Profound Hypothermia without Extracorporeal Circulation

The Effects of Cooling Rate and Hemodilution on the Incidence of Ventricular Fibrillation in Dogs*

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During production of profound hypothermia in dogs by extracorporeal cooling of the blood, it was observed that in many of the dogs the heart continued to beat despite temperatures of 14 to 20°C. It was further observed that when the extracorporeal pump was stopped, the hearts continued to beat, maintaining a small but effective output. As evidenced by the absence of acidosis, cardiac output appeared to be sufficient, at low body temperatures, to supply the dog’s metabolic needs.

That some dogs can maintain a sinus or nodal rhythm below temperatures of 20°C is well known. However, ventricular fibrillation has always occurred in a certain percentage of animals. We were surprised that only 5 per cent of our dogs cooled by extracorporeal means developed ventricular fibrillation, and we wondered whether this low incidence of fibrillation could be explained by the techniques we were employing. This technique differs from previously reported techniques accompanied by high percentages of fibrillation. The differences include the use of hemodilution, a slow rate of cooling, and careful control of the base deficit. An experiment was designed, therefore, to test the effects of hemodilution and slow cooling on the incidence of ventricular fibrillation in dogs cooled to profound levels of hypothermia by external cooling alone without the circulatory support of an extracorporeal pump.

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Method

Fifty-five adult female mongrel dogs varying in weight from 15 to 20 lbs. were cooled by external means to a temperature of 20°C. The temperatures then drifted to 17° to 18°C, and the animals were slowly warmed by diathermy. Diathermy was chosen so that core temperature might be maintained above that of the peripheral mass during rewarming. In this way, better perfusion of tissues was provided for and the metabolic deficit was minimized. Catheters were placed into the aortic root and inferior vena cava near the right atrium. The arterial and venous blood pressures were measured by means of a Statham strain gauge and were monitored on a Grass polygraph with the electrocardiogram. Arterial \( P_{O_2}, P_{CO_2}, \) and \( pH \) were frequently determined (employing a Severinghaus Blood-Gas Electrode Unit) and the base deficit was calculated by the Astrup chart. Base deficit was corrected when necessary by administration of sodium bicarbonate. Esophageal, rectal and subcutaneous temperatures were monitored on a Yellow Springs telethermometer.*

All body hair was removed with electric clippers prior to cooling. Sodium pentothal (thiopental sodium—25 mg./Kg.) was used to induce anesthesia and was supplemented by controlled inhalation of a mixture of \( N_2O \) (75 per cent) and \( O_2 \) (25 per cent). Anectine® (succinylcholine) was administered for muscle relaxation; atropine was given prior to induction. Constant inspiratory pressure and respiratory rate were controlled with a Bird Mark 8 respirator. As a body temperature of 30°C. was approached, the \( N_2O-O_2 \) inhalation mixture was changed to 100 per cent \( O_2 \) which was given for the remainder of the experiment.

The dogs were divided into 3 groups:

Group I: Ice-cooled, hemodiluted (19 dogs). Each animal was placed on a wire rack, and cooled in ice. The layer of ice surrounding the body soon

* Yellow Springs Instrument Co., Yellow Springs, Ohio.
melted and the water drained off, so that, in essence, these dogs were cooled by circulating air. When their body temperature was approximately 32°C, 50 per cent of their calculated blood volume was withdrawn in 50-cc. increments and replaced with Ringer’s lactate solution at ambient temperature. The withdrawn blood was returned by transfusion during the rewarming procedure.

**Group II:** Ice-cooled, non-hemodiluted (18 dogs). The protocol for this group was the same as for Group I, with the exception that withdrawal of blood and replacement with Ringer’s lactate solution was not done.

**Group III:** Ice water-cooled, non-hemodiluted (18 dogs). In this group, cooling took place in an ice water “slush” so that nearly freezing water was always in contact with the dog’s skin. The protocol in other respects was identical with that of Group II.

Since the purpose of this experiment was to test the effect of the variations in these groups on the incidence of fibrillation or arrest, no attempt was made to resuscitate a dog whose heart was fibrillating or arrested.

## Results

Eighteen of the 19 dogs in Group I survived. Fibrillation occurred in the 19th dog. There were no cases of cardiac arrest (Table 1). Of the 18 dogs in Group II, fibrillation occurred in 3, resulting in only 15 survivors. From Group III only 9 of the 18 dogs survived, with 6 instances of fibrillation and 3 of cardiac arrest (Table 1).

The rate of cooling was different in all 3 groups (Fig. 1). The most rapid cooling took place in Group III, the slowest cooling in Group II.

The hematocrits were determined throughout the procedure. After rewarming, there was a 15 to 20 per cent increase over the initial hematocrit in Groups II and III. In Group I, the hematocrit decreased from 40 to 50 per cent after hemodilution and returned to approximately the initial level after transfusion during the rewarming phase.

