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Postanaesthetic Shivering

Epidemiology, Pathophysiology, and Approaches to Prevention and Management

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Contents

Abstract

Along with nausea and vomiting, postanaesthetic shivering is one of the leading causes of discomfort for patients recovering from general anaesthesia. The distinguishing factor during electromyogram recordings between patients with postanaesthetic shivering and shivering in fully awake patients is the existence of clonus similar to that recorded in patients with spinal cord transection. Clonus coexists with the classic waxing and waning signals associated with cutaneous vasoconstriction (thermoregulatory shivering). The primary cause of postanaesthetic shivering is peroperative hypothermia, which sets in because of anaesthetic-induced inhibition of thermoregulation. However, shivering associated with cutaneous vasodilatation (non-thermoregulatory shivering) also occurs, one of the origins of which is postoperative pain.

Apart from causing discomfort and aggravation of pain, postanaesthetic shivering increases metabolic demand proportionally to the solicited muscle mass and the cardiac capacity of the patient. No link has been demonstrated between the occurence of shivering and an increase in cardiac morbidity, but it is preferable to avoid postanaesthetic shivering because it is oxygen draining.

Prevention mainly entails preventing peroperative hypothermia by actively rewarming the patient. Postoperative skin surface rewarming is a rapid way of obtaining the threshold shivering temperature while raising the skin temperature

and improving the comfort of the patient. However, it is less efficient than certain drugs such as meperidine, clonidine or tramadol, which act by reducing the shivering threshold temperature.

Postanaesthetic shivering is an involuntary movement that may affect one or several muscle groups, and which generally occurs in the early recovery phase after general anaesthesia.

Recent studies have made it possible to identify some of the causes of postanaesthetic shivering. With the findings of these studies, we have proposed a physiopathological explanation for their occurrence at recovery from a general anaesthesia. Among the different consequences of postanaesthetic shivering, the principal one is an increase in oxygen uptake. However, the relationship between this increase and the occurrence of undesirable effects on vital functions remains a controversial subject. This is probably as a consequence of the difficulties in establishing a link between variations of oxygen uptake and undesirable events, and also disassociating the proper effects of postanaesthetic shivering from those of coexistent hypothermia.

A systematic search of an electronic database (Medline), using the keywords 'postanaesthetic shivering' or 'postoperative shivering or shaking' revealed a large number of trials on the prevention or the treatment of postanaesthetic shivering. Retaining only the randomised studies versus placebo, many drugs were identified as acting on postanaesthetic shivering. They can be classified into three categories: those that have an experimentally and clinically demonstrated effect on thermoregulation; those for which there are a lot of elements, making it possible to suppose that they also act by this way; and a third category made up of various treatments that belong to different classes and whose mechanisms of action on the postanaesthetic shivering remain unknown. In order to try to clarify and to classify the various treatments on a basis of their respective potencies, we calculated the number needed to treat (NNT) for each one of them.

1. Epidemiology

According to studies, the incidence of postanaesthetic shivering ranges between 6.3 and 66%.[1-12] Some authors[3,5,13,14] consider males more prone to postanaesthetic shivering, whereas others make no distinction between genders.[6,7] However, being a young adult seems to be a determinant factor.[1,3,6,14] Other risk factors identified are the length of the anaesthesia or surgery (the longer the more likely),[1,3,14] and if no active perioperative rewarming procedure is used.[15,16] However, while some authors[4,8,12,17-19] did not find a relationship between a drop in body temperature and the incidence of postanaesthetic shivering, others found the link exists.[5-7,10,14] In fact, mild perioperative hypothermia does not necessarily occur before the appearance of postanaesthetic shivering but it encourages it, and the more serious the hypothermia, the higher the probability of postanaesthetic shivering.[2]

Lastly, the incidence of postanaesthetic shivering differs depending on the anaesthetic used. The use of a halogenated agent[3,6,7] or pentothal,[8,18] or the administration only peroperatively of small quantities of opiates[3] encourage the appearance of shivering. In contrast, the incidence of shivering is less common with the use of propofol.[12,18,20]

2. Pathophysiology

2.1 Origins of Postanaesthetic Shivering

Several hypotheses have been raised to explain the occurrence of postanaesthetic shivering. These include perioperative hypothermia,[4,5,10,15,16] postoperative pain,[7] perioperative heat loss,[1,6,7] the direct effect of certain anaesthetics, hypercapnia or respiratory alkalosis, the existence of pyrogens, hypoxia, early recovery of spinal reflex activity and sympathetic overactivity.

