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Effects of Epidural Anesthesia on Cardiovascular Response and Survival in Experimental Hemorrhagic Shock in Dogs

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The purpose of the present study was to assess the effects of epidural anesthesia on cardiovascular responses and survival in experimental hemorrhagic shock in dogs. Thirty mongrel dogs were randomly assigned to one of three groups on the basis of anesthetic technique: the upper-level group (n = 10), receiving general anesthesia plus upper-level (mainly thoracic region) epidural anesthesia; the lower-level group (n = 10), receiving general anesthesia plus lower-level (mainly lumbar region) epidural anesthesia; and the control group (n = 10), receiving general anesthesia alone. After withdrawal of blood, the changes in mean arterial pressure (40 mmHg) and cardiac index were similar in all groups. In the upper-level group, a lower heart rate and systemic vascular resistance than the control group were maintained throughout in the presence of severe hypotension. A significant difference in survival was seen between the upper-level and control groups over the 100-min observation period as a whole ($P < 0.05$ by the Generalized Wilcoxon test), since, at the end of the period, only two of the ten animals in the control group survived, whereas nine of ten in the upper-level group survived ($P < 0.001$ by the Kaplan-Meier test). This result demonstrates that, in dogs lightly anesthetized with halothane and nitrous oxide, upper thoracic level epidural anesthesia significantly improves survival in experimental hemorrhagic shock (compared with survival in dogs with lumbar epidural or no epidural anesthesia) when the epidural is performed before hemorrhage and when the mean arterial pressure is constant. This survival benefit may be related to the significantly lower catecholamine concentrations attained during upper-level epidural anesthesia. (Key words: Anesthetic techniques: epidural. Physiology: hemorrhagic shock. Sympathetic nervous system: epinephrine; norepinephrine.)

THE USE OF α-adrenergic blocking agents has been advocated as potentially useful in hemorrhagic shock.[1–6] The rationale underlying the usefulness is that they relieve vasoconstriction due to sympathetic overactivity following acute blood loss. There are, however, few studies, if any, assessing the influence of epidural anesthesia, which produces vasodilation by a different mechanism, in hemorrhagic shock.

It was demonstrated by Klassen *et al.*,[7] using the multiple-microsphere technique, that cervicothoracic epidural blockade had improved endocardial blood flow and a decrease in the determinants of myocardial oxygen consumption in dogs. Yeager *et al.*[8] reported that the use of epidural anesthesia in a group of high-risk surgical patients is associated with more stable intraoperative hemodynamics and decreased postoperative morbidity. We hypothesized that epidural anesthesia might be of use in circumstances where hemorrhage was expected because sympathetic overactivity was suppressed when it was employed.

This study was undertaken in dogs to clarify the following questions: What are the effects of epidural anesthesia on cardiovascular responses and survival in experimental hemorrhagic shock? Is there any difference between the effects of upper- and lower-level epidural anesthesia? The animals received both general anesthesia and either no additional anesthesia or epidural anesthesia in the upper- and lower-spinal cord segments, and were then subjected to hemorrhage.

The principle finding of the study was that epidural anesthesia, especially in the upper-spinal cord segments, significantly improved survival following experimental hemorrhagic shock in dogs.

Materials and Methods

Thirty healthy adult mongrel dogs (10–13 kg) were studied. The experimental protocol was approved by the Animal Care Committee of Kanazawa University School of Medicine.

General Procedure

General anesthesia was induced with ketamine, 10 mg/kg im. After tracheal intubation facilitated with succinylcholine, 2 mg/kg im, the lungs were mechanically ventilated with a volume respirator. Tidal volume was adjusted to obtain an arterial P_{CO_2} of approximately 40 mmHg. Anesthesia was maintained with 0.5% halothane and 50% nitrous oxide in oxygen. The femoral arteries were cannulated bilaterally. One arterial catheter was connected to a blood bag reservoir containing 20 ml of citrate-phosphate-dextrose solution for blood withdrawal. The other was used for arterial pressure measurement and blood sampling. A pulmonary artery thermodilution catheter (American Edwards, Santa Ana, TX) was inserted into the pulmonary artery *via* the right femoral vein. The two pressure catheters were connected to a polygraphic recorder (Nihon Kohden, Tokyo). After catheterization, the dogs received heparin, 200 IU/kg. Body temperature was maintained using a warming lamp. Muscle relaxation was obtained by intermittent injections of 0.1 mg/kg doses

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of pancuronium bromide. During the experiments, the animals were infused with 0.2 ml · kg^{-1} · min^{-1} of lactated Ringer's solution.

