Anesthesiology
74:303–308, 1991

Beneficial Effect of Upper Thoracic Epidural Anesthesia in Experimental Hemorrhagic Shock in Dogs: Influence of Circulating Catecholamines

Keizo Shibata, M.D., Yasunori Yamamoto, M.D.,† Tsutomu Kobayashi, M.D.,‡ Seiitsu Murakami, M.D.§*

The question as to whether reduction of plasma catecholamine concentration contributes to the beneficial effects of upper thoracic epidural anesthesia on survival during hemorrhagic shock was examined. Twenty-six dogs were anesthetized with halothane and nitrous oxide, and blood was withdrawn to reduce the mean arterial blood pressure (MAP) to 40 mmHg. The 12 dogs in group A received both upper thoracic epidural anesthesia before the hemorrhage and intravenous infusion of epinephrine (450 ng · kg^{-1} · min^{-1}) and norepinephrine (150 ng · kg^{-1} · min^{-1}) during hemorrhage. The 14 dogs in group B received none of these. At 20 min after the start of the bleeding, plasma catecholamine concentrations were increased in both groups more than ten-fold. There were no significant intergroup differences with respect to these concentrations at any point during the experimental period. During the 100-min period of hemorrhage, 1 of the 12 animals in group A and 10 of the 14 in group B died. A significant difference in survival was seen between the two groups over the 100-min hypotensive period ($P < 0.01$ by the generalized Wilcoxon test). These results suggest that the survival benefit of upper thoracic epidural anesthesia cannot be explained simply by differences in the level of catecholamines in the plasma, and that perhaps differences in the level of catecholamines at the nerve endings or other factors may be more important. (Key words: Anesthetic technique: thoracic epidural. Physiology: hemorrhagic shock. Sympathetic nervous system: epinephrine; norepinephrine.)

IN A PREVIOUS STUDY,[1] we observed that when upper thoracic epidural anesthesia was administered before hemorrhage (at a mean arterial blood pressure [MAP] of 40 mmHg), survival in dogs anesthetized with halothane and nitrous oxide and subjected to experimental hemorrhagic shock was significantly improved and that plasma catecholamine concentrations remained significantly lower. It has been documented in animals that anesthetics influenced not only sympathoadrenal responses to hemorrhage but also survival rates during hemorrhagic hypotension.[2–5] Theye *et al.*,[4] comparing survival rates for dogs bled while anesthetized with cyclopropane, halothane, or isoflurane, reported that survival times were correlated inversely with the relative sympathoadrenal reactivity associated with the particular agent and that lesser survival times were associated with an earlier appearance of increased concentrations of catecholamine.

The purpose of the current study was to investigate whether reduction of plasma catecholamine concentration contributes to the beneficial effects of upper thoracic epidural anesthesia on survival during hemorrhagic shock. We therefore compared survival, hemodynamics, and some indications of stress in hemorrhaged dogs receiving both upper thoracic epidural anesthesia and intravenous catecholamine infusions to these parameters in dogs receiving neither.

Materials and Methods

Twenty-six adult mongrel dogs (9.5–13 kg) were studied. The experimental protocol was approved by the Animal Care Committee of Kanazawa University School of Medicine.

General Procedure

The method of preparation used was similar to that previously reported.[1] Briefly, anesthesia was induced with ketamine (10 mg/kg intramuscularly); the trachea was intubated; and the lungs were mechanically ventilated to maintain arterial carbon dioxide tension (Pa_{CO_2}) between 35 and 40 mmHg. Anesthesia was maintained with halothane (end-tidal 0.5%) and nitrous oxide (50%) in oxygen. The femoral arteries were cannulated bilaterally. One arterial catheter was connected to a blood bag reservoir containing 20 ml citrate–phosphate–dextrose solution for blood withdrawal; the other was used for arterial blood pressure measurement and blood sampling. A triple-lumen pulmonary artery thermodilution catheter (American Edwards, Santa Ana, TX) was inserted *via* the right femoral vein. The two pressure catheters were connected to a polygraphic recorder (Nihon Kohden, Tokyo, Japan) using transducers. In all animals, the vertebral arches of T7–T8 were surgically exposed and an epidural catheter introduced into the epidural space. The position of this catheter was confirmed radiographically with 2 ml iopamidol.