For slightly more than 10 years, different studies have provided clearer insight into the origins of

postanaesthetic shivering. First of all, the recording of postanaesthetic shivering electromyographic (EMG) patterns enables the identification of three types of EMG signals:[21-23] tonic EMG activity, spontaneous EMG clonus similar to pathological clonus observed in patients with spinal cord transection, and waxing and waning signals identical to those obtained during cold-induced shivering in non-anaesthetised patients. Furthermore, waxing and waning in unstimulated volunteers is always preceded by cutaneous vasoconstriction confirming their central thermoregulatory origin. One hypothesis used to explain the clonic movements is that they correspond to spinal reflex hyperactivity, which results from the inhibition of descending cortical control by residual concentrations of anaesthetics.[22] These EMG signals are compatible with the clinical descriptions of abnormal reflexes observed during the early recovery phase.[4]

Recently, Horn et al.[24] observed 120 patients who were divided into two groups according to the intraoperative temperature management. Forty patients became hypothermic while the others (n = 80) were actively rewarmed in order to obtain a postoperative core temperature higher than the measured preoperative temperature. The authors noticed that the frequency of shivering was approximately 50% (20 patients) in the control group compared with 22% (20 patients) in the rewarmed group. In the latter group, 55% of patients (11 patients) displayed shivering associated with vasodilatation. This means that 15% of actively rewarmed patients (11 out of 80) present shivering which does not correspond to a thermoregulatory response.

Therefore, we can say that there are two types of postanaesthetic shivering. The first corresponds to thermoregulatory shivering that is associated with cutaneous vasoconstriction and which is the physiological response to the hypothermia developed during the perioperative period. The second corresponds to shivering associated with cutaneous vasodilatation or non-thermoregulatory shivering. The mechanisms responsible for non-thermoregulatory shivering are not fully known. However, the existence of a link between postoperative pain and the incidence of postanaesthetic shivering[7] has been confirmed by a study comparing the frequency of postanaesthetic shivering after knee arthroscopy in patients who received and those who did not receive intra-articular lidocaine at the end of the operation.[25] The existence of greater pain in patients who did not receive local anaesthesia was accompanied by a higher incidence of postanaesthetic shivering.

Of all the different hypothesis raised to explain the incidence of postanaesthetic shivering, only perioperative hypothermia and pain have been clearly verified. Furthermore, it is indeed a drop in core temperature that facilitates the emergence of shivering and not a reduction in the heat content of the patient. In fact, the initial decrease in central temperature during the inhibition of thermoregulation by anaesthetics is first of all due to an internal redistribution of the heat content, which is carried out with a quasi zero heat balance.[26] As hypothermia and pain are known to initiate sympathetic overactivity,[27,28] it is difficult to specifically evaluate the influence of sympathetic overactivity on postanaesthetic shivering.

On the basis of several factors, we can assume that there is a relationship between a possible early recovery of spinal reflex activity facilitated by the residual effect of anaesthetics on the inhibiting control exercised by supraspinal structures and the incidence of postanaesthetic shivering. This link provides an explanation for the existence of EMG-recorded clonus. Furthermore, there is a lower frequency of postanaesthetic shivering with propofol compared to other anaesthetics such as pentothal[18] or halogenated agents,[20] which cannot be explained by the differences of effect on thermoregulation.[26] However, it is plausible that the effect of low concentrations of propofol is less significant on certain central structures such as the reticular formation compared to these other drugs, thus enabling a faster 'recovery' of the descending inhibiter control.

