Egyptian Journal of Anaesthesia (2013) **29**, 213–217

Egyptian Society of Anesthesiologists

Egyptian Journal of Anaesthesia

www.elsevier.com/locate/egja
www.sciencedirect.com

Research Article

Is this the time for Magnesium sulfate to replace Meperidine as an antishivering agent in spinal anesthesia?

Mohamed Elsonbaty *, **Ahmed Elsonbaty, Dalia Saad**

Faculty of Medicine, Cairo University, Egypt

Received 4 June 2012; revised 17 March 2013; accepted 21 March 2013
Available online 12 April 2013

KEYWORDS

Shivering;
Meperidine;
Magnesium sulfate;
Spinal anesthesia;
Regional anesthesia

Abstract *Background & Aim:* Shivering is one of the serious complications during spinal anesthesia. Mepreidine is considered the most common drug used for control of shivering. The aim of this study is to detect if Magnesium sulfate can replace Mepreidine, in the prevention of shivering in patients undergoing spinal anesthesia during knee arthroscopy.

Methods: The study included 50 patients scheduled for elective knee arthroscopy, aged 20–50 years under spinal anesthesia. The patients were randomly divided into two equal groups. Patients in Group (M) ($n = 25$) received single intravenous bolus dose of Meperidine 0.5 mg/kg while patients in group (Mg) ($n = 25$) received intravenous (IV) $MgSO_4$ in a dose of 50 mg/kg over 20 min followed by 0.5 mg/kg/min both. The both test drugs were administered after establishment of spinal anesthesia. The incidence and severity of shivering were recorded during the operation and in the recovery room.

Results: Shivering occurred in 68% of patients in group (M) when compared to group (Mg) where only 28% suffered from shivering. This difference in % was found to be statistically significant. Regarding the complications, local allergy significantly occurred in group (M) in five patients when compare to one patient in group (Mg). There was no significant difference between group (M) and group (Mg) regarding the body core temperature.

Conclusion: $MgSO_4$ was found to be an effective way for the control shivering and it could replace Meperidine in middle age patients under spinal anesthesia.

1. Introduction

Shivering is an oscillatory involuntary muscular activity [1] that may occur during knee arthroscopy, which is an unpleasant sensation for all patients [2], surgeons, and anesthetist. It interferes with the proper visualization of the field which resulting in ligament or vascular injury and results in inappropriate ECG and pulse oximeter monitoring as well [3].

The main value of shivering is to increase metabolic heat production [4]. Also it increases the oxygen consumption from

* Corresponding author. Tel.: +20 1111111847.
E-mail address: jijsonbaty@yahoo.com (M. Elsonbaty).

Peer review under responsibility of Egyptian Society of Anesthesiologists.

Production and hosting by Elsevier

1110-1849 © 2013 Egyptian Society of Anesthesiologists. Production and hosting by Elsevier B.V. Open access under CC BY-NC-ND license.
http://dx.doi.org/10.1016/j.egja.2013.03.002

500% [5,6] up to 600% of the basal level [7], lactic acid, and CO_2 production with consequence increase in the cardiac output and minute ventilation [8].

Shivering during knee arthroscopy occurs due to hypothermia which may be either due to irrigation of fluid at room temperature, or due to the effect of spinal or epidural anesthesia [9] which are the common anesthetic techniques of choice in knee arthroscopy. Regional anesthesia results in sympathetic and somatic neural blockade on both vasomotor tone and shivering below the level of the blockade [10].

Magnesium sulfate is found to be effective in management of post-operative shivering after general anesthesia [11]. In the present study, we compared the antishivering action between Meperidine and Magnesium sulfate in middle age patients under spinal anesthesia.

2. Materials and methods

This study was performed between January 2010 and June 2010 after approval of ethical committee of anesthesia department (Faculty of Medicine Cairo University). The selected patients were scheduled for unilateral knee arthroscopy under spinal anesthesia. Patients included in the study were ASA I and II aged between 20 and 50 years, with no history of allergy to Meperidine or Magnesium sulfate. Exclusion criteria included patients with history of allergy, obese with body mass index (BMI) □30 generalized infection or localized infection at level of blockade, neurologic disease, coagulation disorder, and patients refusing regional anesthesia.