* Assistant Professor.
† Staff Anesthesiologist.
‡ Associate Professor.
§ Professor and Chairman.

Received from the Department of Anesthesiology, School of Medicine, Kanazawa University, Kanazawa, Japan. Accepted for publication October 4, 1990.

Address reprint requests to Dr. Shibata: Department of Anesthesiology, School of Medicine, Kanazawa University, 13-1 Takara-machi, Kanazawa 920, Japan.

Experimental Protocols and Data Acquisition

Twenty minutes after surgical procedures had been completed, baseline measurements were obtained. The hemodynamic variables, including MAP, heart rate (HR), pulmonary capillary wedge pressure (PCWP), central venous pressure, and cardiac output, were measured at end-expiration with the atmospheric pressure as the reference. Cardiac index (CI) was calculated using standard formulas. The dog's body surface area was calculated according to the method of Berry *et al.*[6] Arterial blood was obtained for analysis of arterial *p*H, blood gases, and arterial concentrations of epinephrine, norepinephrine, lactate, pyruvate, aldosterone, adrenocorticotrophic hormone (ACTH), and plasma renin activity.

The animals were randomly assigned to two groups: group A (n = 12) received both upper thoracic epidural anesthesia and intravenous infusion of catecholamines, and group B (n = 14) received neither and served as controls. After baseline measurements had been made, 2 ml of either 1% mepivacaine (group A) or normal saline (group B) was injected *via* the epidural catheter, and half of this dose was given every 50 min thereafter. Twenty minutes after the epidural injection, the hemodynamic and biochemical analyses were repeated. Then, withdrawal of blood was started in all animals, and the MAP was maintained at 40 mmHg by adjusting the blood levels of the reservoir to a constant level above the heart.

In group A, continuous infusion of catecholamines diluted in lactated Ringer's solution (0.2 $ml \cdot kg^{-1} \cdot min^{-1}$ for the lactated Ringer's solution, 450 $ng \cdot kg^{-1} \cdot min^{-1}$ for epinephrine, and 150 $ng \cdot kg^{-1} \cdot min^{-1}$ for norepinephrine) was started simultaneously with the start of bleeding. The infusion was performed through the right atrial port of a pulmonary arterial catheter and continued until the end of the experiment. In group B, lactated Ringer's solution alone was infused at the same rate (0.2 $ml \cdot kg^{-1} \cdot min^{-1}$). During the hemorrhagic period, the blood reservoir was frequently shaken to prevent the sedimentation of blood cells. Hemodynamic measurements and blood samples were taken every 20 min during the 100-min hypotensive period.

Sample Analysis

Arterial blood gases and acid–base status were measured with an automatic analyzer (ABL-2, Radiometer, Copenhagen, Denmark). Blood for determinations of catecholamines, aldosterone, ACTH, and plasma renin activity was placed in iced 7-ml sodium ethylenediaminetetraacetic acid (EDTA) vacuum tubes prior to centrifugation for 10 min at 2,000×g and 4° C. Plasma was decanted and stored at −20° C until analysis. Plasma catecholamine assays were performed with high-performance liquid chromatography (HPLC).[7] Intraassay variation was less than 6% for each catecholamine. Plasma renin activity[8] and the concentrations of plasma aldosterone[9] and ACTH[10] were determined by radioimmunoassay. Intraassay variation was less than 12% for each mediator. For the determination of the arterial lactate and pyruvate concentrations, a 3-ml blood sample was treated with 6 ml 0.6 M perchloric acid and kept at 4° C until enzymatic analysis.[11,12] Intraassay variation was less than 5% for each concentration.

Statistical Analysis

Analysis of variance (ANOVA) and the Bonferroni procedure were used to define differences within and between groups. A generalized Wilcoxon test of Kaplan-Meier curves was used to evaluate the effects of epidural blockade on overall survival. Levels of $P < 0.05$ were considered to be statistically significant. Values were expressed as means ± SD.

