Administration of Warmed Intravenous Fluids for Medetomidine-induced Hypothermia in Normal Dogs

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SUMMARY: The effects of warmed fluid therapy on medetomidine (MED)-induced hypothermia in normal dogs were evaluated. Animals were intramuscularly administered physiological saline solution (control) or 40 μg/kg of MED. At the same time, each treated dogs were intravenously administered 10 ml/kg/hr of Ringer’s solutions at room temperature (RT) or after warming the fluids with either Animec (ANI) or Medi-Temp (MEDI) for 4 hours. In the MED-ANI group, the tendency to normalize hypothermia was observed, but no significant differences were recorded in rectal temperature between the MED-ANI and MED-RT groups. The results did not significantly support the reduction in MED-induced hypothermia by warmed fluids.

Key words: dog, hypothermia, warmed fluid

Introduction

Medetomidine (MED) is a widely used a sedative agent in veterinary practice, but has been reported to induce severe hypothermia. Many studies suggest that attempts should be made to conserve body heat and prevent marked reductions in body temperature. Therefore, we investigated the effect of administering warmed fluids. The effect of warmed fluid therapy has been minimally reported in human medicine. Fluid-warming equipment for veterinary use is also commercially available. To the author’s knowledge, there have been no reports on the effectiveness of administration of warmed fluids for the treatment of hypothermia in veterinary medicine, even though warmed fluid effectiveness has been described in some textbooks. The purpose of this study was to investigate the effects of intravenous administration...
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Materials and Methods

The subjects included in this study were five clinically normal beagle dogs (two intact and three neutered males), aged 5.4 ± 0.5 years (mean ± S.D.), with a body weight of 14.2 ± 1.2 kg (mean ± S.D.). All dogs were standard figure. This experiment was approved by the Animal Research Committee of Kurashiki University of Science and the Arts, Okayama, Japan (No. 21–26).

Two types of fluid-warming equipment were used. The Animal Fluid Warmer (ANIMEC AM-2S; ELLTEC Co. Ltd., Nagoya, Japan) is an electrically powered warmer consisting of a dry heating plate that supplies heat to the infusion- or blood-tubing set (will be referred to as ANI in this report). The temperature setting is fixed at 37°C and cannot be changed by the user. Temperature sensors in contact with the tubing control heat and regulate temperature. The second equipment was a blood- and fluid-warming unit (Medi-Temp III FW600; Gaymer Industries Inc., NY, USA) that was also made of a dry heating system (will be referred to as Medi-Temp in this report). This device is placed on a cassette for standard flow (Medi-Temp III Standard Set; Gaymer Industries Inc., NY, USA), and the temperature of the fluid can be adjusted from 38°C to 43°C in one-degree increments so that it can be used for a wide range of procedures. Owing to the design of each equipment, the length of the tube from the device to the animal was not same. In our study, the length of each ANIMEC tube was 30 cm, and each Medi-Temp was 127 cm.

The experiment was divided into six sets, and the five beagles were repeatedly used, by following a randomised block design. There was at least 1 week between treatments for each dog. Treatment involved intramuscular administration of 1.0 ml of physiological saline solution (control) per dog or 40 μg/kg of MED hydrochloride (Domitor; Zenoaq, Fukushima, Japan) per dog. At the same time, all treated dogs were intravenously received 10 ml/kg/h of lactated Ringer’s solution for 4 hr with ANI set at default (37°C), Medi-Temp (MEDI) set at 42°C, and no warming instrument at room temperature (RT, i.e. 22°C). Rectal temperature, heart rate, respiratory rate, and blood pressure were measured at 0 hour (hr) (baseline) and at 0.25, 0.5, 0.75, 1, 2, 3, 4, 5, 6, 7, 8 and 24 hr after injection of the test agents. We performed the measurement at 24 hr after injection to confirm that any effects of medetomidine disappeared, and an experiment was finished safely. Rectal temperature (considered to be representative of body temperature) was measured with an electronic thermometer (Sure-Temp; Welch Allyn, NY, USA). Heart rate and respiratory rate were measured with a stethoscope. Blood pressure was measured with an electronic oscillometric blood pressure measuring device (PetMap; Ramsey Medical Inc., FL, USA). The cuff of size 4.5 to 5.5 was applied to the left forelimb for each measurement. All dogs were acclimatized to the experimental room and were fasted for 12 hr before treatment. The experimental room temperature was set at 22°C by air conditioner through the all procedures. Sedative duration was also measured by observation of the behavioural response. The time from initiation of lateral recumbency until recovery to the prone position by itself was measured as a behavioural response to the sedative effect. The dogs were rested in a cage before and during the study. They were moved to the examination table for measurements and then returned to the cage.

