Anesthesiology
78:317–325, 1993

Spinal Cord Perfusion Pressure in Dogs after Control of Proximal Aortic Hypertension during Thoracic Aortic Cross-clamping with Esmolol or Sodium Nitroprusside

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Background: Spinal cord perfusion pressure may be reduced when sodium nitroprusside is used to control proximal aortic hypertension during thoracic aortic clamping. The effect of esmolol infusion on spinal cord perfusion pressure during thoracic aortic clamping is unknown. This study compares spinal cord perfusion pressure following control of proximal hypertension with either sodium nitroprusside or esmolol during thoracic aortic clamping.

Methods: The thoracic aorta was cross-clamped for 30 min in 18 dogs anesthetized with halothane. A control group (n = 6) received no treatment of proximal hypertension during cross-clamping. In two other groups, proximal arterial pressure was controlled (100 mmHg) by infusion of either sodium nitroprusside (n = 6) or esmolol (n = 6). Brachial and femoral arterial pressures, spinal cord perfusion pressure, pulmonary artery occlusion, central venous pressures, and cardiac output were monitored. Neurologic assessment was performed 24 h following surgery.

Results: Femoral arterial pressure was lower with nitroprusside (14 ± 3 mmHg) compared to esmolol (24 ± 4 mmHg) after 15 min of aortic cross-clamping. Cerebrospinal fluid pressure increased during aortic cross-clamping in the sodium nitroprusside group (from 7 ± 5 to 16 ± 6 mmHg) but not in esmolol or control groups. Spinal cord perfusion pressure was lower with nitroprusside at 15 min of aortic cross-clamping (2 ± 4 mmHg) compared to control (15 ± 7 mmHg) and esmolol groups (17 ± 11 mmHg). Esmolol infusion reduced cardiac output and increased ventricular filling pressures compared to control and nitroprusside groups.

Conclusions: Esmolol was associated with greater spinal cord perfusion pressure, but adverse hemodynamic effects, when compared with nitroprusside during thoracic aortic cross-clamping. When only surviving dogs (4 control, 5 esmolol, 6 nitroprusside) are considered, the incidence of neurologic deficit was greater in nitroprusside-treated dogs than in either control or esmolol-treated dogs. No difference in outcome was present when all dogs are considered. (Key words: Pharmacology: sodium nitroprusside. Spinal cord: paraplegia. Surgery: thoracic aorta. Sympathetic nervous system: beta-adrenergic antagonist; esmolol.)

POSTOPERATIVE paraplegia remains a significant problem following cross-clamping of the thoracic aorta. This complication is due to infarction of the motor neurons in the anterior spinal cord, with the reported incidence of paraplegia varying from 6% to 40%.[1] The reduction in distal aortic pressure after cross-clamping reduces spinal cord perfusion pressure (SCPP), which is an important determinant of spinal cord integrity.[2,3] Spinal cord perfusion pressure is defined as the difference between the mean distal aortic pressure and cerebrospinal fluid pressure (CSFP).

Because of the abrupt changes in afterload associated with clamping and declamping of the thoracic aorta, a pharmacologic agent with rapid onset and short duration of action may be indicated to control proximal arterial hypertension. Postoperative neurologic dysfunction has been reported following use of sodium nitroprusside to control proximal hypertension. Sodium nitroprusside, a vasodilator, increases cerebral blood flow[4] and CSFP.[5] Therefore, a reduction in SCPP may occur when sodium nitroprusside is infused during thoracic aortic cross-clamping. Esmolol is a recently introduced rapidly acting beta adrenoreceptor antagonist without vasodilatory properties; it has both rapid

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Received from the Departments of Anesthesia and Surgery, Royal College of Surgeons in Ireland, Beaumont Hospital, Dublin. Accepted for publication October 6, 1992. Performed at the Department of Anesthesia and Surgery, Beaumont Hospital, Dublin. Presented in part at the International Anesthesia Research Society Meeting, San Francisco, California, March 13–17, 1992.

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onset and a brief duration of action once discontinued. The objectives of this study were to assess the use of esmolol to control proximal aortic hypertension during thoracic aortic cross-clamping and to compare the hemodynamic effects and spinal cord perfusion pressure with those following sodium nitroprusside.