Results

There were no significant intergroup differences with respect to body weight between groups A and B (10.9 ± 1.1 and 10.7 ± 0.9 kg, respectively) or maximum bleeding volume (36.7 ± 10.2 and 34.4 ± 9.3 ml/kg, respectively). Iopamidol injected prior to mepivacaine spread epidurally from level C5.4 ± 1.1 to level T8.6 ± 1.8 in group A animals.

Hemodynamic Variables and Blood Gas Analysis

Pa_{CO_2} and Pa_{O_2} did not differ significantly between the two groups at any point during the experimental period. The hemodynamics and other blood gas analyses are presented in table 1. All baseline variables were similar for the two groups. After epidural injection, the HR of dogs in group A remained lower than that of dogs in group B. During an initial 60-min hypotensive period, there were no significant intergroup differences in any variable except the HR. However, at 80 and 100 min after the start of hemorrhage, a significantly greater CI, arterial *p*H, and bicarbonate concentration were observed in group A than in group B. Thus, during the later hypotensive period, both the hemodynamics and the acid–base balance were maintained better in group A dogs than in group B dogs.

Biochemical Measurements

The changes in the biochemical measurements are presented in table 2. All baseline values were similar in the two groups. After bleeding, no significant intergroup

TABLE 1. Hemodynamic Variables and Blood Gas Analyses

Variable/ Group	Baseline	Post-TEA	Time after Start of Hemorrhage (min) 20	40	60	80	100
MAP (mmHg)							
A	126 ± 19	100 ± 19*†	40 ± 3*	40 ± 3*	39 ± 3*	38 ± 2*	39 ± 2*
B	121 ± 13	122 ± 13	40 ± 3*	40 ± 3*	39 ± 4*	36 ± 3*	37 ± 1*
PCWP (mmHg)							
A	11 ± 3	10 ± 2	8 ± 2*	8 ± 2*	8 ± 2*	8 ± 2*	8 ± 2*
B	10 ± 3	10 ± 3	7 ± 3*	7 ± 3*	7 ± 3*	7 ± 4*	7 ± 6*
Heart rate (beats per min)							
A	164 ± 14	130 ± 14*†	150 ± 21*†	149 ± 17*†	150 ± 14*†	149 ± 16*†	151 ± 14*†
B	164 ± 21	165 ± 21	180 ± 23*	193 ± 30*	208 ± 32*	194 ± 40*	209 ± 26*
CI ($l \cdot min^{-1} \cdot m^{-2}$)							
A	3.4 ± 0.6	2.7 ± 0.9	1.0 ± 0.2*	1.0 ± 0.2*	1.0 ± 0.2*	1.0 ± 0.2*†	1.1 ± 0.2*†
B	3.2 ± 0.6	3.2 ± 0.6	1.0 ± 0.2*	0.9 ± 0.2*	0.8 ± 0.2*	0.7 ± 0.1*	0.8 ± 0.1*
*p*Ha							
A	7.28 ± 0.04	7.30 ± 0.04	7.29 ± 0.03	7.21 ± 0.04*	7.17 ± 0.06*	7.17 ± 0.06*†	7.15 ± 0.06*†
B	7.32 ± 0.06	7.31 ± 0.05	7.29 ± 0.06	7.18 ± 0.07*	7.14 ± 0.07*	7.07 ± 0.10*	7.07 ± 0.09*
HCO_3^- (mM)							
A	18.3 ± 2.0	18.3 ± 1.8	15.6 ± 1.2	13.7 ± 1.6*	12.9 ± 2.1*	12.8 ± 2.1*†	13.3 ± 2.5*†
B	18.3 ± 1.8	18.5 ± 1.7	14.2 ± 2.2*	12.5 ± 2.2*	11.5 ± 2.7*	9.5 ± 2.6*	9.1 ± 3.1*

Values are means ± SD.
Post-TEA = 20 min after epidural injection; MAP = mean arterial pressure; PCWP = pulmonary capillary wedge pressure; CI = cardiac index; *p*Ha = arterial *p*H.
* $P < 0.05$ *versus* baseline values; † $P < 0.05$ *versus* group B at the same stage.

differences were seen except in the lactate concentration. Arterial lactate concentrations increased progressively in both groups, but a significantly lower concentration was observed in group A than in group B at 80 and 100 min after the start of hemorrhage.