This double-blinded randomized study included 50 patients who were equally divided into two equal groups: Meperidine group (M) and Magnesium sulfate group (Mg).

All routine investigations were done including complete blood picture, coagulation profile, liver function tests, kidney function tests, blood grouping, and ECG, and written informed consents were obtained.

Demographic data including age, weight, height, (BMI) and ASA, also intra-operative data include (level of sensory blockade, total irrigation fluid, and total surgical time) were recorded.

Preoperative hemodynamic data were recorded namely mean blood pressure (MBP), heart rate (HR), arterial oxygen saturation (SPO_2), skin temperature (Ts), and tympanic temperature (Tc).

No premedication was given to both groups. Peripheral intravenous line was inserted and (15 mL/kg) Ringer's lactate solution warmed up to 37 °C was given to all patients prior to performance of spinal anesthesia, and all subsequent intravenous fluids and irrigation fluids given during the procedure were also warmed.

Oxygen was administered via face mask (5 L/min). All through the procedure and during the recovery time, the operating room temperature was maintained between 22 °C and 25 °C.

Midline Spinal anesthesia approach was performed to all patients in the sitting position at the L3–L4 or L4–L5 interspaces using 25-gauge Quincke needle using 2.5 mL hyperbaric bupivacaine, 5 mg/mL.

After confirming the establishment of the spinal anesthesia level by pinprick, the patients were secured in the supine position and wrapping the other limb in cotton towels and the same standard tourniquet for knee was applied.

In group M [1], patients received single bolus dose of Meperidine 0.5 mg/kg diluted in 10 mL syringe intravenously after establishment of spinal anesthesia.

In group Mg [2], patients received intravenous (IV) infusion of $MgSO_4$ 50 mg/kg over 20 min followed by 0.5 mg/kg/min infusion after establishment of spinal anesthesia.

The (MBP), (HR), (SPO_2), (Ts), and (Tc) were measured and recorded intermittently intra-operatively and in the recovery room (every 15 min).

The incidence and severity of shivering were recorded during the operation and in the recovery room. Shivering was graded with a scale described by (Bedside Shivering Assessment Score) (BSAS) as follows [12]:

1. *None*: no shivering noted on palpation of the masseter, neck, or chest wall.
2. *Mild*: shivering localized to the neck and/or thorax only.
3. *Moderate*: shivering involves gross movement of the upper extremities (in addition to neck and thorax).
4. *Severe*: shivering involves gross movements of the trunk and upper and lower extremities.

Also any complications were recorded:

Hypotension was defined as a decrease in the (MBP) to less 20% less than the baseline value, which was treated with 5–10 mg of intravenous ephedrine.

Bradycardia was defined as a decrease in HR less than 50 b/min which was treated with 0.5 mg IV atropine.

2.1. Statistical analysis

The collected data were analyzed by Statistical Package for Social Science (SPSS) version 16. Parametric data were expressed as mean ± SD. The comparison the mean ± SD of two groups was done using the paired and unpaired student's *t* test. Nonparametric data was expressed as number and percentage of the total number of patients. Determining the extent of a single observed series of proportions, difference from a theoretical or expected distribution was done using the Chi square test and repeated-measures analysis of variance followed by Bonferroni's post hoc testing. *P*-value < 0.05 was considered statistically significant.

2.2. Outcome measures

The primary outcome measure was the dose of Magnesium sulfate that prevented the shivering and at the same time did not produce hypotension. The second outcome was the use of Magnesium sulfate in avoiding complications secondary to the use of Meperidine.

3. Results

All the demographic data including age, sex, weight, height, body mass index and ASA status (Table 1), operative data surgical time, and total irrigation fluid (Table 2) were comparable between both groups.

As regards the level of sensory blockade in both groups, minimal level was T10 and maximal level was T4 with no significant difference between the two groups.

Table 1 Demographic data.