Methods

This study was approved by the Committee for Animal Experimentation of the Royal College of Surgeons in Ireland. Eighteen fasting mongrel dogs weighing (20.4 ± 1.91 kg) were anesthetized with 25 mg/kg sodium thiopental. Normocapnic controlled ventilation, with oxygen and 1% halothane, at a fresh gas flow of 100 $ml \cdot kg^{-1} \cdot min^{-1}$ was commenced. A warming blanket was used to maintain normothermia during the procedure. Catheters were inserted into the right brachial and femoral arteries to measure brachial and femoral arterial pressures, respectively. An Edwards 7-French thermodilution pulmonary artery catheter inserted *via* the left external jugular vein was used to measure pulmonary artery occlusion pressure and central venous pressure (CVP). Cardiac output (CO) was measured in triplicate after injection of 10 ml of ice cold saline at end expiration. A 22-G spinal needle was inserted into the cisterna magna to measure CSFP. Core body temperature was recorded utilizing the thermistor of the pulmonary artery catheter. All pressures were monitored using a Hewlett Packard quartz transducer (Andover, MA, model 129 0A OPT 006) and displayed on a Hewlett Packard monitor (model 78534C). All transducers were zeroed at the level of the cisterna magna, and calibrated electronically prior to use, with the animal in the right lateral position. Arterial blood gases were analyzed by a Corning 300 acid base laboratory (coefficient of variation 1.5%).

When all monitoring catheters were *in situ,* 500 ml 0.9% NaCl at 37° C was infused over 30 min. A thoracotomy was performed in the fifth left intercostal space, and the descending aorta was identified just distal to the origin of the left subclavian artery. Hemodynamic data including proximal arterial pressure *via* the brachial artery, distal arterial pressure (DAP) *via* the femoral artery, CVP, pulmonary artery occlusion pressure, and cerebrospinal fluid pressures were documented. Cardiac output and temperature were recorded, and an arterial sample was taken for blood gas analysis. Spinal cord perfusion pressure was calculated by subtracting cerebrospinal fluid pressure from mean femoral arterial pressure. Five minutes after collection of this set of data, the thoracic aorta was cross-clamped for 30 min (with a noncrushing clamp) just distal to the origin of the left subclavian artery. All the hemodynamic indexes were recorded at 5-min intervals for the duration of cross-clamping.

The dogs were divided into three groups. In group 1 (n = 6), no attempt was made to control proximal systemic blood pressure. In group 2 (n = 6), proximal mean arterial pressure was maintained at 100 mmHg following aortic cross-clamping using a 0.01% sodium nitroprusside infusion. In group 3 (n = 6), an 0.05% esmolol infusion was used to maintain mean blood pressure at 100 mmHg following aortic cross-clamping. All drug infusions were discontinued 5 min before release of the aortic cross-clamping.

Five minutes before clamp release, arterial blood was withdrawn from the brachial artery for blood gas analysis. The aorta was then declamped and hemodynamic measurements were obtained at 5-, 15-, and 30-min intervals after declamping. Further arterial blood gas samples were obtained at 5 and 30 min after clamp release.

Thirty minutes after aortic cross-clamping release, all intravascular catheters used for monitoring were removed and the 1% inspired halothane was discontinued. Intermittent positive pressure ventilation with 100% oxygen was continued until the animals were awake, when their tracheas were extubated. The dogs were transferred to a warm (22° C) pen and 0.3 mg intramuscular buprenorphine was administered for postoperative analgesia. Twenty-four hours after surgery, the dogs underwent neurologic assessment and grading, using Tarlov's criteria,[6] by an assessor who was blinded to group allocation.

The animals were then killed by lethal injection of sodium thiopental.

All data values are expressed as mean ± SD. A two-way analysis of variance with repeated measures was performed to detect significant intergroup differences and intragroup changes with time. *Post hoc* testing was performed by partial F test when analysis of variance detected significant ($P < .05$) intergroup difference or intragroup change. Bonferroni's correction of P values ($P/n < .05$, where n = number of comparisons) was performed where multiple comparisons were made. Kruskal-Wallis analysis of variance was used to analyze Tarlov scores for the three groups as a whole. Dunn's procedure was used for intergroup comparison of Tarlov scores.

Results

The three groups were comparable with respect to body weight and temperature measured before aortic cross-clamping. Hemodynamic function including CVP, pulmonary artery occlusion pressure, mean arterial pressure, CSFP, and acid-base status were similar in all groups prior to aortic cross-clamping (tables 1 and 2).