Epidural Anesthesia

The dogs were then randomly assigned to one of three groups according to anesthetic technique: the upper-level group (n = 10), receiving general anesthesia plus upper-level epidural anesthesia; the lower-level group (n = 10), receiving general anesthesia plus lower-level epidural anesthesia; and the control group (n = 10), receiving general anesthesia alone. The vertebral arches of either T7-8 (upper-level and control groups) or L6-7 (lower-level group) were surgically exposed. The epidural space was identified by the loss of resistance technique. A catheter was introduced 3 cm into the epidural space in a cephalad direction and sutured in place. The position of the catheter was confirmed radiographically using 2 ml of iopamidol. The wound was closed in layers.

Experimental Protocols and Data Acquisition

After the surgical procedures, the animals were left for a period of approximately 30 min to allow blood gases and hemodynamic parameters to stabilize. Baseline readings were then taken of the mean arterial blood pressure (MAP), heart rate (HR), pulmonary capillary wedge pressure (PCWP), central venous pressure (CVP), and cardiac output. Cardiac index (CI) and systemic vascular resistance (SVR) were calculated using standard formulas. The dog's body surface area[9] was calculated as: 0.112 (body weight)$^{2/3}$. An arterial blood sample was obtained for analyses of arterial *p*H, blood gases, and arterial epinephrine, norepinephrine, lactate, and pyruvate concentrations. Following baseline measurements, 2 ml of either 1% mepivacaine (upper- and lower- level groups) or normal saline (control group) was injected *via* an epidural catheter over a period of 1 min. After 20 min, measurements and blood samples were taken again and the dogs were bled into blood bags for up to 20 min. A MAP of 40 mmHg was maintained throughout the experiment by adjusting the blood level of the reservoir to a constant level above the heart. Measurements and samples were taken repeatedly at 20, 40, 60, 80, and 100 min following hemorrhage. A second epidural injection of half the previous dose was administered 50 min after the first.

Data Analysis

Arterial blood gases and acid-base status were measured using an automatic analyzer (ABL-2, Radiometer, Copenhagen, Denmark). Blood for catecholamine determinations was put in iced 7-ml sodium EDTA vacuum tubes before being placed in a refrigerated centrifuge for 10 min at 2000*g*. Plasma was decanted and stored frozen prior to analysis. Plasma catecholamine assays were performed using high-performance liquid chromatograph (HPLC) equipped with post-column delivertizing fluorometric detection system described by Yui *et al.*[10] Within-assay variation was less than 6% for each catecholamine. For the determination of the arterial lactate and pyruvate concentrations, a 3-ml blood sample was treated with 6 ml of 0.6 M perchloric acid and kept 4° C until analyzed enzymatically.[11,12] Within-assay variation was less than 5% for each concentrations.

Statistical Analysis

Significant differences among group means were determined by using ANOVA and the Bonferroni modification of the *t* test as described.[13,14] The significant differences in survival between the two groups was determined over the entire 100-min observation period with the Generalized Wilcoxon test, and differences in survival at specific times in this period were isolated with the Kaplan-Meier test. $P < 0.05$ was considered to be statistically significant. Values were expressed as means ± SD.

Results

No significant differences existed among the three groups with respect to body weight or maximum bleeding volume (table 1). Radiographic findings indicated that contrast medium was spreading from approximately C6 to T10, and from T9 to L7 segments, in the upper- and lower- level groups, respectively.

TABLE 1. Characteristics of Dogs Studied

	n	Weight (kg)	Spread of Contrast Material	Maximum Bleeding Volume (ml/kg)
Upper-level group	10	11.1 ± 0.9	C6.2 ± 1.2–T9.6 ± 1.7	31.5 ± 10.6
Lower-level group	10	10.3 ± 0.3	T9.2 ± 1.1–L6.8 ± 0.4	29.2 ± 8.1
Control group	10	10.7 ± 0.7	—	34.3 ± 12.6

Spread of contrast material = the spread of a similar volume of radigraphic contrast material in the epidural space as described in Methods. C, T, L = spinal.