All data were analysed simultaneously using the Prism statistical software (Version 5; GraphPad Software, CA, USA). The Friedman test was used to determine and compare the time effect within the same treatment groups, and to examine the treatment effect at each time point. When a significant difference was obtained by the Friedman test, Dunn’s test was used to compare the means. A P value of < 0.05 was considered significant.

Results

In the control groups, the rectal temperature decreased slightly during fluid administration for 4 hr in all the dogs (Fig. 1. A). The reduction in body temperature was less than 1°C. Statistical analysis showed a significant temperature reduction at 1, 2, 3, 4 and 6 hr after administration compared with the initial value in the
control-RT group \( (P<0.05) \). In contrast, the statistically significant reduction was observed only at 0.75 hr after administration in the control-ANI group, and at 0.5, 5 and 6 hr after administration in the control-MEDI group \( (P<0.05) \). We observed no significant differences in rectal temperatures between the control groups. In all the MED groups, a decrease in rectal temperature was recorded after MED administration (Fig. 1.B). A significant temperature reduction from the initial value was observed at 4 hr after MED administration in all the MED groups \( (P<0.05) \). The lowest rectal temperatures (mean \( \pm \) S.D.) recorded at 4 hr after administration were 36.4 \( \pm \) 0.7 °C in the MED-ANI group, 35.9 \( \pm \) 0.5 °C in the MED-MEDI group, and 35.8 \( \pm \) 0.5 °C in the MED-RT group. At 2 to 7 hr after MED administration, the rectal temperature of the MED-ANI group tended to be maintained higher than that of the MED-RT group by 0.5°C, but there were no significant differences in rectal temperatures between the MED groups.

There were no significant differences in the heart rates between the MED groups, but bradycardia was observed after MED administration in all the MED groups (Table 1). The heart rates were significantly different only at 6 hr after administration between the control-RT and -ANI groups.

No significant changes in respiratory parameters were observed between any of the control groups (Table 2). At 3 hr after MED administration, the respiratory rate significantly decreased in all the MED groups \( (P<0.05) \). There were no significant differences in the respiratory rates between the MED groups.

In all the control and MED groups, no significant changes were recorded in the mean, systolic, and diastolic blood pressure. In all MED-ANI and -MEDI groups, however, the tendency of transient increase followed by decrease was observed in mean, systolic, and diastolic blood pressure.

In all MED treated groups, each sedative duration (mean \( \pm \) S.D.) evaluated by behavioural response was 3.0 \( \pm \) 0.5 hr in MED-RT, 3.0 \( \pm \) 1.8 hr in MED-ANI and 3.0 \( \pm \) 0.8 hr in MED-MEDI groups. No significant differences between all MED groups were observed.

**Discussion**

In this study, a decrease in rectal temperature was observed in all dogs treated with MED, which is consistent with previous reports\(^7, 8\). And, the lowest rectal temperature was recorded at 4 hr after MED administration. This tendency was not observed in...
Table 1. Heart rate following the administration of medetomidine (40 μg/kg) or physiological saline solution in dogs