Following aortic cross-clamping, mean brachial artery pressure decreased to 100 mmHg within 5 min of cross-clamping in both treatment groups (fig. 1). Mean arterial pressure was maintained, at this level, throughout the period of cross-clamping. The mean proximal arterial pressure was significantly greater in the control group compared to both esmolol and sodium nitroprusside groups throughout aortic cross-clamping. After aortic cross-clamping release, mean arterial pressure decreased significantly ($P < .05$) in the sodium nitroprusside group compared to both other groups for the first 15 min after release of cross-clamping. No significant intragroup change in femoral artery pressure occurred during aortic cross-clamping (fig. 1). Femoral arterial pressure was greater with esmolol (28 ± 11 mmHg) than in the nitroprusside group (13 ± 3 mmHg) after 15 min of aortic cross-clamping, but was not different between the groups at other measurement times.

Cerebrospinal fluid pressure was similar in all groups prior to aortic cross-clamping (fig. 1). Significant increase in CSFP was observed after aortic cross-clamping in the nitroprusside group from 7 ± 5 mmHg to 16 ± 6 mmHg at 30 min of aortic cross-clamping. When

Table 1. Hemodynamic and Spinal Cord Perfusion Data with Aortic Cross-clamping

	Baseline	15 min after Clamping	30 min after Aortic Clamping	30 min after Aortic Declamping
Nitroprusside				
BAP (mmHg)	116 ± 23	107 ± 14*	100 ± 10*	96 ± 19
FAP (mmHg)	—	14 ± 3†	19 ± 7	—
CSFP (mmHg)	7 ± 5	16 ± 6‡	16 ± 6‡	10 ± 7
SCPP (mmHg)	—	−2 ± 4*,†	3 ± 8	—
CO (L/min)	3.2 ± 0.9	5.0 ± 0.7†	—	4.2 ± 0.7
PAOP (mmHg)	7 ± 2	12 ± 5	12 ± 6	4 ± 2
CVP (mmHg)	64 ± 2	10 ± 4	9 ± 3	4 ± 3
Esmolol				
BAP (mmHg)	122 ± 13	104 ± 5§	97 ± 16§	104 ± 24
FAP (mmHg)	—	28 ± 11	33 ± 15	—
CSFP (mmHg)	7 ± 3	11 ± 5	9 ± 4	5 ± 3
SCPP (mmHg)	—	17 ± 11†	24 ± 15	—
CO (L/min)	3.6 ± 1	0.8 ± 0.1†,§,¶	—	3.7 ± 1
PAOP (mmHg)	8 ± 5	22 ± 3¶	23 ± 5¶	5 ± 2
CVP (mmHg)	4 ± 4	16 ± 4§,¶	12 ± 3¶	3 ± 3
Control				
BAP (mmHg)	121 ± 10	141 ± 9*,§	146 ± 8*,§	108 ± 5
FAP (mmHg)	—	24 ± 4	26 ± 9	—
CSFP (mmHg)	8 ± 5	9 ± 3	9 ± 3	7 ± 3
SCPP (mmHg)	—	15 ± 5*	17 ± 8	—
CO (L/min)	4 ± 2.2	3.3 ± 1.2§	—	3.9 ± 2.6
PAOP (mmHg)	6 ± 3	15 ± 7	15 ± 3	5 ± 3
CVP (mmHg)	4 ± 4	6 ± 2§	7 ± 3	4 ± 3

Values are mean ± SD.

BAP = brachial artery presssure; FAP = femoral artery pressure; CSFP = cerebrospinal fluid pressure; SCPP = spinal cord perfusion pressure; CO = cardiac output; PAOP = pulmonary artery occlusion pressure; CVP = central venous pressure.

* $P < .05$, nitroprusside *versus* control (between-group).

† $P < .05$, nitroprusside *versus* esmolol (between-group).

‡ $P < .05$, nitroprusside (within-group).

§ $P < .05$, esmolol *versus* control (between-group).

¶ $P < .05$, esmolol (within-group).

