: control group; M: magnesium sulfate group; ML: magnesium sulfate combined with lidocaine group. The box-and-whisker plots show the range and quartiles. The boxes extend from the 25th percentile to the 75th percentile, with a line at the median. The whiskers show the highest and lowest values; * $p<0.0001$ versus the M and ML groups.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CONSORT2010Checklist.doc