The electrocardiographic readings varied in all 3 groups. Fig. 2 shows the electrocardiogram of one of the Group I dogs during cooling and rewarming. There was a progressive lengthening of most intervals during cooling with preservation of an isoelectric ST segment. A slow nodal rhythm was present at 19°C with a root aortic pressure of 50/25 mm. Hg.

The Group II dogs showed more T-wave changes, as can be seen in Fig. 3. The Group III dogs showed the most marked changes in the electrocardiographic patterns. There were many variations in the pacemaker, frequent elevation of the ST segment, and often fibrillation (6 out of 19 dogs). Fig. 4 shows one such case where ventricular fibrillation, interspersed with several effective systolic ejections, occurred at 19°C. A comparison of the frequency of ectopic beats in the 3 groups (Table 2) shows that 10 of the 19 dogs in Group I had none, and 4 had greater than 100 ectopic beats; 3 of the 18 dogs in Group II had no ectopic beats and 9 had greater than 100 ectopic beats; 2 of the 18

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**TABLE 1**

The incidence of survival, fibrillation and cardiac arrest in 55 dogs undergoing hypothermia

<table>
<thead>
<tr>
<th>No. of Dogs</th>
<th>Survived</th>
<th>Cardiac Fibrillation</th>
<th>Cardiac Arrest</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Ice hemodiluted</td>
<td>19</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>II. Ice non-hemodiluted</td>
<td>18</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>III. Ice water non-hemodiluted</td>
<td>18</td>
<td>9</td>
<td>6</td>
</tr>
</tbody>
</table>

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**Fig. 1.** A comparison of the differences in cooling time in the 3 experimental groups: Group I—cooled in ice and hemodiluted; Group II—cooled in ice but not hemodiluted; Group III—cooled in ice water but not hemodiluted.
Fig. 2. Representative EKG and blood pressure tracings seen in Group I animals during hypothermia.

Fig. 3. Representative EKG and blood pressure tracings seen in Group II animals during hypothermia.
dogs in Group III had no ectopic beats, but 12 had greater than 100 ectopic beats.

Discussion

The mechanisms by which hemodilution may be beneficial in hypothermia are obvious. The hematocrit normally increases during cooling with escape of fluid into the extracellular space. Concomitant with this increased hematocrit is a remarkable increase in viscosity, and the resultant perfusion through the capillaries is drastically curtailed. The coronary circulation should be no exception. Hemodilution decreases both hematocrit and viscosity despite the lowered temperature and, therefore, insures better tissue perfusion. The decrease in circulating cells does not appear to represent a problem at a lowered temperature because of the increased solubility of oxygen in plasma.

An explanation for the difference between results in Groups II and III is not quite so obvious. If, however, one considers the externally cooled preparation to be analogous to the extracorporeal preparation, it becomes apparent that the skin and subcutaneous fat are, in reality, heat exchangers. When the temperature in this tissue layer is monitored by a subcutaneous needle thermistor, a marked difference is noted between dogs cooled in ice and dogs cooled in ice water. This was illustrated by the following experiment.

Thermistors were placed into the walls of the right and left atria in 2 dogs (not included in the 55 dogs of Groups I, II, and III). One dog was cooled in ice and the other in ice water. Subcutaneous and esophageal temperatures were also measured. Fig. 5 shows the results in these 2 dogs after 30 minutes of cooling.

The dog cooled in ice water (slush) had a precipitous drop in skin temperature to a few degrees above zero, while the skin of the dog cooled in ice dropped only about 10 to 12° below the core temperature. The rate of cooling was much faster in the dog cooled in ice water. There was no temperature gradient between the left and right chambers of the heart in the dog cooled in ice and no greater than a 0.5° gradient in the dog cooled in slush. This is within the experimental error of the thermistors employed.

It is thought, therefore, that the lower incidence of fibrillation and arrest in Group II as compared to Group III may have been due to the slower rate of cooling and the smaller temperature gradient between “heat exchanger” and core.

<table>
<thead>
<tr>
<th>TABLE 2</th>
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<p>| A comparison of the frequency of ectopic beats in 55 dogs undergoing hypothermia |</p>
<table>
<thead>
<tr>
<th>No. of Dogs</th>
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<th>&lt;10</th>
<th>&lt;100</th>
<th>&gt;100</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Ice hemodiluted</td>
<td>19</td>
<td>10</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>II. Ice non-hemo- diluted</td>
<td>18</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>III. Ice water non- diluted</td>
<td>18</td>
<td>2</td>
<td>1</td>
<td>3</td>
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</table>
Summary

By means of hemodilution with Ringer's lactate solution and slow cooling by exposure to cold air, dogs can safely be cooled to 18°C. and rewarmed with diathermy. It is suggested that clinical application of the factors of slow external cooling, small periphery-to-core temperature gradients, hemodilution, and rewarving with diathermy may provide a means of safely cooling patients externally to temperatures far lower than those currently in use. The slow cardiac rate and small systolic ejection would present the neurosurgeon with ideal operative conditions for aneurysms and other difficult intracranial vascular lesions. The avoidance of heparinization and extracorporeal circulation presents an obvious advantage.

References