

Magnesium Sulfate Stops Postanesthetic Shivering^a

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INTRODUCTION

Shivering is common during recovery from general anesthesia. All general anesthetics produce a dose-dependent decrease in the core temperature, thereby reducing the threshold for thermoregulatory vasoconstriction.¹ Postanesthetic shivering causes complications, including increased oxygen consumption and elevation of intraocular and intracranial pressures.² During recovery, brain anesthetic concentrations decrease rapidly, leaving the patients hypothermic but no longer anesthetized.³ This triggers vasoconstriction and shivering.

The classical pharmacological approach to the treatment of postanesthetic shivering is administration of meperidine.⁴ It is far more effective than equianalgesic doses of other opioids. It was previously reported that clonidine, an alpha-2 adrenergic receptor agonist, and ketanserin, a 5-hydroxytryptamine receptor antagonist, are effective treatment for postanesthetic shivering.^{5,7} Magnesium sulphate has been effectively used for treating patients with severe tetanus; recently, we also used the drug as a treatment for postanesthetic shivering.

METHODS

With approval of the University of Istanbul Ethics Committee and informed consent from the subjects, we evaluated seventy-five, ASA physical status I or

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TABLE 1. Sedation and Shivering Scales

| | |
|-----------------|---|
| Sedation scale | |
| Grade 0 | cooperative, oriented |
| Grade 1 | responds to commands only |
| Grade 2 | asleep with brisk response to loud noise |
| Grade 3 | asleep with sluggish response to loud noise |
| Grade 4 | asleep, no response |
| Shivering scale | |
| Grade 0 | no sign of shivering |
| Grade 1 | vasoconstriction, cyanosis and piloerection |
| Grade 2 | visible tremor only in one muscle group |
| Grade 3 | visible tremor in more than one muscle group |
| Grade 4 | intense shivering, tremor of the head and arms and piloerection |

II adult patients shivering during postoperative recovery. All patients received general anesthesia, and only patients with intense shivering were included. Patients were prospectively and randomly assigned to one of three groups ($n = 25$ each): 1) meperidine (0.5 mg/kg, iv bolus); 2) magnesium sulphate (30 mg/kg, iv bolus); and, 3) isotonic saline. Postoperatively, they were transferred to the recovery room and covered with a single wool blanket. Shivering was evaluated visually by a blinded observer on a four-point scale, with zero indicating no shivering and four indicating intense, continuous shivering (TABLE 1).

Monitoring

Oxygen saturation, arterial blood pressure, heart rate (PROPAQ 106 EL, Protocol-Oregon[®]), respiratory rate, and distal esophageal (core) temperature (Protocol-Oregon[®]) were recorded at admission and in the 5th, 10th, 20th, and 30th minutes of bolus injection. Venous serum magnesium levels were measured before and 20 minutes after magnesium sulphate injection.

Data Analysis

The data were analyzed using repeated measures of ANOVA and Sheffé's F tests. Data are presented as means and SD; a $p < 0.05$ was considered statistically significant.

RESULTS

The morphometric characteristics of patients and operation conditions did not differ in the three groups (TABLE 2). Before the bolus injection, baseline blood magnesium levels were comparable in the three groups. Injection of magnesium sulphate increased the plasma concentrations significantly, but the levels remained within the normal range.

Patients given meperidine and magnesium sulphate had significantly shorter duration of shivering than those given saline ($p < 0.01$). Meperidine acted faster

TABLE 2. The Characteristics of the Patients and Anesthetic Agents Used in the Three Groups^a

| | Isotonic Saline (n = 25) | Pethidine (n = 25) | MgSO ₄ (n = 25) |
|------------------------------------|-----------------------------|-----------------------|-------------------------------|
| Age (yr) | 31 ± 14 | 33 ± 13 | 27 ± 10 |
| Weight (kg) | 65 ± 10 | 68 ± 14 | 66 ± 13 |
| Female/male | 13/12 | 13/12 | 15/10 |
| Operation time (min) | 100 ± 41 | 114 ± 67 | 100 ± 50 |
| Operation room temperature (°C) | 21 ± 1 | 21 ± 1 | 21 ± 1 |
| Recovery room temperature (°C) | 25 ± 1 | 25 ± 1 | 25 ± 1 |
| N ₂ O | 21 | 21 | 20 |
| Enflurane | 10 | 10 | 12 |
| Isoflurane | 6 | 10 | 10 |
| Halothane | 3 | 6 | 7 |
| Propofol | 2 | 4 | 2 |

^a Data are presented as means ± SD.

than magnesium sulphate, but both were effective 10 minutes after the bolus injection. Shivering scores at ten minutes were 1.4 ± 1.1 for magnesium sulphate and 0.29 ± 0.8 for meperidine. Twenty minutes after injections, shivering was observed in 4% of the patients given magnesium, 4% of those given meperidine, and 76% of those given saline. Shivering intensity as a function of time differed significantly among saline and other therapeutics (FIG. 1).