	Variable each group (n = 25)	Mean ± std. deviation	P value
Age	Group (M) Group (Mg)	38.36 ± 8.36 39.64 ± 8.78	0.60
Sex (M/F)	Group (M) Group (Mg)	10/15 12/13	0.39
ASA (/ll)	Group (M) Group (Mg)	11/14 15/10	
Weight (kg)	Group (M) Group (Mg)	73.36 ± 10.19 78.6 ± 10.31	0.77
Height (cm)	Group (M) Group (Mg)	175.36 ± 13.56 180.64 ± 8.42556	0.105
BMI	Group (M) Group (Mg)	24.18 ± 4.38 24.27 ± 4.10	0.935

Data were express as mean (±SD), P value < 0.05 is considered significant. Group (M) = Meperidine group. Group (Mg) = Magnesium sulfate group, BMI = body mass index.

Table 2 Operative data.

	Group (M) n = 25	Group (Mg) n = 25	P value
Anesthesia time (min)	84.2(13.81)	86.52(15.894)	0.57
Surgical time (min)	68.08(12.524)	71.4(14.108)	0.38
Total irrigation fluid (L)	2.7(0.9165)	3.18(1.008)	0.09

Data are expressed as mean (±SD), P value < 0.05 is considered significant. Group (M) = Meperidine group. Group (Mg) = Magnesium sulfate group.

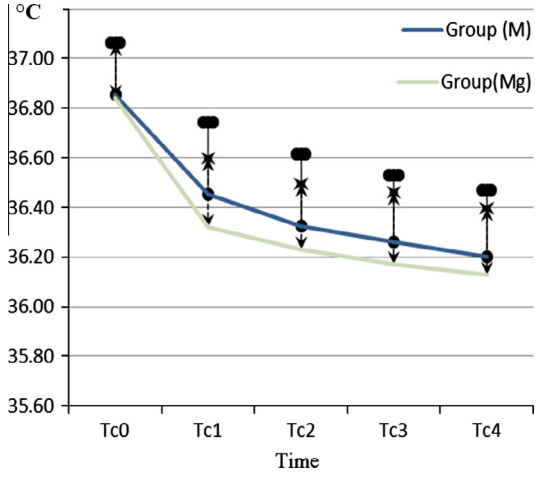

Figure 1 Core temperature change over time in both groups, Tc0 = basal core temperature, Tc1 = core temperature 1, Tc2 = core temperature 2, Tc3 = core temperature 3, Tc4 = core temperature 4 (interval 15 min).

Both group showed a decrease in body core temperature with an insignificant lower values in group (Mg) when compared to group (M) in Fig. 1.

Shivering was observed in seven patients (28%) in Magnesium sulfate group and 17 patients (68%) in Meperidine group with a statistically difference (p < 0.05) as was Table 3.

Table 3 Shivering score among groups.

Shivering score	Group (M) n = 25	Group (Mg) n = 25
0	8(32.0%)	18(72.0%)
1	7(28.0%)	5(20.0%)
2	7(28.0%)	1(4.0%)
3	3(12.0%)	1(4.0%)

Concerning the associated local allergy, it was observed in five patients in group (M) and only in one patient in group (Mg). This difference was found to be statistically significant (Table 4).

On the other hand, no statistically significant difference was observed between both groups with respect to the incidence of other complications.

4. Discussion

Shivering under regional anesthesia occurs in about 56.7% [13], mainly due to impairment of afferent thermal input [10] as a thermoregulatory response to hypothermia.

Subsequent complications included hypoxia, cardiac complications as tachycardia, increased intracranial, and intraocular pressure. Therefore, treatment of shivering is crucial. Many physical methods used to control shivering include increased ambient room temperature, radiant heaters, warm IV fluid and wrapping the nonsurgical area in cotton towels [14], but all these methods proved not to be enough to prevent shiver-

Table 4 Incidence of adverse side effect.

	Group (M) $n = 25$	Group (Mg) $n = 25$	P value
Itching	2	0	0.149
Hypotension	2	1	0.557
Local allergy	5	1	0.018*
Generalized allergy	0	0	

P value < 0.05 is considered significance.
* Significant difference.

ing. Many pharmacological methods have been tested in reducing perioperative hypothermia [13] and suppressing post-anesthetic shivering; however, none of these have received universal acceptance.