Among the other hypotheses raised to define the causes of postanaesthetic shivering, some of them such as hypercapnia or hypoxia are unlikely to be involved since they reduce the thresholds for the appearance of shivering in volunteers.[29,30] The same applies to respiratory alkalosis since arterial blood samples taken during postanaesthetic shivering have a normal or slightly acid pH. Secondly, the residual effects of anaesthetic agents rather tend to possess respiratory depressant effects that facilitate hypercapnia in patients recovering from anaesthesia.

2.2 Consequences of Postanaesthetic Shivering

The first clinical consequence of postanaesthetic shivering is discomfort for the patient. Moreover, the patient has a stressful sensation of coldness that is systematically associated with postanaesthetic shivering.[7,8,23] Most patients mention shivering and the sensation of coldness as priorities when queried about the events that should be avoided after an operation.[31] Another consequence of postanaesthetic shivering on the comfort of the patient is the increased pain caused by muscular contractions on the operated site. Lastly, after ophthalmological surgery, postanaesthetic shivering increases intra-ocular pressure that can be pernicious.[32]

The main effect of postanaesthetic shivering is the increase in oxygen consumption (VO_2). By affecting several muscular groups for periods of 45 minutes or more, postanaesthetic shivering triggers an increase in metabolic demand, which generally translates into higher VO_2 combined with increased minute ventilation. Sometimes, but this is quite rare, metabolic demand can exceed the capacity to deliver oxygen peripherally and result in anaerobic metabolism. However, the impact of the VO_2 increase on perioperative cardiac morbidity is difficult to evaluate.

It is important to stress that mild perioperative hypothermia *per se*, increases postoperative cardiac morbidity.[33] With regard to VO_2 increase, the figures reported in the literature are very variable, ranging from 7 to >700%.[5,9,13,17,34-43] The heterogeneous samples, measuring methods and differences between clinical situations (table I) can explain such significant differences.

Firstly, the increase of VO_2 linked to shivering is proportional to the affected muscular mass. Therefore, the VO_2 values recorded during postanaesthetic shivering will be higher if the patients are young male adults.[34,37] Furthermore, taking heterogeneous samples in terms of age induces the risk of obtaining equally heterogeneous results.[41]

In the same way, clinical situations vary significantly from one study to another. In particular, several studies were carried out in shivering patients during recovery after cardiac surgery,[9,38-40,43] when alterations in the left ventricular function usually exist[44] which limit the adaptation of cardiac output to metabolic constraints and, therefore, the increase of VO_2. In addition, VO_2 measurements may be discontinuous and the VO_2 peak cannot be recorded.[9,13,17,37,39,41,42]

Another element that makes it difficult to compare the different studies is the choice of the reference value that allows calculation of the percentage of variation. It could be a theoretical value,[17,36,37] solely attributed to postanaesthetic shivering, i.e. the postoperative increase in VO_2, and without taking into account other factors such as non-shivering thermogenesis (even it is a marginal phenomenon in adults), stress or pain. In other studies, the patients are their own control,[9,34,38,41] and the reference is generally that measured at the end of the anaesthesia leading to an increase in the percentage of variation in so far as the anaesthesia reduces oxygen consumption.[34]

Lastly, some studies compare the VO_2 of patients presenting or not presenting with postanaesthetic shivering.[13,39,42] In these cases, VO_2 is approximately 40% higher in the patients with postanaesthetic shivering than in the control group. However, in these studies, the patients are >65 years of age, and only 25% of patients shivered in the routine thermal care group,[13] or the measurement was taken post-extracorporeal circulation,[39]

Table I. Studies evaluating oxygen consumption (VO_2) among shivering patients during the recovery period