Esophageal temperatures before the bolus injections were similar in all three groups: $35.5 \pm 0.5^\circ\text{C}$ in saline, $35.6 \pm 0.5^\circ\text{C}$ in magnesium sulphate, and $35.6 \pm 0.4^\circ\text{C}$ in the meperidine group. Rewarming was slower in the meperidine and magnesium groups than in the patients given saline ($p < 0.05$, FIG. 2). Core temperatures increased significantly in all patients in the first 20 postoperative minutes (TABLE 3, $p < 0.05$).

DISCUSSION

Intraoperative hypothermia is associated with numerous complications including myocardial ischemia,¹² ventricular arrhythmias,¹³ increased bleeding and transfusion requirement,¹⁴ impaired resistance to surgical wound infections,¹⁵ and decreased drug metabolism.¹⁶⁻¹⁸ Intraoperative hypothermia also causes postoperative shivering.¹⁹⁻²¹ Shivering increases metabolic rate,²² an increase that has been claimed to cause respiratory embarrassment and myocardial ischemia.²³ However, shivering usually increases metabolic rate only slightly in the patients at greatest risk for ischemia,¹⁹ and postoperative myocardial ischemia is not correlated with the incidence of shivering.¹² It thus seems likely that postoperative myocardial ischemia is not related directly to shivering. Nonetheless, shivering increases plasma norepinephrine concentrations threefold,²⁴ and patients find shivering uncomfortable, frequently remembering it as being among the worst aspects of hospitalization. For this reason alone, prompt treatment of postoperative shivering is appropriate.

Our major result is that administration of a modest intravenous bolus of magnesium sulphate essentially obliterated postoperative shivering. Although intravenous meperidine administration stopped shivering slightly faster than magnesium, both drugs were rapidly effective. Under the circumstances of this study, there certainly was no clinically important difference between the efficacy and onset of the two drugs. In contrast, most saline-treated patients continued to shiver. These results confirm and extend the findings of Miyakawa *et al.*²⁵ and Beliaev *et al.*,²⁶ who also found that magnesium sulphate rapidly stopped shivering.

The patients in this study had initial postoperative core temperatures near 35.5°C. However, 35.5°C is not much less than the normal shivering threshold.²⁷ It thus remains likely that magnesium sulphate will prove less effective in patients having lower core temperatures. Alternatively, administration of larger doses may be required in such patients. A limitation of our study is thus that we failed to evaluate different doses of magnesium sulphate and that our patients were only slightly hypothermic. Our results, nonetheless, suggest that magnesium sulfate is an effective treatment in typical postoperative patients.

The mechanism by which magnesium sulphate arrests shivering remains unclear. It seems unlikely that the effect was entirely peripheral. Although we did not formally assess muscular strength, treated patients were not obviously weak and certainly displayed no difficulty breathing or moving. However, the alternative hypothesis, that magnesium sulphate reduced the central threshold for shivering is also unsatisfactory, because plasma concentrations of the drug increased only

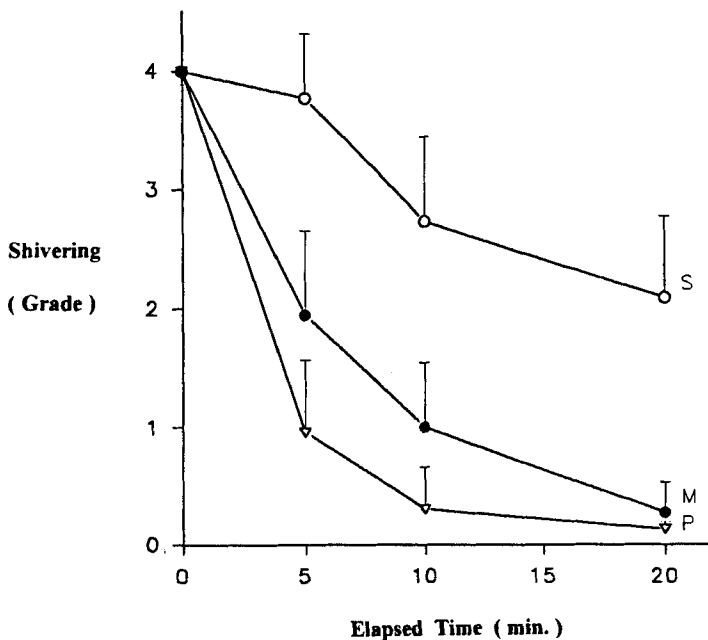


FIGURE 1. Shivering intensity as a function of time. S, saline; M, magnesium sulfate; P, meperidine.