Table 2. Temperature and Arterial Blood Gas Data

	Baseline	25 min after Aortic Clamping	5 min after Aortic Declamping	30 min after Aortic Declamping
Nitroprusside				
Temperature (° C)	37.5 ± 0.9	36.2 ± 0.9*		36.2 ± 1.1*
*p*H	7.39 ± 0.1	7.33 ± 0.06	7.15 ± 0.06*	7.27 ± 0.07
P_{CO_2} (mmHg)	31.5 ± 9	25.5 ± 5.3	39 ± 9	33 ± 6.8
HCO_3 (mM)	18.5 ± 1.7	12.8 ± 1.1*	12.9 ± 1.5*§	14.8 ± 2.7*
Esmolol				
Temperature (° C)	37.9 ± 0.5	36.7 ± 0.7†		37.3 ± 0.5
*p*H	7.46 ± 0.1	7.33 ± 0.08	7.19 ± 0.11†	7.33 ± 0.07
P_{CO_2} (mmHg)	28.5 ± 9	24.8 ± 7.5	36.8 ± 9.8†	33 ± 7.5
HCO_3 (mM)	19.2 ± 2.6	12.6 ± 2.9†	13.8 ± 1.9†¶	17 ± 2.3
Control				
Temperature (° C)	38.4 ± 0.8	37.7 ± 0.9		38.0 ± 0.9
*p*H	7.41 ± 0.14	7.33 ± 0.09	7.27 ± 0.07‡	7.38 ± 0.03
P_{CO_2} (mmHg)	36 ± 12.8	36.8 ± 9.8	40.5 ± 8.3	35.3 ± 3.7
HCO_3 (mM)	21.5 ± 1.5	17.8 ± 3.2‡	18.9 ± 1.6‡§¶	19.5 ± 2.2

Values are mean ± SD; n = 5 for blood gas data in nitroprusside group; n = 6 for esmolol and control groups.

* $P < .05$, nitroprusside (within-group).

† $P < .05$, esmolol (within-group).

‡ $P < .05$, control (within-group).

§ $P < .05$, nitroprusside *versus* control (between-group).

¶ $P < .05$, esmolol *versus* control (between-group).

nitroprusside was discontinued at clamp release, CSFP rapidly returned to pre-clamping levels. No significant intergroup differences in CSFP were observed during aortic cross-clamping.

No significant intragroup change in spinal cord perfusion pressure occurred during aortic cross-clamping (fig. 2). In both the control and esmolol groups, mean SCPP was greater than 15 mmHg throughout the cross-clamping period. In the sodium nitroprusside group, SCPP was less than 10 mmHg throughout the cross-clamping period. Spinal cord perfusion pressure was significantly less in the nitroprusside group after 5, 15, 20, and 25 min of aortic cross-clamping when compared with the esmolol group and at 15 and 20 min when compared with the control group. Five dogs in the sodium nitroprusside group had zero SCPP for more than 15 min of cross-clamping time.

Cardiac output measurements were not available in three dogs in the esmolol group 5, 25, and 30 min after aortic cross-clamping. Cardiac output values at these times for all three groups were excluded from statistical analysis. Cardiac output was similar in the three groups prior to aortic cross-clamping (fig. 3, table 1). In the control group, CO was unchanged during the entire procedure. Cardiac output decreased in the esmolol group from a pre-clamping mean of 3.6 ± 0.5 L/min to a nadir of 0.6 ± 0.1 L/min. Cardiac output was lower in the esmolol group when compared with control at 15 and 20 min of aortic cross-clamping and with nitroprusside at 10, 15, and 20 min of aortic occlusion and 15 min after aortic declamping. Sodium nitroprusside infusion was associated with a progressive increase of CO for 15 min after clamp release.

Pulmonary artery occlusion pressure in the control group was significantly increased at 5, 20, and 25 min of aortic cross-clamping (fig. 3, table 1). Pulmonary artery occlusion pressure increased progressively during aortic cross-clamping in the esmolol group from a baseline of 8 ± 2 mmHg to a maximum of 23 ± 2 mmHg. Pulmonary artery occlusion pressure was significantly greater in the esmolol group at 10, 20, and 25 min of aortic cross-clamping than in the nitroprusside group. Five minutes after aortic clamp release, pulmonary artery occlusion pressure was still significantly increased in the esmolol group compared to baseline, nitroprusside, and control values. Central venous pressure was unchanged in the control and nitroprusside groups. In the esmolol group, CVP was ele-