Values are mean ± SD. No significant differences existed among the three groups with respect to Weight or Maximum bleeding volume.

Hemodynamics

The hemodynamic responses are presented in table 2. After epidural injection, the MAP and HR in the upper-level group decreased progressively and remained lower than in both the lower-level and control groups. After withdrawal of blood, both CI and PCWP decreased. The changes in CI and PCWP were similar in all groups except for the CI measured 80 min following hemorrhage. With upper-level epidural anesthesia, a lower HR was maintained throughout in the presence of severe hypotension. At the same time, the stroke volume in the upper-level group was approximately twice that of the other two groups.

On the other hand, no significant difference in hemodynamic values was seen between the lower-level epidural and control groups. Thus, after hemorrhage, upper-level epidural anesthesia was followed by hemodynamic effects different from those following lower-level anesthesia.

Blood Gas Analysis

The changes of arterial blood gas data are presented in table 3. Arterial P_{CO_2} and P_{O_2} did not differ significantly among the three groups at any point during the experimental period. After hemorrhage, arterial *p*H decreased progressively in all groups. In the upper-level group, a significantly greater arterial *p*H than in both the lower-level and control groups was observed at 40 min after hemorrhage. The mean arterial *p*H in the upper-level group was maintained at a level significantly greater than that in the two groups throughout the remainder of the study. Similarly, the mean arterial bicarbonate level in the upper-level group significantly exceeded that in the control group.

The decrease in arterial *p*H and bicarbonate with lower-level epidural anesthesia, was similar to that in the control animals. Thus, in the upper-level epidural group, acid-base balance was maintained better than, or at least as well as in the other two groups.

Arterial Concentrations of Catecholamines, Lactate, and Pyruvate

The changes in the arterial concentrations of epinephrine, norepinephrine, lactate, and pyruvate are presented in table 4. Upper-level epidural anesthesia was associated with significantly lower plasma catecholamine concentrations than were found in the control animals, as well as in the lower-level group. The catecholamine response to hypovolemia was consequently abolished in the upper-level group throughout the experimental period. A pronounced increase in plasma catecholamine concentrations were seen in the lower-level group. However, these concentrations remained significantly lower in the lower-level group than in the control group, but significantly higher than in the upper-level group throughout the remainder of the study.

Blood lactate concentrations increased progressively in all groups after withdrawal of blood, but a significantly

TABLE 2. Hemodynamics in the Upper- (U) and Lower- (L) Level Epidural, and Control (C) Groups

			Time after Blood Loss (min)			
	Baseline	Post-ED	20	40	60	80
MAP (mmHg)						
U	128 ± 22	84 ± 26*†	41 ± 8	36 ± 5	36 ± 7	36 ± 6
L	142 ± 27	127 ± 25†	39 ± 4	39 ± 5	37 ± 5	35 ± 2
C	116 ± 13	116 ± 12	40 ± 4	40 ± 6	41 ± 6	35 ± 4
HR (beats/min)						
U	187 ± 33	137 ± 28*†	118 ± 9*†	109 ± 15*†	108 ± 19*†	108 ± 27*†
L	189 ± 32	172 ± 33†	171 ± 35†	168 ± 25†	167 ± 24†	169 ± 27†
C	168 ± 21	166 ± 21	178 ± 21	188 ± 34	202 ± 45	165 ± 39
PCWP (mmHg)						
U	11 ± 5	9 ± 5	7 ± 3	6 ± 2	5 ± 2	5 ± 1
L	12 ± 8	9 ± 4	6 ± 2	5 ± 2	5 ± 2	4 ± 2
C	11 ± 4	11 ± 4	7 ± 4	7 ± 4	7 ± 4	7 ± 2
CI ($l \cdot min^{-1} \cdot m^{-2}$)						
U	3.2 ± 0.4	2.4 ± 1.1	1.2 ± 0.4	1.0 ± 0.2	0.9 ± 0.1	0.9 ± 0.1*
L	2.9 ± 0.4	2.4 ± 0.9	0.9 ± 0.2	0.9 ± 0.3	1.0 ± 0.3	0.9 ± 0.3
C	2.8 ± 0.5	2.8 ± 0.5	0.9 ± 0.2	0.8 ± 0.2	0.8 ± 0.2	0.6 ± 0.1
SVR ($dynes \cdot s \cdot cm^{-5}$)						
U	5400 ± 1300	4700 ± 1300	4800 ± 1800	4500 ± 1400*	4700 ± 1000*	5000 ± 800*
L	6300 ± 1600	7200 ± 2500	7300 ± 1400	6900 ± 1800	5700 ± 1600	6000 ± 2000
C	6200 ± 1600	6200 ± 1600	6300 ± 2000	7200 ± 1900	7700 ± 2500	8000 ± 1800