References	Type of study	Sample size (n)	Comparative VO_2 value	Mean VO_2 increase	Comments
Bay et al.[17]	Descriptive Shivering (A) or non-shivering (B) patients	A = 11 B = 14	Theoretical value	A: 151% B: 4%	A: as 180% to 490% of basal value B: as 71% to 135% of basal value
MacIntyre et al.[37]	Descriptive	14	Theoretical value	380%	At rest after shivering, VO_2 is equal to 1.5 times of theoretical value
Just et al.[36]	Effect of IV naloxone on VO_2 in rewarmed (A) or not rewarmed (B) patients	A = 7 B = 7	Theoretical value	A = 25% B = 114%	
Guffin et al.[9]	Effect of IV meperidine or morphine on shivering and VO_2 during recovery	20	End of anaesthesia	105%	Post ECC
Roe[41]	Descriptive	24	End of anaesthesia	80%	Patients aged from 18 to 79y
Ciofolo et al.[34]	Descriptive	10	End of anaesthesia	230%	Compared with theoretical value, the mean increase is 80% and is up to 200% in 3 patients
Viale et al.[38]	Descriptive	11	End of anaesthesia	92%	Post ECC. The highest VO_2 value among shivering patients ranged from 19 to 53% of preoperative VO_{2max} value
Rodriguez et al.[42]	Comparative. Routine thermal care (A) *vs* patients receiving curare (B)	A = 8 B = 8	Maximal VO_2 value	40%	
Frank et al.[13]	Comparative. Routine thermal care (A) *vs* actively rewarmed (B) patients	A = 52 B = 59	Maximal VO_2 value	38%	In group A, 25% of patients shivered and 2% in group B
Zwischenberger et al.[39]	Comparative. Patients were allowed to shiver (A) or not (B) during recovery	A = 12 B = 12	Maximal VO_2 value	35%	Post ECC

ECC = extracorporeal circulation; **IV** = intravenous; **VO_{2max}** = maximum oxygen consumption.

or the shivering inhibition in the control group was probably not complete.[42]

It seems reasonable to assume that postanaesthetic shivering increases VO_2 by approximately 40 to 120%. Mild perioperative hypothermia doubles the incidence of morbid cardiac events among patients who either have coronary artery disease or are at high risk for coronary disease.[33] In contrast, Frank et al.[33,45] did not find any relationship between the incidence of myocardial ischaemia and postanaesthetic shivering, which is a specific consequence of hypothermia. However, many authors have observed significant decreases in vein oxygen saturation (SvO_2)[9,39,41,46] in patients with postanaesthetic shivering or a higher consumption of inotropic drugs.[39] This indicates, in certain situations, the inability of the ventricular function to cope with the increase in metabolic demand.[47]

3. Prevention and Management

Hypothermia is responsible for postanaesthetic shivering in most patients. The way in which it occurs in the peroperative phase is known and consistent with a combination of competitive inhibition of thermoregulatory responses by the anaesthetics, with a decrease in metabolism, and exposure to a cold environment.[48] Schematically, the drop in core temperature occurs in three stages. The first stage is immediately after anaesthesia induction and consists in an internal transfer of core heat to the periphery, known as internal redistribution. The temperature decrease takes place without heat loss. The second stage is a drop in core temperature the result of heat losses (via the cutaneous route, by the exposure of viscera or by the perfusion of cold solutions) being higher than heat gains. Finally, after a decrease in body temperature

that varies depending on the anaesthetic products and concentrations used, cutaneous vasoconstriction occurs. During this period, the core temperature is almost stable but the heat content of limbs continues to fall, thereby aggravating the hypothermia. At recovery and the waning of the effect of the anaesthetic drugs, thermoregulation is no longer inhibited and other physiological responses to cold such as shivering appear. Therefore, prevention of peroperative hypothermia will not only have a beneficial effect on the patient[33,49,50] but will also automatically reduce the incidence of postanaesthetic shivering.

3.1 Peroperative Hypothermia Prevention

Hypothermia prevention during general anaesthesia entails limiting the effects of internal redistribution, and reducing and making up for the heat losses.