<table>
<thead>
<tr>
<th>Time after administration (hr)</th>
<th>Group</th>
<th>0</th>
<th>0.25</th>
<th>0.5</th>
<th>0.75</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control-RT</td>
<td>96.8 ± 29.8</td>
<td>96.8 ± 32.2</td>
<td>100.0 ± 37.7</td>
<td>89.6 ± 28.3</td>
<td>90.4 ± 27.5</td>
<td>91.2 ± 24.8</td>
<td>83.2 ± 27.9</td>
<td></td>
</tr>
<tr>
<td>Control-ANI</td>
<td>106.4 ± 27.9</td>
<td>99.2 ± 27.3</td>
<td>103.2 ± 29.4</td>
<td>103.2 ± 26.1</td>
<td>104.0 ± 29.7</td>
<td>97.6 ± 31.3</td>
<td>96.8 ± 23.2</td>
<td></td>
</tr>
<tr>
<td>Control-MEDI</td>
<td>101.6 ± 37.7</td>
<td>95.2 ± 25.9</td>
<td>89.6 ± 24.7</td>
<td>94.0 ± 31.5</td>
<td>95.2 ± 26.2</td>
<td>95.2 ± 29.4</td>
<td>95.2 ± 28.1</td>
<td></td>
</tr>
<tr>
<td>MED-RT</td>
<td>83.2 ± 21.9</td>
<td>47.2 ± 14.8</td>
<td>43.2 ± 12.4</td>
<td>38.4 ± 9.2</td>
<td>40.8 ± 11.1</td>
<td>39.2 ± 7.1</td>
<td>36.8 ± 5.2 a</td>
<td></td>
</tr>
<tr>
<td>MED-ANI</td>
<td>82.4 ± 39.4</td>
<td>41.6 ± 23.7</td>
<td>36.0 ± 15.2 a</td>
<td>36.0 ± 13.2</td>
<td>39.2 ± 12.4</td>
<td>36.8 ± 11.1</td>
<td>36.8 ± 7.6 a</td>
<td></td>
</tr>
<tr>
<td>MED-MEDI</td>
<td>82.4 ± 38.8</td>
<td>56.4 ± 23.7</td>
<td>44.0 ± 13.5</td>
<td>44.0 ± 12.6</td>
<td>46.0 ± 10.5</td>
<td>44.0 ± 17.2</td>
<td>36.8 ± 10.3</td>
<td></td>
</tr>
</tbody>
</table>

Each value represent the mean ± S.D. (n=5). a: significantly different from the base line (P<0.05). b: significantly different between the control-RT and -ANI groups. (P<0.05).

Table 2. Respiratory rate following the administration of medetomidine (40 μg/kg) or physiological saline solution in dogs

<table>
<thead>
<tr>
<th>Time after administration (hr)</th>
<th>Group</th>
<th>0</th>
<th>0.25</th>
<th>0.5</th>
<th>0.75</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control-RT</td>
<td>49.6 ± 30.6</td>
<td>45.6 ± 32.6</td>
<td>36.0 ± 11.3</td>
<td>30.4 ± 6.0</td>
<td>35.2 ± 8.1</td>
<td>35.2 ± 5.9</td>
<td>30.4 ± 4.5</td>
<td></td>
</tr>
<tr>
<td>Control-ANI</td>
<td>41.6 ± 10.4</td>
<td>40.8 ± 13.9</td>
<td>40.0 ± 11.6</td>
<td>35.2 ± 3.3</td>
<td>37.6 ± 11.8</td>
<td>37.6 ± 9.2</td>
<td>32.0 ± 2.8</td>
<td></td>
</tr>
<tr>
<td>Control-MEDI</td>
<td>48.0 ± 28.1</td>
<td>39.2 ± 12.7</td>
<td>38.4 ± 13.4</td>
<td>33.6 ± 10.4</td>
<td>32.8 ± 4.3</td>
<td>35.2 ± 12.1</td>
<td>37.6 ± 12.8</td>
<td></td>
</tr>
<tr>
<td>MED-RT</td>
<td>39.2 ± 11.4</td>
<td>28.8 ± 13.6</td>
<td>25.6 ± 13.4</td>
<td>17.6 ± 4.5</td>
<td>18.4 ± 9.6</td>
<td>18.4 ± 9.6</td>
<td>16.0 ± 9.3 a</td>
<td></td>
</tr>
<tr>
<td>MED-ANI</td>
<td>36.8 ± 7.6</td>
<td>32.8 ± 14.8</td>
<td>24.0 ± 6.3</td>
<td>29.6 ± 22.3</td>
<td>18.4 ± 6.6</td>
<td>19.2 ± 5.2</td>
<td>14.4 ± 4.5 a</td>
<td></td>
</tr>
<tr>
<td>MED-MEDI</td>
<td>34.0 ± 16.3</td>
<td>28.4 ± 16.6</td>
<td>18.0 ± 8.0</td>
<td>17.6 ± 4.5</td>
<td>16.8 ± 1.7</td>
<td>18.0 ± 7.2</td>
<td>13.6 ± 3.5 a</td>
<td></td>
</tr>
</tbody>
</table>