SURVIVAL DATA

Survival curves for the two groups are shown in figure 1. At the end point of the 100-min hypotensive period, only 4 of the 14 animals in group B survived, whereas 11

TABLE 2. Biochemical Measurements

Measurement/ Group	Baseline	Post-TEA	Time after Start of Hemorrhage (min) 20	40	60	80	100
Epinephrine (ng/ml)							
A	2.0 ± 1.1	1.3 ± 0.6	31 ± 18*	29 ± 21*	31 ± 18*	30 ± 23*	26 ± 13*
B	2.1 ± 1.8	2.6 ± 1.9	33 ± 27*	32 ± 19*	31 ± 28*	36 ± 23*	22 ± 13*
Norepinephrine (ng/ml)							
A	0.4 ± 0.1	0.2 ± 0.1	5.1 ± 2.1*	4.9 ± 2.3*	5.6 ± 2.6*	5.7 ± 4.2*	5.5 ± 2.6*
B	0.4 ± 0.2	0.4 ± 0.2	4.1 ± 3.3*	4.8 ± 3.2*	5.6 ± 4.7*	6.5 ± 4.2*	3.9 ± 3.0*
Lactate (mg/dl)							
A	20 ± 5	20 ± 4	30 ± 6*	44 ± 16*	50± 18*	50 ± 15*†	65 ± 38*†
B	21 ± 10	23 ± 10	36 ± 12*	56 ± 23*	66 ± 17*	81 ± 15*	83 ± 29*
Pyruvate (mg/dl)							
A	0.6 ± 0.2	0.6 ± 0.2	0.7 ± 0.2	0.9 ± 0.3	1.1 ± 0.4	1.1 ± 0.4	1.5 ± 1.0
B	0.6 ± 0.3	0.7 ± 0.3	1.0 ± 0.4	1.2 ± 0.5	1.2 ± 0.5	1.1 ± 0.4	1.3 ± 0.6
PRA ($ng \cdot ml^{-1} \cdot hr^{-1}$)							
A	3.3 ± 1.7	3.1 ± 1.8	6.2 ± 3.0	25 ± 10*	42 ± 15*	47 ± 13*	44 ± 13*
B	3.7 ± 1.3	4.4 ± 1.7	6.6 ± 6.4	18 ± 10*	23 ± 12*	38 ± 12*	40 ± 10*
Aldosterone (ng/dl)							
A	5.8 ± 3.8	10 ± 6.4	37 ± 14*	52 ± 19*	53 ± 14*	56 ± 13*	60 ± 31*
B	7.4 ± 4.4	10 ± 9.4	47 ± 26*	66 ± 31*	74 ± 26*	94 ± 27*	95 ± 28*
ACTH (pg/ml)							
A	45 ± 27	54 ± 17	120 ± 24*	130 ± 23*	138 ± 32*	149 ± 47*	176 ± 57*
B	54 ± 18	43 ± 24	141 ± 67*	142 ± 81*	154 ± 85*	170 ± 67*	193 ± 63*

Values are means ± SD.
PRA = plasma renin activity. See footnote to table 1 for other abbreviations.
* $P < 0.05$ *versus* baseline values; † $P < 0.05$ *versus* group B at the same stage.