Meperidine (a phenylpiperidine compound) has been discussed to be an effective opioid agent for management of shivering and is considered the master drug used for management of perioperative shivering. The antishivering action of Meperidine is unclear. It is found to decline the threshold of shivering through multimodal mechanisms, κ-opioid receptors, α_{2B}-adrenoreceptor agonist, and NMDA receptor antagonism [15–17].

Kurz et al. compared the antishivering characteristic of Meperidine with low dose naloxone blocking μ receptor and high dose naloxone blocking both μ and κ receptor; they found that the Meperidine with low dose naloxone was not affected, but the antishivering activity was decreased when high dose was used which indicates that the antishivering effect of Meperidine is partially mediated through κ-opioid receptors [18] and not through the μ-receptor that why it is more effective than other opioid agents as alfentanil as antishivering agent [19]. However, Sajedi and Nazemroaya [20] found that there were no differences in efficacy to control post-operative shivering among Meperidine, alfentanil, sufentanil, fentanyl, and tramadol in management of shivering grade and V, and they concluded that this group of drugs may have other antishivering mechanism rather than their opioid receptors action.

In the present study, it was observed that five patients in the Meperidine group suffered from local redness. This was consistent with the study done by Blunk et al. [21]. They observe that in the spite of using small dose of Meperidine, local itching and redness around the site of injection and rarely flushing, severe hypotension, and tachycardia as a result of mast cell activation and histamine release may attenuate its use as an antishivering agent. They requested the need to find another agent with less side effects especially during regional anesthesia [21]. Concerning the antishivering effect, we observe that although Meperidine is effective in management of perioperative shivering, Magnesium sulfate was founded to be significantly more effective.

Magnesium sulfate is a noncompetitive antagonist of *N*-methyl-D-aspartate (NMDA) receptors, and also, it is naturally occurring calcium antagonist [22]. It was found to be effective in prevention of shivering [11]. The exact mechanism by which it prevents shivering is not clear. It may be due to blocking of NMDA receptors leading to a decrease in norepinephrine, and 5-HT and both have role in thermoregulatory control. Magnesium sulfate is an attractive choice for shivering control because hypomagnesemia commonly is observed during induced hypothermia [23].

Another action of $MgSO_4$ is modulation of NMDA receptors at the level of dorsal horn of the spinal cord which affects the ascending nociceptive transmission [24].

Although Kizilirmak et al. used 30 mg/kg IV bolus of Magnesium sulfate which is considered smaller than that we used, they found it enough to stop post-operative shivering after general anesthesia. This may be due to its use in the post-operative period when there is no more hypothermia [11]. Gozdemir et al. [25] studied the effect of Magnesium sulfate on Perioperative shivering during spinal anesthesia, and they found that Magnesium sulfate is considered an excellent agent with less side effect than Meperidine. In our study, we used smaller dose of Magnesium sulfate than that used in Gozdemir et al. study and it was found to be effective.

Using of this, dose of Magnesium sulfate was not associated with any hemodynamic unstability as higher dose would cause vasodilatation and subsequent hypotension.

5. Conclusion

It was found that Magnesium sulfate is significantly effective than Meperidine in management of shivering during spinal anesthesia with lower incidence of side effect.