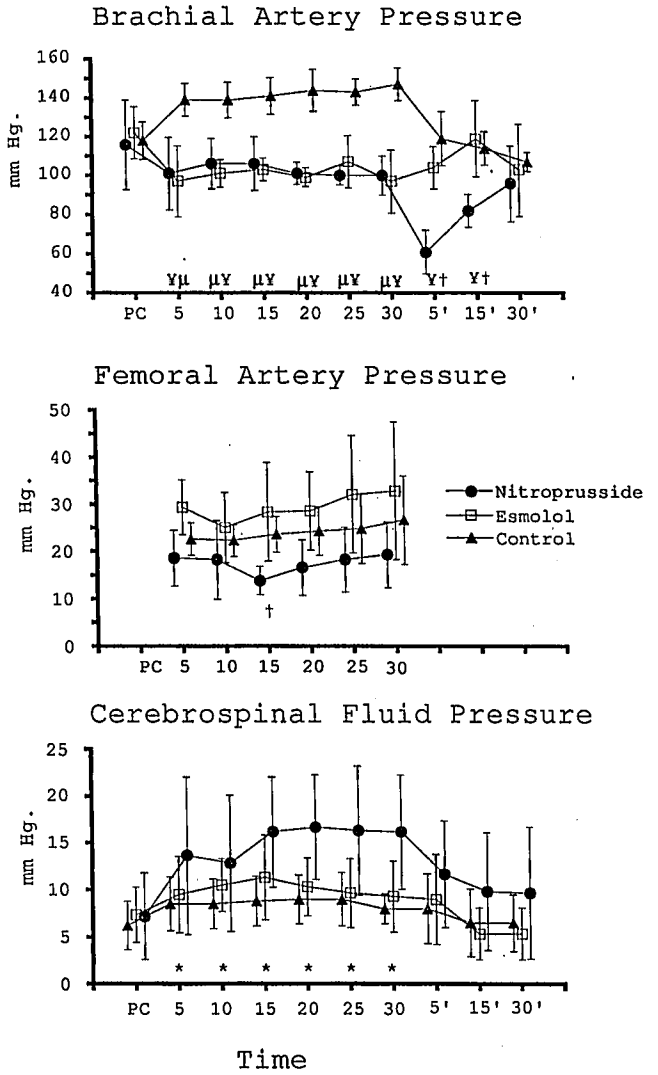

Fig. 1. Brachial artery, femoral artery, and cerebrospinal fluid pressures. All values are expressed as mean ± SD. Time is denoted by PC for pre-clamping, 5 to 30 for duration in minutes of aortic cross-clamping, and 5′ to 30′ for time in minutes after aortic declamping. Significant within-group changes ($P < .05$) are indicated by * for nitroprusside. Significant between-group differences ($P < .05$) are indicated by ‡ for nitroprusside *versus* control, μ for esmolol *versus* control, and † for nitroprusside *versus* esmolol.

vated from 10 to 30 min of aortic cross-clamping. Central venous pressure was greater in the esmolol than the control group at 10 and 15 min of aortic cross-clamping (fig. 3).

There was no significant differences between groups in core temperature before aortic cross-clamping (table 2). In the nitroprusside group, core temperature was significantly lower after 25 min of aortic clamping and 30 min after aortic declamping when compared to baseline values. In the esmolol group, core temperature was lower than baseline after 25 min of aortic cross-clamping. No changes occurred in the control group's core temperature. There were no significant intergroup differences in core temperature. Core body temperatures were maintained above 35.5° C in all animals, apart from one, in the sodium nitroprusside group, in which core temperature dropped to 34.7° C.

Arterial blood gas analysis was not performed in one dog in the nitroprusside group. pH, arterial carbon dioxide tensions, and plasma bicarbonate levels were similar in all groups prior to aortic cross-clamping (fig. 4, table 2). In all three groups, plasma bicarbonate was reduced after 25 min of aortic cross-clamping. At clamp release, pH and plasma bicarbonate were lower in all groups when compared with baseline values. Plasma bicarbonate was lower in both treatment groups compared with the control group 5 min after clamp release. Otherwise, no significant intergroup differences in pH, carbon dioxide tension, and bicarbonate were noted. Plasma bicarbonate was still lower than baseline levels in the nitroprusside group 30 min after aortic clamp release. In the esmolol group alone, significant increase in carbon dioxide occurred at cross-clamping release.