Each value represent the mean ± S.D. (n=5). a: significantly different from the base line (P<0.05).

control groups although the decrease in rectal temperature was also shown. This changes of rectal temperature was considered to be characteristic of MED-induced hypothermia. This is the first observation of medetomidine-induced hypothermia for such long duration, as far as authors know. Similar to rectal temperature, the decreases of heart rate and respiratory rate were also observed obviously for 2 to 4 hr in this study. Additionally, it was also reported that the effects of medetomidine on insulin secretion and other endocrine functions sustained for 2 hr or more after administration1. Therefore, duration of these physiological changes induced by medetomidine was longer compared with that of sedative effect. The decrease in rectal
temperature was greater than 1°C. The rectal temperature of dogs treated with MED was maintained at a minimum of 36.4 ± 0.7°C when the dogs were administered fluids warmed by ANI, whereas the lowest body temperature of MED-treated dogs was less than 36°C when fluids were administered at RT or warmed by MEDI. In addition, in all the MED groups, the use of ANI for warming tended to reduce the decrease in rectal temperature compared with the administration of fluid at RT and MEDI. Therefore, our results suggest the possibility that administration of fluids warmed with ANI may reduce MED-induced hypothermia. We used MEDI set at 42°C in this study. Although it was a higher setting compared to ANI, which was set at 40°C maximum, the suppressive effect on medetomidine-induced hypothermia was shown in the MED-ANI group only. In the MED-MEDI group, the tendency for changes in body temperature was similar to that in the MED-RT group. We thought the reason for this result was that fluids warmed by MEDI became cold as fluids moved through the tube. Differences in the length of the tube from the device to the animal could influence this result. In our study, the length of each ANI tube was 30 cm, and each Medi-Temp was 127 cm. The MEDI tubes could not be shortened. However, we did not observe significant differences in rectal temperature between the MED-ANI and MED-RT groups. The decrease in temperature induced by α2-adrenoceptor agonists, including MED, can be attributed to CNS depression in combination with a reduction in muscular activity. In addition, our results do not suggest that the administration of warmed fluids induces thermogenesis. We considered that the warmed fluids only supply a certain amount of heat to the body through the peripheral venous route. This anti-hypothermic effect of warmed fluids was conservative rather thermogenic. We could not determine the precise mechanism of this effect in this study. Hence, fluid administration also induced significant decrease of rectal temperature regardless of fluid temperature. It was suggested that heat loss depending on the counter current heat change mechanism might be accelerated as a result of increase in circulating blood volume induced by fluid administration. Therefore, warmed fluid administration might have the inconsistent effects on rectal temperature. We considered this is a reason why warmed fluid administration could not reduce the MED-induced hypothermia sufficiently.

In both the MED-ANI and MED-MEDI groups, we did not observe any remarkable effects of administration of warmed fluids on the heart rate, respiratory rate and sedative duration, as compared with the MED-RT group; that administration of warmed fluid did not affect any physiological parameters except for rectal temperature was considered advantageous. Especially, it was clinically important that warmed fluid administration did not shorten or prolong sedative effect induced by MED. As mentioned in results, the heart rates were significantly different at 6 hr after administration between the control-RT and -ANI groups. However, we could not reveal that reason. On the other hand, we did not observe any significant transient increase or sustained decrease in the blood pressure in the dogs after MED administration. It was different from the previous report. Thus, the effect of warmed fluid administration on blood pressure in dogs treated with MED has not been discussed.

The change in rectal temperature was not greater than 1°C in all the control groups; however, some significant decreases were observed. Therefore, the administration of warmed fluids to normal dogs without MED treatment, using the commercially available methods, does not clinically affect their rectal temperature. The results suggest that the use of ANI or MEDI does not induced hyperthermia compared to administration at RT.

This study showed that warmed fluid therapy results in clinically insignificant changes in rectal temperature only. The possibility of using warmed fluid therapy should be seriously considered, and a more detailed investigation is necessary to confirm this.

References