Preoperative skin surface rewarming efficiently limits the effects of internal redistribution.[51] Covering the patient with a forced-air warmer for 30 minutes before the induction of anaesthesia is enough to eliminate the phenomenon of internal redistribution.[52] Another method entails increasing the heat content of the patient by generating endogenous production. Providing the patient with 480kJ in the form of an amino-acid solution resulted in values close to normothermia after hysterectomy.[53]

As patients mainly lose calories through radiation and convection on the skin surface, it also helps to raise the operating room temperature (>23°C).[54] This method is especially useful when the patient is uncovered (i.e. at the beginning and end of the operation). Indeed, the mere fact of covering the patient as much as possible with the surgical drapes, which are excellent insulators, is sufficient to significantly reduce the loss of heat from the skin. However, when the surgical field is very large or if a large amount of viscera is exposed, room temperature remains an important factor to limit heat loss. When a perfusion of a large volume of crystalloid or colloid or of cold blood products are needed, intravenous solution rewarming prevents the patient from cooling down. At least, losses via the respiratory paths are small and the use of exchange filters is sufficient to prevent it.

However, reducing calorific losses is not enough if we want patients to be close to normothermia when they come out of the operating room. Indeed, in addition to the internal redistribution mentioned in section 3 above, the use of passive means will not prevent the heat balance from being negative, therefore an active heat transfer is necessary. The cutaneous path is the most efficient. It offers the largest surface area for exchange and can be used throughout the operation. Forced warm air systems are more efficient than water circulation blankets. During abdominal surgery, covering one-third of the cutaneous surface is enough for the patient to be close to normothermia when they leave the operating room.[55] Furthermore, under general anaesthesia, heat transfer is more rapid and more efficient because of peripheral vasodilatation.

3.2 Physical Treatment

Cheng et al.[56] have shown that a linear relationship exists between core temperature and the average skin temperature at the threshold for the appearance of shivering in the non-anaesthetised patient. On the basis of the slope of the straight regression line linking these two parameters, it has been established that the threshold temperature for shivering is equal to the sum of 20% of the mean skin temperature and 80% of the core temperature. Under light general anaesthesia, the cutaneous factor levels off at 18%.[57] This factor has not yet been calculated at recovery, but it is unlikely that it will be different. In practice, this means that, to inhibit postanaesthetic shivering, the average skin temperature must be raised by at least 4°C to be as efficient as a 1°C increase in core temperature. In addition, heat transfer from the periphery and the deep tissues is hindered by cutaneous vasoconstriction.[58] Radiant heat systems applied in the recovery room are efficient ways of preventing postanaesthetic shivering[59-61] or rapidly inhibiting it when it occurs.[62,63] The use of a forced air warmer in the

recovery room can reduce[64,65] the frequency of postanaesthetic shivering and was found in all patients to reduce the duration.[64,65] In all patients and regardless of the means used, increasing the skin temperature significantly improves thermal comfort.[62,66]

3.3 Medical Treatment

There are numerous effective drugs for preventing or stopping postanaesthetic shivering. These include α_2-agonists,[20,67-71] opiates,[37,69,71-80] tramadol,[37,81] ketanserin,[67,82,83] magnesium sulfate,[84,85] corticosteroids,[86] physostigmine,[69] doxapram,[79,87] methylphenidate,[88] nefopam,[89,90] and serotonin (5-hydroxytriptamine) 5-HT_3 antagonists.[91]

3.3.1 Opiates

The results of clinical studies with μ-receptor agonists are contradictory. The use of alfentanil 250μg in patients with postanaesthetic shivering has been shown to be both effective[74] and ineffective.[92] Morphine 2 to 10mg was ineffective,[9,76,93] whereas doses ranging from 1 to 4 mg/kg followed by a continuous perfusion of 0.2 to 0.5 mg/kg/h were effective in 60% of patients.[75] A dose of 25μg (0.36 μg/kg for 70kg) of fentanyl had no effect on postanaesthetic shivering,[76] whereas a dose of 1.7 μg/kg,[72] was effective in approximately 75% of patients. However, several studies have shown that μ-receptor agonists inhibit postanaesthetic shivering. Alfentanil acts centrally by increasing the interthreshold range in volunteers,[94] and in the postoperative period, there is a linear relationship between the threshold temperature of postanaesthetic shivering and the plasma sufentanil concentration.[73]