References

[1] Bhattacharya P, Bhattacharya L, Jain R, Agarwal R. Post anaesthesia shivering. Indian J Anaesth 2003;47(2):88–93.
[2] Kurz A, Sessler DI, Narzt E, et al. Perioperative hemodynamic and thermoregulatory consequences of intraoperative core hypothermia. J Clin Anesth 1995;7:359–66.
[3] Barker SJ, Shah NK. Effects of motion on the performance of pulse oximeters in volunteers. Anesthesiology 1996;85:774–81.
[4] Witte JD, Sessler DI. Perioperative shivering physiology and pharmacology. Anesthesiology 2002;96:467–84.
[5] Hemingway A. Shivering. Physiol Rev 1963;43:397–402.
[6] Yi JW, Lee BJ, Han JH. Effects of intrathecal meperidine on prevention of shivering during spinal anesthesia for herniorrhaphy. Korean J Anesthesiol 2005;49:484–9.
[7] Giesbrecht GG, Sessler DI, Mekjavic IB, Schroeder M, Bristow GW. Treatment of immersion hypothermia by direct body-to-body contact. J Appl Physiol 1994;76:2373–9.
[8] 8- Talakoub R, Noori Meshkati. Sh tramadol versus meperidine in the treatment of shivering during spinal anesthesia in cesarean section. JRMS 2006;11(3):151–5.
[9] Ozaki M, Kurz A, Sessler DI, et al. Thermoregulatory thresholds during spinal and epidural anesthesia. Anesthesiology 1994;81:282–8.
[10] Kurz A, Sessler DI, Schroeder M, Kurz M. Thermoregulatory response thresholds during spinal anesthesia. Anesth Analg 1993;77:721–6.

[11] Kizilirmak S, Karakas SE, Akca O, et al. Magnesium sulfate stops postanesthetic shivering. Ann NY Acad Sci 1997;813:799–806.
[12] Badjatia N, Strongilis E, Gordon E, et al. Metabolic impact of shivering during therapeutic temperature modulation, the bedside shivering assessment scale. Stroke 2008;39:3242–7.
[13] Jeon YT, Jeon YS, Kim YC, Bahk JH, Do SH, Lim YJ. Intrathecal clonidine does not reduce post-spinal shivering. Acta Anaesthesiol Scand 2005;49:1509–13.
[14] Sessler DI, Schroeder M. Heat loss in humans covered with cotton hospital blankets. Anesth Analg 1993;77:73–7.
[15] Kurz A, Ikeda T, Sessler DI, Larson M, Bjorksten AR, Dechert M, Christensen R. Meperidine decreases the shivering threshold twice as much as the vasoconstriction threshold. Anesthesiology 1997;86:1046–54.
[16] Takada K, Clark DJ, Davies MF, et al. Meperidine exerts agonist activity at the alpha2B adrenoceptor subtype. Anesthesiology 2002;96:1420–6.
[17] Ebert B, Andersen S, Krogsgaard-Larsen P. Ketobemidone, methadone and pethidine are non-competitive *N*-methyl-D-aspartate (NMDA) antagonists in the rat cortex and spinal cord. Neurosci Lett 1995;187:165–8.
[18] Kurz M, Belani K, Sessler DI, Kurz A, Larson M, Blanchard D, Schroeder M. Naloxone, meperidine, and shivering. Anesthesiology 1993;79:1193–201.
[19] Wrench IJ, Cavill G, Ward JEH, Crossly AWA. Comparison between alfentanil, pethidine and placebo in the treatment of post-anaesthetic shivering. Br J Anaesth 1997;79(4):541.
[20] Sajedi, Nazemroaya. Comparing the effectiveness of antishivering action of meperidine alfentanil, sufentanil, fentanyl and tramadol after general anesthesia. Shiraz E Med J 2006; 7(3):9–12.
[21] Blunk JA, Schmelz M, Zeck S, et al. Opioid-induced mast cell activation and vascular responses is not mediated by μ-opioid receptors: an in vivo microdialysis study in human skin. Anesth Analg 2004;98:364–70.
[22] Schulz-Stubner S, Wettmann G, Reyle-Hahn SM, Rossaint R. Magnesium as part of balanced general anaesthesia with propofol, remifentenil and mivacurium: a double-blind prospective study in 50 patients. Eur J Anaesthesiol 2001;18:723–9.
[23] Polderman KH, Peerdeman SM, Girbes ARJ. Hypophosphatemia and hypomagnesemia induced by cooling in patients with severe head injury. J Neurosurg 2001;94:697–705.
[24] Dickenson AH. Spinal cord pharmacology of pain. Br J Anaesth 1995;75:193–200.
[25] Gozdemir M, Usta B, Demircioglu RI, Muslu B, Sert H, Karatas OF. Magnesium sulfate infusion prevents shivering during transurethral prostatectomy with spinal anesthesia: a randomized, double-blinded, controlled study. J Clin Anesth 2010;22:184–9.