Post-ED = 20 min after epidural injection; MAP = mean arterial pressure; HR = heart rate; PCWP = pulmonary capillary wedge pressure; CI = cardiac index; SVR = systemic vascular resistance.

Values are mean ± SD.
* Significant difference *versus* control group ($P < 0.05$).
† Significant difference between groups U and L ($P < 0.05$).

TABLE 3. Blood Gas Analysis in the Upper- (U) and Lower- (L) Level Epidural, and Control (C) Group

	Baseline	Post-ED	Time after Blood Loss (min) 20	40	60	80
pH_a (units)						
U	7.31 ± 0.05	7.31 ± 0.06	7.33 ± 0.06	7.31 ± 0.07*†	7.28 ± 0.04*†	7.26 ± 0.04*†
L	7.29 ± 0.09	7.30 ± 0.03	7.29 ± 0.03	7.14 ± 0.09†	7.19 ± 0.06†	7.19 ± 0.06†
C	7.32 ± 0.06	7.31 ± 0.06	7.31 ± 0.06	7.20 ± 0.08	7.13 ± 0.08	7.03 ± 0.1
Pa_{CO_2} (mmHg)						
U	38 ± 5	36 ± 5	33 ± 6	32 ± 5	33 ± 3	34 ± 3
L	37 ± 3	35 ± 4	35 ± 2	35 ± 5	36 ± 3	36 ± 5
C	38 ± 6	37 ± 6	33 ± 5	34 ± 6	35 ± 5	33 ± 9
Pa_{O_2} (mmHg)						
U	181 ± 24	180 ± 34	204 ± 39	192 ± 51	211 ± 40	207 ± 39
L	164 ± 52	160 ± 42	162 ± 43	150 ± 44	178 ± 48	178 ± 46
C	192 ± 62	185 ± 52	182 ± 37	187 ± 43	175 ± 41	173 ± 43
HCO_3^- (mEq/L)						
U	18.5 ± 2.2	18.3 ± 2.1	16.6 ± 1.7	15.0 ± 0.8*†	15.0 ± 0.9*	14.9 ± 1.1*
L	19.1 ± 2.3	19.0 ± 2.1	14.8 ± 2.3	11.7 ± 2.4†	13.0 ± 2.4	13.1 ± 3.3
C	18.0 ± 2.1	18.1 ± 2.0	14.9 ± 2.6	12.6 ± 2.6	11.4 ± 3.4	7.7 ± 3.0

pH_a = arterial pH. Values are mean ± SD.
* Significant difference *versus* control group ($P < 0.05$).
† Significant difference between groups U and L ($P < 0.05$).

lower lactate concentration was observed in the upper-level group than in the control group. In the lower-level group, the blood lactate concentration was maintained significantly lower than in the control group after the fortieth minute, and was significantly greater after 60 min than in the upper-level group. In contrast, there were no significant differences in blood pyruvate concentration among the three groups.

SURVIVAL DATA

Survival curves for the three groups are shown in figure 1. A significant difference in survival was seen between the upper-level and control groups over the 100-min observation period as a whole ($P < 0.05$ by the Generalized Wilcoxon test), since, at the end of this period, only two of the ten animals in the control group survived, whereas nine of the ten in the upper-level group survived ($P < 0.001$ by the Kaplan-Meier test). On the other hand, the difference between the lower-level and control groups failed to reach statistical significance.