Three dogs, two in the control group and one in the esmolol group, died in the immediate postoperative period. The four survivors in the control group were neurologically intact (Tarlov 4; fig. 5). In the esmolol group, four dogs were neurologically intact (Tarlov 4) and the fifth dog was paraplegic (Tarlov 0). In the sodium nitroprusside group, all dogs demonstrated some degree of neurologic dysfunction, ranging from five

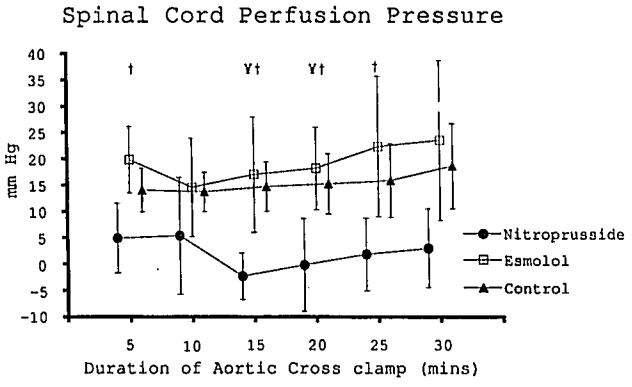

Fig. 2. Spinal cord perfusion pressure during aortic cross-clamping. All values are expressed as mean ± SD. Significant between-group differences ($P < .05$) are indicated by ‡ for nitroprusside *versus* control and † for nitroprusside *versus* esmolol.

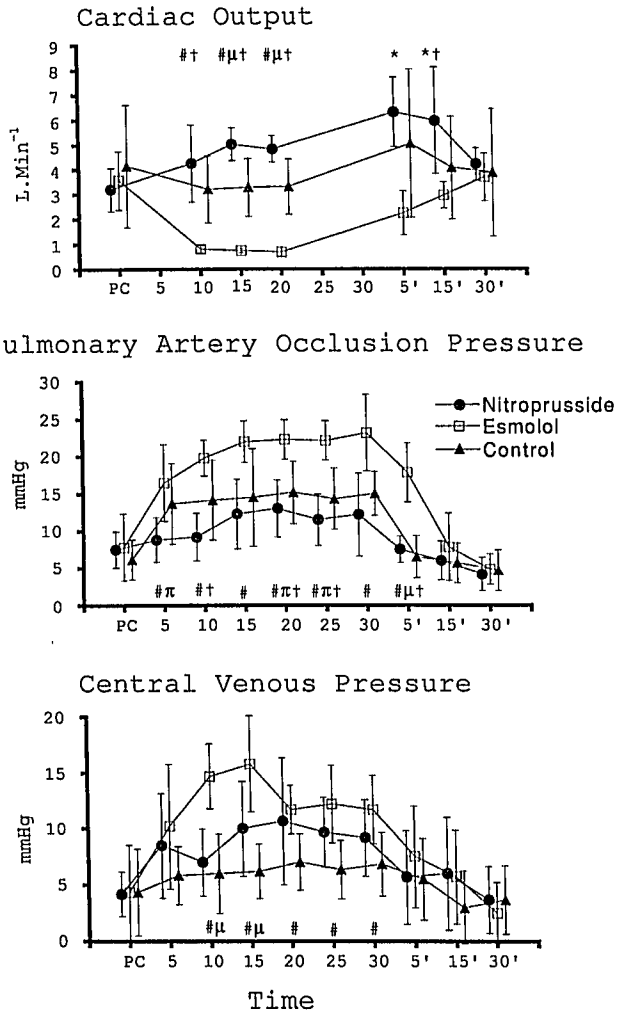

Fig. 3. Changes in cardiac output, pulmonary artery occlusion pressure, and central venous pressure over time. All values are expressed as mean ± SD. Time is denoted by PC for preclamping, 5 to 30 for duration of aortic cross-clamping, and 5′ to 30′ for times after aortic declamping. Significant within-group changes ($P < .05$) are indicated by * for nitroprusside, # for esmolol, and π for control. Significant between-group differences ($P < .05$) are indicated by μ for esmolol *versus* control and † for nitroprusside *versus* esmolol.

with paraplegia (Tarlov 0) to one with a paraparesis (Tarlov 3). The incidence of neurologic deficit in the sodium nitroprusside group was significantly greater than that of the control group and esmolol groups, whereas neurologic outcome in the esmolol and control groups were similar. However, when nonsurviving dogs, in control and esmolol groups, are considered as having a marked neurologic deficit and are included in analysis, then no difference in neurologic outcome between groups is apparent.