Change in Temperature

(C)

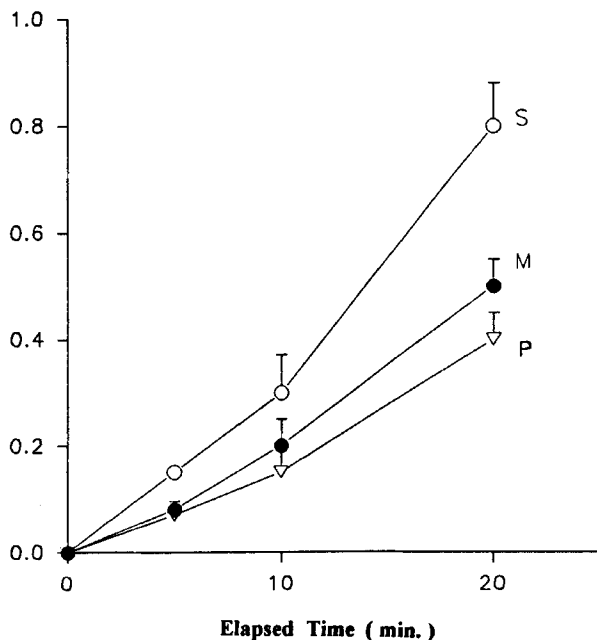


FIGURE 2. Change in temperature as a function of time in the saline (S), magnesium sulfate (M), and meperidine (P) groups.

slightly and remained within the normal range. Most likely, concentrations did increase sufficiently to have a central effect, but had returned towards normal values at 20 elapsed minutes when blood was sampled.

Our data and previous results indicate that magnesium sulphate joins a variety of other drugs that have been proved effective treatments for postoperative shivering. Meperidine is certainly the prototypical treatment for shivering.⁹ However, clonidine,^{28,29} ketanserin,²⁹ and methylphenidate³⁰ are also effective. Meperidine decreases the shivering threshold centrally,³¹ apparently *via* its activity at the kappa opioid receptor.³² Clonidine also decreases the shivering threshold,³³ presumably by its action on central alpha receptors. In contrast, the mechanism by which methylphenidate and magnesium sulphate stop shivering remains unknown.

The purpose of shivering, of course, is to increase metabolic production of heat, thereby speeding rewarming. It is thus not surprising that treated patients warmed at a slower rate than those given saline placebo. Prolonged hypothermia was similarly observed in previous investigations of antishivering drugs.^{28,29} From a clinical point of view, however, shivering should be treated even if treatment slows rewarming, because shivering *per se* is uncomfortable and potentially harmful. Body heat content can be increased more effectively by active cutaneous warming in patients whose hypothermia is a concern.³⁴

TABLE 3. The Effect of Meperidine and Magnesium Sulfate on Postanesthetic Shivering, Sedation Level, Respiratory Rate, Heart Rate, Systolic (SAP) and Diastolic Arterial Pressures (DAP) Compared to Saline-Treated Group

| Time | Isotonic Saline | | Meperidine | | Magnesium Sulfate | |
|--------------------------------|-----------------|-------------|------------|--------------|-------------------|--------------|
| | 0 | 20 min | 0 | 20 min | 0 | 20 min |
| Shivering score (Grade 0-4) | 4 | 2.1 ± 1.4 | 4 | 0.13 ± 0.6** | 4 | 0.26 ± 0.5** |
| Sedation score (Grade 0-4) | 1.6 ± 0.5 | 0.86 ± 0.35 | 1.4 ± 0.4 | 2.2 ± 0.48** | 1.69 ± 0.68 | 0.9 ± 0.45 |
| Respiratory rate/min | 19 ± 6 | 18 ± 5 | 20 ± 4 | 15 ± 2** | 20 ± 7 | 19 ± 3 |
| Heart rate/min | 80 ± 14 | 99 ± 4 | 88 ± 17 | 79 ± 11 | 88 ± 11 | 79 ± 8 |
| SAP (mm-Hg) | 125 ± 14 | 130 ± 18 | 131 ± 18 | 129 ± 19 | 123 ± 21 | 127 ± 23 |
| DAP (mm-Hg) | 78 ± 8 | 83 ± 10 | 77 ± 10 | 80 ± 9 | 75 ± 11 | 78 ± 9 |
| Body temperature (°C) | 35.5 ± 0.5 | 36.5 ± 0.3 | 35.6 ± 0.5 | 36.4 ± 0.5* | 35.6 ± 0.4 | 36.3 ± 0.4* |
| Blood Mg (mmol/l) | 0.78 ± 0.1 | 0.78 ± 0.2 | 0.76 ± 0.1 | 0.76 ± 0.1 | 0.74 ± 0.1 | 1.05 ± 0.1* |

* $p < 0.05$; ** $p < 0.01$.

In summary; magnesium sulphate has a logical place in the treatment of post-anesthetic shivering. Although its onset time is slightly longer than that of meperidine, it was ultimately as effective in stopping the tremor.

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