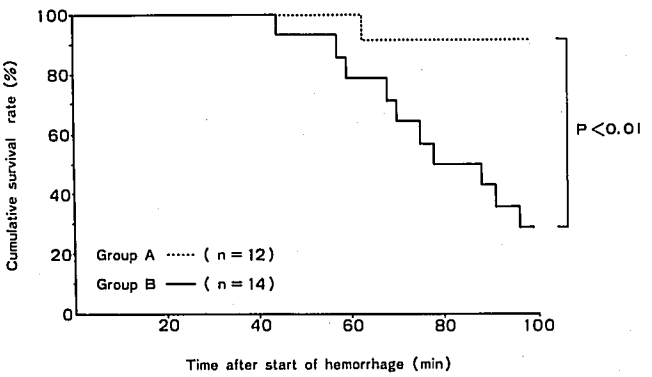

FIG. 1. Curves of 100-min survival after the start of hemorrhage in the two groups. Group A (n = 12) received both upper thoracic epidural anesthesia and intravenous infusion of catecholamines; group B (n = 14) received neither and served as controls. The *P* values refer to the statistical significances of the differences in survival between the two groups over the entire 100-min hypotensive period.

of the 12 animals in group A survived. Most animals died as a result of ventricular fibrillation (1 animal in group A and 9 in group B). Ventricular fibrillation was preceded by frequent premature ventricular contractions (1 animal in group A and 5 in group B) or bradycardia (4 animals in group B). In group B, progressive bradycardia was observed in 1 animal only. Overall survival was significantly better in group A than in group B ($P < 0.01$).

Discussion

The infusion rates of catecholamines in group A animals were determined with other animals in a similar experimental model in a preliminary investigation. The preliminary investigation was designed so that subsequent concentrations of plasma catecholamines would approach as closely as possible those of group B animals (those not receiving upper thoracic epidural anesthesia). From the current study, it is therefore difficult to explain the survival differences between the animals receiving and not receiving upper thoracic epidural anesthesia by the level of catecholamines in the plasma alone.

In the current study, we did not subject a group of animals to catecholamine infusion without upper thoracic epidural anesthesia. A question therefore remains as to whether the addition of exogenous catecholamines would decrease the survival rate during hemorrhagic shock. With their addition, plasma catecholamine concentrations would be much higher than those of the group B animals of the current study. This situation is outside the purpose of the current study, which was to compare the survival rate at identical levels of circulating catecholamines. The above questions, however, need to be ruled out by further studies in order to elucidate the actions of upper thoracic epidural anesthesia.

Increased sympathetic activity is an important compensatory mechanism during hemorrhagic shock, while the increase of catecholamines has potentially damaging effects on the heart.[13,14] Hackel *et al.*[15,16] observed that methods to decrease the effects of catecholamines—methods including cardiac denervation, adrenalectomy, and administration of β-adrenergic blockade—reduced the myocardial damage. Carlson *et al.*[17] demonstrated in hemorrhaged dogs that α-adrenergic blockade delayed subendocardial flow reduction and that β-adrenergic blockade reduced myocardial oxygen consumption. Furthermore, we have found in a previous study[1] that survival in dogs subjected to hemorrhagic shock was significantly improved when upper thoracic epidural anesthesia was administered before hemorrhage. These considerations lead us to believe that the increase of survival rate seen in group A may have resulted from upper thoracic epidural anesthesia and not from the exogenous catecholamine infusion.

Few investigations have examined the influences of upper thoracic epidural anesthesia administered prior to severe hemorrhage. This form of anesthesia appears to have several actions that make it attractive as a means of protection from hemorrhagic insult. The first is its interference with the excessive response of the sympathoadrenal system to hypovolemia. Harrison *et al.*[18] reported that the release of norepinephrine is suppressed in hemorrhagic shock. The adrenal medulla is innervated from segment T4 to L2,[19] and therefore the increase of catecholamines due to sympathetic hyperactivity is prevented under the sympathetic blockade of these segments.[20,21]

The sympathetic nerves to the heart leave the spinal cord chiefly *via* ventral roots T1–T5. Therefore, the second action of upper thoracic epidural anesthesia is prevention of reflex tachycardia.[1,22] During the hypotensive period, the HR of group A animals did not increase, while that of group B animals rose significantly, even in cases in which the circulating catecholamine levels were identical between the two groups. A large increase in the HR would contribute to excessive myocardial work and to further increase of the oxygen requirement. Blomberg *et al.*[23] demonstrated that upper thoracic epidural anesthesia had beneficial effects on the determinants of myocardial oxygen consumption in patients with coronary artery disease. It would be pertinent to examine whether a HR decrease contributes to the survival benefits of upper thoracic epidural anesthesia during hemorrhagic shock; such studies are currently being conducted in this laboratory.