Discussion

This study demonstrates that both sodium nitroprusside and esmolol produce rapid and effective control of proximal arterial pressure during experimental cross-clamping of the descending thoracic aorta. The use of sodium nitroprusside was associated with a SCPP significantly lower than in either esmolol or control

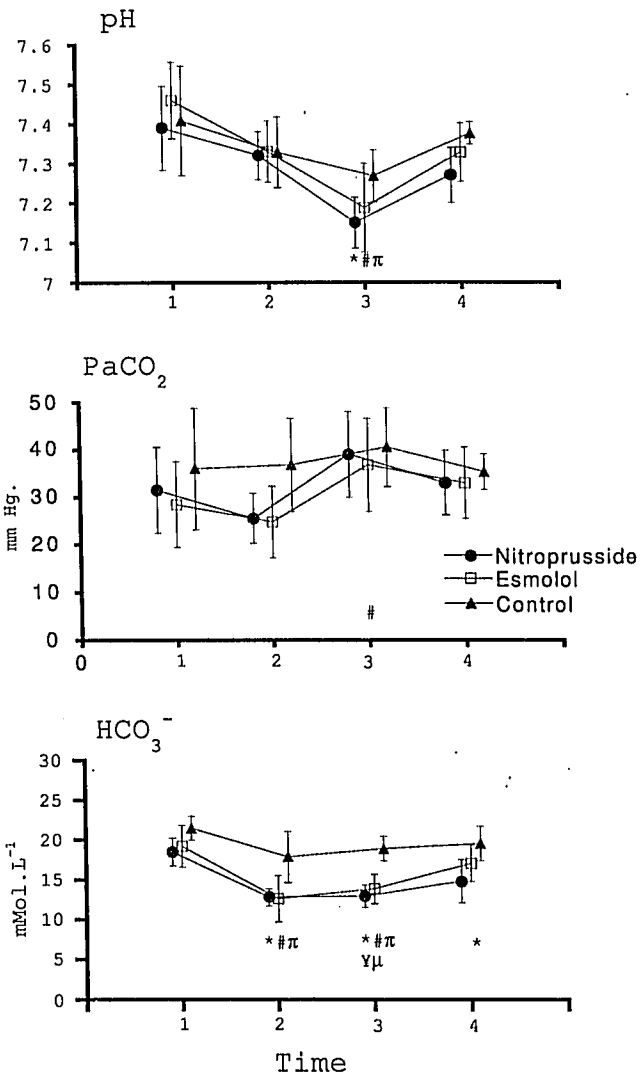

Fig. 4. Results of arterial blood gas analysis. All values are expressed as mean ± SD. Time is denoted as follows: 1 = before aortic cross-clamping; 2 = after 25 min of aortic cross-clamping; 3 = 5 min after aortic declamping; 4 = 30 min after aortic declamping. Significant within-group changes ($P < .05$) are indicated by * for nitroprusside, # for esmolol, and π for control. Significant between-group differences ($P < .05$) are indicated by ‡ for nitroprusside *versus* control, μ for esmolol *versus* control, and † for nitroprusside *versus* esmolol.

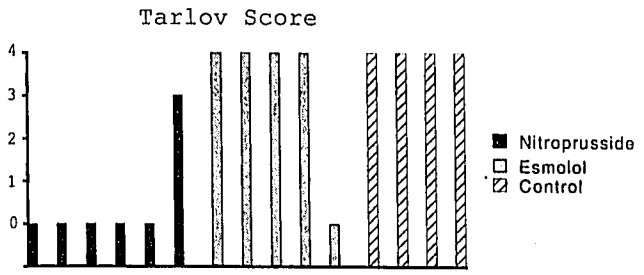

Fig. 5. Tarlov scores at 24 h for 15 surviving animals. Scores are denoted as follows: 0 = spastic paraplegia with no movement of lower limbs; 1 = spastic paraplegia and slight movement of lower limb joints; 2 = good movement of lower limbs but unable to stand; 3 = able to stand but unable to walk normally; 4 = complete recovery.

groups. Esmolol infusion decreased CO and increased ventricular filling pressures compared with control and nitroprusside groups.