In fact, only meperidine (pethidine) presents a constantly remarkable effect on postanaesthetic shivering.[37,69,71-73,76-80] In volunteers, it raises the threshold for sweating and lowers that of cutaneous vasoconstriction.[95] In particular, meperidine has a strong anti-shivering effect since at an equivalent concentration, it lowers the shivering threshold by twice that of cutaneous vasoconstriction.[95] In the postoperative period, a plasma meperidine concentration of 0.6 mg/L, which is an average concentration for analgesia, lowered the shivering threshold by approximately 1.6°C.[73]

There are several arguments which favour the action of meperidine via κ-opioid receptors: (i) in mammals, thermoregulation seems to be principally under the dependence of κ-receptors,[96] (ii) only strong doses of naloxone raise the inhibiting effect on shivering of meperidine 1 mg/kg,[97] and (iii) the equipotent ratios on shivering between meperidine and μ-receptor agonists are lower than for analgesics.[73,94] However, this hypothesis is contradicted by the effects of nalbuphine (a κ-receptor agonist) which inhibits postanaesthetic shivering[98] but, in contrast to meperidine, it has no particular anti-shivering effect and acts more by lowering the setpoint than by increasing the interthreshold range.[99] Another hypothesis is that its superiority is attributable to a non-opiate property of meperidine. Indeed, it has a local anaesthetic activity and a central anticholinergic action. However, none of these properties seem to have an effect on the postanaesthetic shivering.[24,72,100]

3.3.2 α_2-Adrenergic Agonists

In volunteers, clonidine 75μg lowered the threshold for cutaneous vasoconstriction and shivering by 0.5°C.[101] However, it appears to have little or no effect on the threshold for sweating.[102,103] Dexmedetomidine, an α_2-agonist with a receptor specificity 10 times higher than clonidine, also lowers the threshold for vasoconstriction and shivering without changing the sweating threshold.[104]

When recovering from general anaesthesia, clonidine 75μg as a bolus injection stopped postanaesthetic shivering within 5 minutes in all patients.[67] In contrast, a clonidine 5 μg/kg perfusion over 1 hour had no effect, probably because the period required to obtain an effective concentration is too long.[105]

The results of prophylactic administration of clonidine varies with studies. In peripheral surgery, the injection of clonidine 150μg[68] at the beginning of the operation resulted in the incidence of postanaesthetic shivering being divided by three,

whereas in another study,[70] clonidine 2 μg/kg only resulted in a decrease of 13% (61 *vs* 74%).

When clonidine 1.5 or 3 μg/kg is administered at the end of the operation, the frequency of postanaesthetic shivering is significantly lower.[20,69,71] Increasing the doses above this value appears to result in an even greater decrease in the frequency of postanaesthetic shivering.[106] In patients undergoing cardiac surgery, the administration of clonidine 200 to 300μg as a premedication and during surgery reduced the incidence of postanaesthetic shivering by a factor of 3.5.[80]

Premedication with intramuscular dexmedetomidine 2.5 μg/kg in patients scheduled for hysterectomies resulted in a reduction in the incidence of shivering by five compared with those who have received midazolam 0.08 mg/kg.[107] This significant effect can be explained by the fact that plasma dexmedetomidine concentrations 3 hours after the end of the anaesthesia range between 0.18 and 0.52 μg/L. This causes a drop in the shivering threshold of 0.4 to 1.2°C.[104] In cardiac surgery, the administration of a continuous perfusion of dexmedetomidine until the end of the surgery, reduced the frequency of postanaesthetic shivering by 57% to 33%.[108]

The mechanism in which α_2-agonists work is probably central. Indeed, the shivering centre is under the inhibiting control of the preoptic anterior hypothalamic region. This control is strengthened