Third, upper thoracic epidural anesthesia prevents a dissociation between myocardial oxygen supply and demand. Hemorrhagic shock has been observed to result in a decrease not only in total coronary blood flow but also in the endocardial–epicardial blood flow ratio.[17,24] Upper thoracic epidural anesthesia in dogs may improve the regional myocardial blood flow distribution by increasing

the flow ratio.[25,26] In a report by Yeager *et al.*[27] assessing the rate of epidural anesthesia on perioperative morbidity, thoracic epidural anesthesia was associated with more stable intraoperative hemodynamics and fewer episodes of myocardial ischemia. The effect might be attributed to the decrease in HR, but the possibility of other mechanisms also exists. Blomberg *et al.*[28] reported that during experimental myocardial ischemia, upper thoracic epidural anesthesia, compared to β-adrenergic blockade, had more favorable effects on central hemodynamics, such as a decrease in the left ventricular end-diastolic pressure without an increase in systemic vascular resistance.

The results of the current study suggest that the level of catecholamines in the plasma is not a key determinant of survival during hemorrhagic shock. Differences in distribution of endogenous and exogenous catecholamines in individual organs are currently unknown. Plasma catecholamines in group A animals originated mainly from those exogenously administered, whereas those in group B animals had overflowed from the sympathetic nerve endings. Therefore, the level of catecholamines released at the nerve endings in tissues such as the myocardium is perhaps much higher in group B than in group A, and it may be strongly argued that the differences at the nerve endings are related to the survival rate.

The relationship between the background anesthetic and catecholamines should be also considered. It is well known that halothane increases myocardial sensitivity to epinephrine-induced arrhythmias more than do other anesthetics.[29] Sumikawa *et al.*[30] reported that the concentration of plasma epinephrine corresponding to the arrythmogenic doses in dogs during halothane anesthesia was 38.7 ng/ml. Since the plasma epinephrine concentrations in our dogs exceeded 30 ng/ml, the sensitization of the myocardium by halothane may have affected the results of the current study.

Thoracic epidural anesthesia has effects on several organs or regulatory systems of the body other than the heart. In the current study, we observed an increase in plasma renin activity after withdrawal of blood in both groups. Stanek *et al.*[20] made a similar observation in dogs under lumbar epidural anesthesia. In all of our animals, plasma concentrations of both aldosterone and ACTH also increased. The arterial *p*H and bicarbonate concentration declined progressively in both groups A and B, but significant intergroup differences in those values were observed at 80 and 100 min after the start of hemorrhage. Acidosis (*p*H ≈6.8–7.4) alone does not appear to be responsible for impaired myocardial function at a *p*H above 6.8 without associated hypoxia.[31] Although the significantly decreased *p*H in the controls (in the current study) did not appear to be the primary cause of the cardiovascular collapse, it may depress cardiac function even further.

Regarding the effects of upper thoracic epidural anesthesia on survival observed in the current study, it should be considered whether comparable hemorrhagic insult was induced in the two groups. The advantages and disadvantages of various experimental models of hemorrhagic shock have been discussed previously.[32] An ideal experimental model should fulfill several requirements: reproducibility, predictable outcome, economic feasibility, and reasonable similarity to clinical reality. It is obvious that few, if any, of the currently known models fulfill all of these requirements. Butterworth *et al.*[33] demonstrated that, in dogs receiving spinal anesthesia and undergoing cardiopulmonary bypass, mixed adrenergic agonists increased both the venous reservoir volume and the MAP in a reversible and dose-dependent manner. In the current study, no significant intergroup differences were seen in plasma catecholamine concentrations during the hemorrhagic period. This may be one explanation for the association of similar degrees of arterial hypotension with similar volumes of blood withdrawal, regardless of the presence or absence of sympathetic blockade. Vasoconstriction in the unblocked areas may also account for this observation.[34,35]

Finally, our experiments did not study effects of the epidural anesthesia used in the presence of preexisting hypovolemia, and consequently, we can make no comment in this regard.