Discussion

Hemorrhagic shock is a potent stimulus to the sympathetic nervous system and results in an immediate re-

TABLE 4. Arterial Levels of Catecholamines, Lactate, and Pyruvate in the Upper- (U) and Lower- (L) Level Epidural, and Control (C) Groups

	Baseline	Post-ED	Time After Blood Loss 20	40	60	80
Epinephrine (ng/ml)						
U	2.2 ± 1.6	0.8 ± 0.5*	1.4 ± 0.8*†	1.4 ± 1.0*†	1.1 ± 0.7*†	1.6 ± 1.2*†
L	1.9 ± 1.2	1.7 ± 1.2	13.1 ± 11.2*†	10.8 ± 8.8*†	10.9 ± 6.5*†	11.4 ± 6.8*†
C	2.7 ± 1.8	2.8 ± 1.9	38.0 ± 33.3	26.2 ± 22.7	36.1 ± 30.7	40.5 ± 26.9
Norepinephrine (ng/ml)						
U	0.5 ± 0.4	0.2 ± 0.1*	0.2 ± 0.1*†	0.2 ± 0.1*†	0.2 ± 0.1*†	0.3 ± 0.2*†
L	0.4 ± 0.2	0.2 ± 0.2	1.5 ± 1.2†	1.4 ± 1.2*†	1.6 ± 1.5*†	1.6 ± 0.9*†
C	0.5 ± 0.3	0.5 ± 0.3	4.2 ± 3.9	4.6 ± 3.5	6.8 ± 4.7	7.9 ± 4.2
Lactate (mg/dl)						
U	25 ± 10	27 ± 11	32 ± 9	35 ± 8*	36 ± 8*†	35 ± 11*†
L	24 ± 11	26 ± 12	33 ± 11	47 ± 17	53 ± 16*†	54 ± 17*†
C	26 ± 11	27 ± 11	38 ± 13	68 ± 23	77 ± 23	103 ± 17
Pyruvate (mg/dl)						
U	0.9 ± 0.5	0.9 ± 0.5	1.0 ± 0.3	1.0 ± 0.3	0.9 ± 0.3	0.9 ± 0.3
L	0.6 ± 0.4	0.8 ± 0.4	0.9 ± 0.4	1.0 ± 0.5	1.2 ± 0.4	1.1 ± 0.5
C	1.0 ± 0.4	1.1 ± 0.5	1.2 ± 0.5	1.4 ± 0.6	1.4 ± 0.5	1.3 ± 0.5

Values are mean ± SD.
* Significant difference *versus* control group ($P < 0.05$).
† Significant difference between groups U and L ($P < 0.05$).