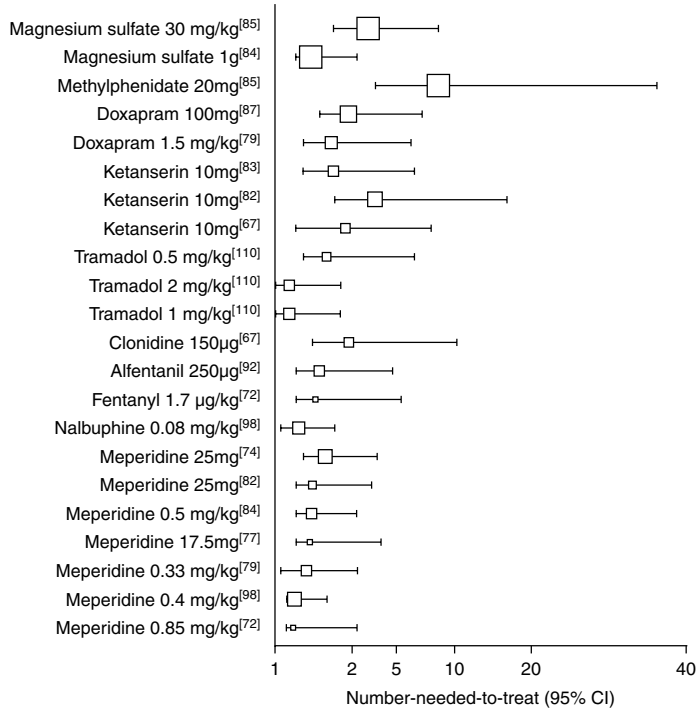

Fig. 1. Number needed to treat from randomised controlled studies using drugs to stop postanaesthetic shivering. The endpoint is cessation of shivering when it occurs during recovery from general anaesthesia. Symbols are 'numbers needed to treat' to stop shivering. Areas of symbols are plotted proportional to the number of analysed patients. Horizontal bars are 95% confidence intervals (CI) calculated the Wilson's equation adapted for a small sample.[114] The upper boundary of the 95% CI around the number to treat places the treatment in the least favourable limit. If this upper limit lies within what would be considered to be a minimal clinically relevant effect (for instance a number needed to treat of 2.5 to stop shivering), the result indicates a definitely useful treatment.

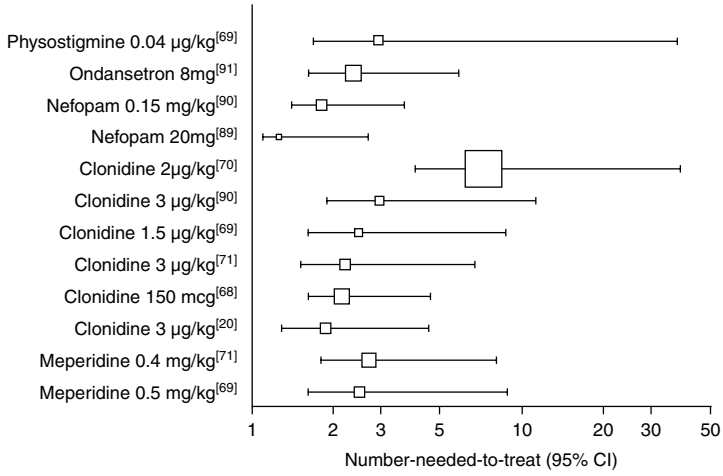

Fig. 2. 'Number needed to treat' from randomised controlled studies using drugs to prevent postanaesthetic shivering. The endpoint is prevention of shivering during recovery from general anaesthesia. Symbols are numbers needed to treat to prevent shivering. Areas of symbols are plotted proportional to the number of analysed patients. Horizontal bars are 95% confidence intervals (CI) calculated the Wilson's equation adapted for a small sample.[114] The upper boundary of the 95% CI around the number to treat places the treatment in the least favourable limit. If this upper limit lies within what would be considered to be a minimal clinically relevant effect (for instance a 'number needed to treat' of 5 to prevent shivering), the result indicates a definitely useful treatment.

by epinephrine and norepinephrine,[109] and the α_2-agonists probably act in the same way.