The exact mechanisms responsible for the survival benefit seen in the current study have not yet been elucidated. Consideration must be given to other factors, such as the level of catecholamines at the nerve endings, HR, regional myocardial blood flow, background anesthesia, and experimental models of hemorrhagic shock. We conclude, however, that upper thoracic epidural anesthesia administered in halothane-anesthetized dogs before hemorrhage, when MAP was constant at 40 mmHg, resulted in a significant improvement in the survival of dogs subjected to hemorrhagic shock, even in cases in which the circulating catecholamine levels were high.

The authors wish to thank Mr. C. W. P. Reynolds for his assistance with the English writing of this paper.

References

1. Shibata K, Yamamoto Y, Murakami S: Effects of epidural anesthesia on cardiovascular response and survival in experimental hemorrhagic shock in dogs. ANESTHESIOLOGY 71:953–959, 1989
2. Weiskopf RB, Bogetz MS, Roizen MF, Reid IA: Cardiovascular and metabolic sequelae of inducing anesthesia with ketamine or thiopental in hypovolemic swine. ANESTHESIOLOGY 60:214–219, 1984
3. Weiskopf RB, Bogetz MS: Cardiovascular actions of nitrous oxide or halothane in hypovolemic swine. ANESTHESIOLOGY 63:509–516, 1985