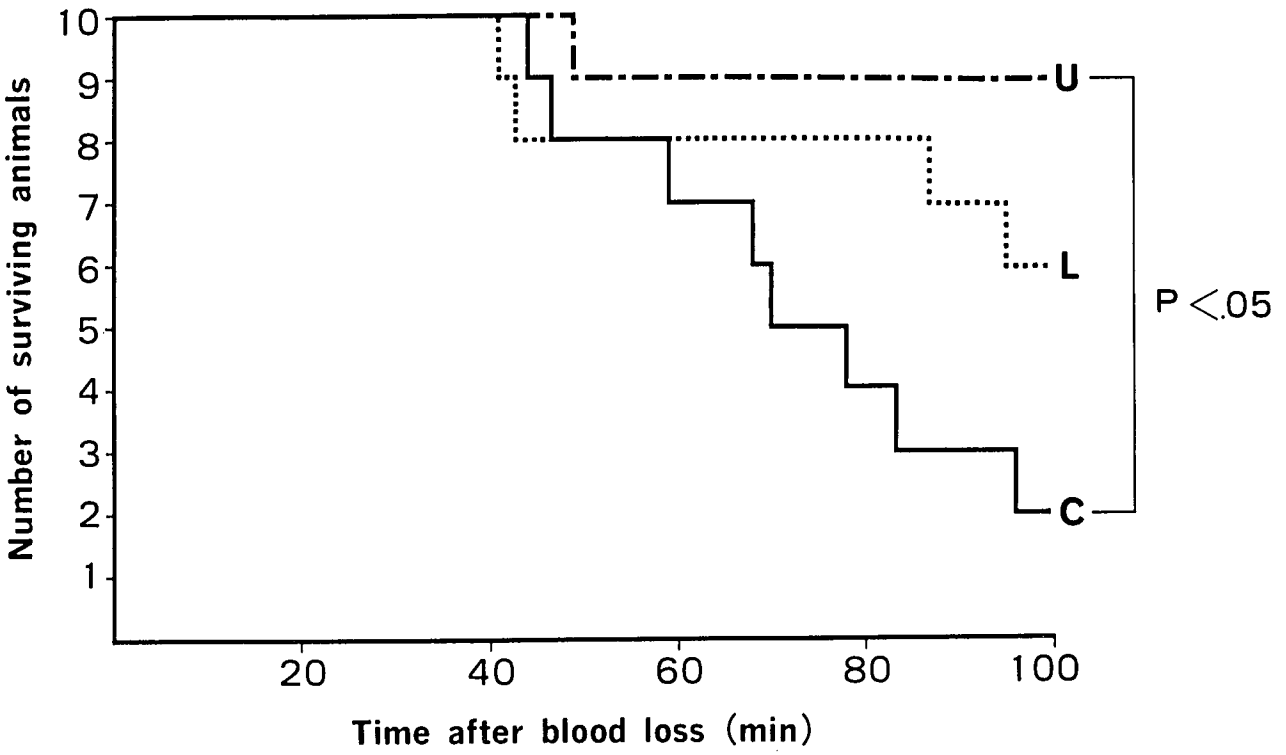

FIG. 1. Curves of 100-min survival after blood loss in the upper- (U) and lower- (L) level epidural, and control (C) groups. The *P* value refers to the statistical significance of the difference in survival between U and C groups over the entire 100-min observation period.

lease of catecholamines from the adrenal medulla. It is characterized by tissue hypoperfusion, hypoxia, increased lactate concentration, and acidosis. Lactate accumulation may be related to the reduction of tissue perfusion and oxygenation in organs using lactate or greater lactate production, or both, in the face of constant or decreased lactate consumption. The peripheral ischemia associated with the shock process may result in a lowered *p*H, which further depresses cardiac function.[1] A portion of the shock syndrome may be related to continued vasoconstriction due to the increased plasma catecholamine concentrations. Lillehei[1] and other investigators[2-6] demonstrated that the α-adrenergic blocker phenoxybenzamine and phentolamine increased survival in animals in irreversible hemorrhagic shock. The rationale underlying the usefulness is thought to be the relief of constriction in the small arteries, arterioles, and smaller venules during hemorrhage, so that venous return is prompted and a subsequent improvement in cardiac output takes place.

Epidural anesthesia, which induces a preganglionic sympathetic blockade, has been reported to interfere with the physiologic response of the sympathoadrenal system to hypovolemia.[15,16] Yeager *et al.*[8] reported that epidural anesthesia was associated with more stable intraoperative hemodynamics with fewer episodes of myocardial ischemia. The mechanisms involved are thought to include afferent sensory blockade, decreased adrenergic tone, and systemic vasodilation with a reduction in cardiac preload and afterload. Epidural anesthesia, which has multiple and potentially beneficial physiologic effects,[17,18] may be of benefit in the prevention of single or multiple system failure. Our interest in the effects of epidural anesthesia on hemodynamics and survival following acute blood loss led to studies of these effects in experimental hemorrhagic shock in dogs.

In this study, reductions of MAP and of CI following induced hypovolemia were similar in all groups. In spite of a pronounced decline of MAP, the epinephrine and norepinephrine concentrations were unchanged during upper-level epidural anesthesia. Similar observations have been made in previous studies.[15,16] More stable cardiovascular responses were observed in the upper-level group than the marked alterations in the control group. Moreover, the arterial *p*H declined progressively in the control group, but remained approximately unchanged in the upper-level group. Decreased *p*H may depress cardiac function even further. The survival in the upper-level group was greater than that in the control group. These results support that upper-level epidural anesthesia may make a significant contribution to hemodynamic and metabolic responses following acute blood loss.