3.3.3 Tramadol, Ketanserin, Nefopam and Ondansetron

Ketanserin, ondansetron, tramadol and nefopam inhibit or prevent postanaesthetic shivering. Generally, ondansetron is used for its antiemetic properties, ketanserin for its vascular effects, and nefopam and tramadol for their analgesic effects. However, in spite of different clinical properties, all four drugs act on the serotonin neuromediator.

Tramadol 1 mg/kg, a non-opioid analgesic, inhibits postanaesthetic shivering.[81,110] In the non-anaesthetised individual, a dose of tramadol 1 mg/kg lowered the setpoint, raised the interthreshold range and reduced the threshold temperature by roughly 0.8°C.[111]

In addition, nefopam 0.15 mg/kg or 20mg, another non-opioid analgesic, has been shown to inhibit and prevent postanaesthetic shivering.[89,90]

Ketanserin 10mg, a 5-HT_2 antagonist, has been shown to inhibit postanaesthetic shivering.[67,82,83]

In the same way, a 5-HT_3 antagonist ondansetron 8mg, was effective in preventing postanaesthetic shivering at recovery of a general anaesthesia.[91] The mechanism by which all these drugs act has not been clarified but could be related to the inhibition of serotonin re-uptake which is supposed to encourage the inhibiting effect of serotonin on the preoptic anterior hypothalamic region.[109]

3.3.4 Other Drugs

Many other drugs seem to have anti-shivering effects, such as methylphenidate 20mg,[88] physostigmine 0.04 mg/kg[69] or doxapram 100mg or 1.5 mg/kg.[79,87] The mechanisms of action of these agents in postanaesthetic shivering remain obscure. They are said to facilitate the 'recovery' of the descending inhibitor control of the supraspinal effecting centres on the spinal centres. Magnesium sulfate 30 mg/kg[84,85] is also effective in inhibiting

postanaesthetic shivering but the mechanism by which it works is not known.

3.3.5 Summary

It is difficult to list and compare the different treatments deemed to efficiently prevent or stop postanaesthetic shivering because of the scarcity of comparative elements between the different studies. Indeed, the residual effects of halogenated products[112] and opiates[36] used in the peroperative phase could interfere with the drugs being evaluated. The heterogeneity and size of samples could influence the validity of tests, as well as the differences in the doses administered. Lastly, postanaesthetic shivering is a spontaneously resolutive phenomenon and the interpretation of studies without a control group is delicate.

In order to be able to compare various drugs used to prevent or stop shivering we calculated the 'number needed to treat' with the 95% confidence interval (CI).[113] We retained the studies where the agent evaluated was compared with a placebo and where the effect was statistically significant. Use of the 'number needed to treat' enables us to calculate the number of patients that must be treated to stop (fig. 1) or prevent (fig. 2) postanaesthetic shivering in a patient. This method has revealed that opiates, particularly meperidine 0.4 to 0.85 mg/kg, are very effective in stopping postanaesthetic shivering. Tramadol 1 or 2 mg/kg and magnesium sulfate 30 mg/kg are interesting alternatives. Only the administration of nefopam seems to be useful in the prevention of postanaesthetic shivering. Clonidine 0.3 μg/kg is only effective in conditions where it is administered at the end of the operation and after the use of a halogenated product in the peroperative phase.

4. Conclusion

The phenomenon of postanaesthetic shivering is tending to decline thanks to the more systematic prevention of hypothermia in the peroperative stage. Prevention of hypothermia consists of limiting heat losses and in actively rewarming the patient. However, if shivering occurs, it must be treated systematically in order to improve patient comfort and analgesia. Skin surface rewarming is less efficient than medical treatment with meperidine, tramadol or, in certain situations, clonidine. Furthermore, secondary effects are rare and the treatments are inexpensive.

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