4. Theye RA, Perry LB, Brzica SM: Influence of anesthetic agent on response to hemorrhagic hypotension. ANESTHESIOLOGY 40:32–40, 1974
5. Longnecker DE, Sturgill BC: Influence of anesthetic agent on survival following hemorrhage. ANESTHESIOLOGY 45:516–521, 1976
6. Berry AJ, Geer RT, Marshall C, Wu WH, Zbuzek VM, Marshall BE: The effect of long-term controlled mechanical ventilation with positive end-expiratory pressure on renal function in dogs. ANESTHESIOLOGY 61:406–415, 1984
7. Yui Y, Fujita T, Yamamoto T, Itokawa Y, Kawai C: Liquid-chromatographic determination of norepinephrine and epinephrine in human plasma. Clin Chem 26:194–196, 1980
8. Haber E, Koerner T, Page LB, Kliman B, Purnode A: Application of a radioimmunoassay for angiotensin I to the physiologic measurement of plasma renin activity in normal human subjects. J Clin Endocrinol Metab 29:1349–1355, 1969
9. Ogihara T, Iinuma K, Nishi K, Arakawa Y, Takagi A, Kurata K, Miyai K, Kumahara Y: A non-chromatographic non-extraction radioimmunoassay for serum aldosterone. J Clin Endocrinol Metab 45:726–731, 1977
10. Orth DN, Nicholson WE: Bioactive and immunoreactive adrenocorticotropin in normal equine pituitary and in pituitary tumors of horses with Cushing's disease. Endocrinology 111:559–563, 1982
11. Gutmann I, Wahlefeld AW: L-(+)-lactate: Determination with lactate dehydrogenase and NAD, Methods of Enzymatic Analysis. Edited by Bergmeyer HU. New York, Verlag Chemie Weinheim and Academic Press, 1974, pp 1464–1468
12. Czok R, Lamprecht W: Pyruvate, phosphoenolpyruvate and D-glycerate-2-phosphate, Methods of Enzymatic Analysis. Edited by Bergmeyer HU. New York, Verlag Chemie Weinheim and Academic Press, 1974, pp 1446–1451
13. Glaviano VV, Klouda MA: Myocardial catecholamines and stimulation of the stellate ganglion in hemorrhagic shock. Am J Physiol 209:751–756, 1965
14. Martin AM, Hackel DB, Entman ML, Capp MP, Spach MS: Mechanisms in the development of myocardial lesions in hemorrhagic shock. Ann NY Acad Sci 156:79–90, 1969
15. Hackel DB, Martin AM, Spach MS, Sieker HO: Hemorrhagic shock in dogs. Arch Pathol 77:575–581, 1964
16. Hackel DB, Ratliff NB, Mikat E: The heart in shock. Circ Res 35: 805–811, 1974
17. Carlson EL, Selinger SL, Utley J, Hoffman JIE: Intramyocardial distribution of blood flow in hemorrhagic shock in anesthetized dogs. Am J Physiol 230:41–49, 1976
18. Harrison DC, Chidsey CA, Braunwald E: Effect of hemorrhagic shock on release of norepinephrine by tyramine. Am J Physiol 206:1262–1266, 1964
19. Cummings JF: Thoracolumbar preganglionic neurons and adrenal innervation in the dog. Acta Anat (Basel) 73:27–37, 1969
20. Stanek B, Schwarz M, Zimpfer M, Raberger G: Plasma concentrations of noradrenaline and adrenaline and plasma renin activity during extradural blockade in dogs. Br J Anaesth 52:305–311, 1980
21. Ecoffey C, Edouard A, Pruszczynski W, Taly E, Samii K: Effects of epidural anesthesia on catecholamines, renin activity, and vasopressin changes induced by tilt in elderly men. ANESTHESIOLOGY 62:294–297, 1985
22. Hotvedt R, Platou ES, Refsum H: Electrophysiological effects of thoracic epidural analgesia in the dog heart in situ. Cardiovasc Res 17:259–66, 1983
23. Blomberg S, Emanuelsson H, Ricksten SE: Thoracic epidural anesthesia and central hemodynamics in patients with unstable angina pectoris. Anesth Analg 69:558–562, 1989
24. Adiseshiah M, Baird RJ: Correlation of the changes in diastolic myocardial tissue pressure and regional coronary blood flow in hemorrhagic and endotoxic shock. J Surg Res 24:20–25, 1978
25. Klassen GA, Bramwell RS, Bromage PR, Zborowska-Sluis DT: Effect of acute sympathectomy by epidural anesthesia on the canine coronary circulation. ANESTHESIOLOGY 52:8–15, 1980
26. Davis RF, DeBoer LWV, Maroko PR: Thoracic epidural anesthesia reduces myocardial infarct size after coronary artery occlusion in dogs. Anesth Analg 65:711–717, 1986
27. Yeager MP, Glass DD, Neff RK, Brinck-Johnsen T: Epidural anesthesia and analgesia in high-risk surgical patients. ANESTHESIOLOGY 66:729–736, 1987
28. Blomberg S, Ricksten SE: Effects of thoracic epidural anaesthesia on central haemodynamics compared to cardiac beta adrenoceptor blockade in conscious rats with acute myocardial infarction. Acta Anaesthesiol Scand 34:1–7, 1990
29. Joas TA, Stevens WC: Comparison of the arrhythmic doses of epinephrine during Forane, halothane and fluroxene anesthesia in dogs. ANESTHESIOLOGY 35:48–53, 1971
30. Sumikawa K, Ishizaka N, Suzaki M: Arrhythmic plasma levels of epinephrine during halothane, enflurane, and pentbarbital anesthesia in the dog. ANESTHESIOLOGY 58:322–325, 1983
31. Goodyer AVN: Left ventricular function and tissue hypoxia in irreversible hemorrhagic and endotoxin shock. Am J Physiol 212:444–450, 1967
32. Zweifach BW, Fronek A: The interplay of central and peripheral factors in irreversible hemorrhagic shock. Prog Cardiovascular Dis 18:147–180, 1975
33. Butterworth JF, Piccione W, Berrizbeitia LD, Dance G, Shemin RJ, Cohn LH: Augmentation of venous return by adrenergic agonists during spinal anesthesia. Anesth Analg 65:612–616, 1986
34. Arndt JO, Hock A, Stanton-Hicks M, Stuhmeier KD: Peridural anesthesia and the distribution of blood in supine humans. ANESTHESIOLOGY 63:616–623, 1985
35. Baron JF, Payen D, Coriat P, Edouard A, Viars P: Forearm vascular tone and reactivity during lumbar epidural anesthesia. Anesth Analg 67:1065–1070, 1988