On the other hand, the hemodynamics and arterial blood gas values in the lower-level group were similar to those in the control animals. Lower-level epidural anes-

thesia had less effect of suppressing sympathetic overactivity than that of upper-level, and no effect of increasing the survival rate during hemorrhagic shock. Thus, there are several differences between the effects of upper- and of lower-level epidural anesthesia on hemodynamic and catecholamine responses.

The sympathetic nervous system plays an important role in regulating regional blood flow. Sympathetic blockade and resulting loss of vasomotor tone can cause considerable changes in the distribution of cardiac output. Vasoconstriction involving large and small arteries in the unblocked area has previously been demonstrated using scintigraphic regional blood volume measurements[19] or pulsed Doppler blood flowmeter.[20] This may be one explanation for the association of similar degrees of arterial hypotension with similar volumes of blood loss, regardless of the absence or presence of sympathetic blockade. Species specificity may also account for this observation. Dogs have gastrointestinal tracts that can act as the shock organ.

It is very difficult to measure directly the extent of the sympathetic blockade in this animal study. Therefore, in the present study, it was assumed to be similar to the spread of a similar volume of radiographic contrast material in the epidural space. The rationale behind this assumption is as follows. Previous studies[7] have reported that the volume of local anesthetic required to provide adequate spread over the cervical and upper thoracic epidural space in dogs (15–25 kg) ranged from 1.5–3 ml, and that the extent and effectiveness of a blockade was confirmed by loss of pain sensation. The degree and onset of bradycardia and hypotension following epidural injection in the upper-level group was similar to those in other studies[21,22] in which thoracic epidural analgesia was performed in dogs. Moreover, in contrast to the lower-level group, the finding that normal reflex tachycardia associated with hypotension had been absent in the upper-level group supported sympathetic blockade of upper four or five thoracic segments.[7,23]

The results of this study indicate that upper-level epidural anesthesia may be associated with inhibition of catecholamine increase despite severe hypovolemia, while lower-level epidural anesthesia did not inhibit the rise in catecholamine concentrations. This finding confirmed the results of a previous study[24] performed during spinal anesthesia. In that study, anesthesia involving only lower thoracic dermatomes failed to inhibit catecholamine release, but when the upper thoracic dermatomes were involved, there was inhibition of catecholamine increase. These results suggest that in dogs upper-level epidural anesthesia has the advantage of suppressing sympathetic overactivity following acute blood loss and produces a higher survival rate and a greater hemodynamic stability related to its inhibition of catecholamine release.

These findings, however, are inconsistent with the clinical findings of Bonica *et al.*[25,26] In their study, healthy volunteers received epidural anesthesia to T5 after the removal of 10 ml/kg blood to simulate mild acute hemorrhage. In contrast to the mild cardiovascular changes before blood removal, severe cardiovascular depression associated with cerebral circulatory insufficiency occurred in the presence of hypovolemia. It is therefore believed that hypovolemia should be considered a contraindication to the use of epidural anesthesia. There are variations in experimental design between the studies of Bonica *et al.* and ours. These include species differences (human subjects vs. dogs), mild versus severe hypovolemia, level of sympathetic blockade, and awake versus anesthetized experimental subjects. In addition, we induced epidural anesthesia prior to hemorrhage, whereas Bonica *et al.* did so following mild hemorrhage.

In conclusion, this study demonstrates that, in dogs lightly anesthetized with halothane and nitrous oxide, upper-level epidural anesthesia significantly improves survival in experimental hemorrhagic shock when it is performed before hemorrhage and when the MAP is constant. It should be further emphasized that this finding might be related to species specificity or to the background anesthetic, and thus further studies should focus on the impact of these two factors. Moreover, it is clear that the beneficial effect of epidural anesthesia is only temporary, and can only postpone the death of the animal. Therefore, especially in the presence of uncorrected hypovolemia, our findings do not preclude the dangers of epidural anesthesia, and it is premature to recommend the clinical application of this technique. This survival benefit may be related to the significantly lower catecholamine concentrations attained during upper-level epidural anesthesia. With regard to the mechanism of this benefit, further studies of many other mediators besides plasma catecholamine concentrations are required.

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