The reported incidence of paraplegia after thoracic aortic cross-clamping varies between 6% and 40%.[1] This complication is due to infarction of the motor neurons in the anterior spinal cord. The blood supply of the thoracolumbar spinal cord originates from the vertebral artery and branches of the intercostal arteries, the largest of which, the artery of Adamkiewcz, arises in the lower thoracic region. The autoregulatory limits of spinal cord blood flow in humans have not been determined. However, in rats, spinal cord blood flow is autoregulated in the same manner as cerebral blood flow[7] and becomes pressure dependent when mean arterial pressures decrease to less than 60 mmHg. During aortic cross-clamping, lumbar SCPP is determined by the gradient between DAP and CSFP and decreases after thoracic aortic occlusion. At aortic occlusion, distal aortic pressure decreases and is often less than 40 mmHg.[8] Simultaneously, an increase in CSFP may occur after thoracic aortic occlusion. This increase may be secondary to proximal arterial hypertension[1,2] or may be associated with manipulation of the aortic arch in a reflex manner.[9] Thus, thoracic aortic cross-clamping may compromise lumbar SCPP. Alternatively, CSFP may increase after thoracic aortic occlusion because of redistribution of blood from the splanchnic bed to the central compartment with resultant increase in CVP.[10,11] Cerebrospinal fluid pressure in dogs increases 0.48 mmHg for each 1-mmHg increase in CVP.[12] In this study, there was no significant change in either CVP or CSFP in the control group during thoracic aortic cross-clamping. In the esmolol group, although CVP increased during aortic cross-clamping, the increase in CSFP did not reach statistical significance. The increase in CSFP in the nitroprusside group during aortic cross-clamping was not associated with a significant change in the CVP. These data do not support the theory that increased CSFP after thoracic aortic cross-clamping is secondary to increase in CVP.

The incidence of neurologic dysfunction following thoracic aortic cross-clamping is thought to depend on the site of cross-clamping, the SCPP achieved during cross-clamping, and the duration of cross-clamping. Grubbs *et al.*[13] demonstrated that the critical level of SCPP below which paraplegia results is 11 mmHg in dogs subjected to 40 min of aortic cross-clamping. Similarly, McCullogh *et al.*[1] showed that, in dogs subjected to either 40 or 60 min of aortic cross-clamping, the mean SCPP in paraplegic animals was 19 mmHg as compared with 34 mmHg in normal animals. Oka and Miyamoto[14] demonstrated that the critical SCPP is related to the duration of aortic cross-clamping. Longer duration of aortic cross-clamping requires higher SCPP if irreversible spinal cord ischemia is to be avoided.

The hemodynamic consequences of aortic cross-clamping include proximal arterial hypertension with associated increased left ventricular afterload, decreased ejection fraction and stroke volume with myocardial ischemia, and acute left ventricular failure.[15] Sodium nitroprusside, a potent vasodilator, is commonly infused to control proximal hypertension following aortic cross-clamping. In this study, sodium nitroprusside produced effective control of proximal aortic hypertension. However, mean aortic pressures were significantly less in the sodium nitroprusside group for 15 min after aortic clamp release.

Sodium nitroprusside has been associated with an increase in cerebral blood flow[8] and CSFP[5] when used to control hypertension during thoracic aortic cross-clamping. Concomitant decrease in distal aortic pressure and increase in CSFP with sodium nitroprusside infusion decreases SCPP and may increase the incidence of paraplegia.[5] In this study, SCPP was significantly lower during thoracic aortic clamping with nitroprusside infusion than with either esmolol or the control group. Although sodium nitroprusside infusion significantly increased CSFP from baseline values, there was no significant between-group difference in CSFP at any time during the study. These results do not support previous assumptions that a cerebral vasodilator, such as nitroprusside, amplifies the increase in CSFP sometimes seen with aortic cross-clamping. These results contrast with those of Marini *et al.*,[5] who showed a

significantly higher CSFP in dogs during thoracic aortic clamping with nitroprusside infusion when compared to a control group. However, in a similar study, Shine[16] did not detect a difference in CSFP between control and nitroprusside infusion groups, despite an increase in CSFP within the nitroprusside group. In the present study, DAP was similar in the control group when compared to either esmolol or nitroprusside groups throughout aortic cross-clamping. Nitroprusside infusion was associated with a lower DAP than the esmolol group at only one measurement during thoracic aortic clamping. This result contrasts with those of Marini[5] and Shine,[16] where nitroprusside infusion during aortic cross-clamping was associated with a lower DAP when compared to a control group. However, in a porcine model, Wadouth *et al.*[17] found that nitroprusside infusion was not associated with lower DAP when compared to a control group. Given the similarity in CSFP and DAP between the three groups, and as SCPP was derived from DAP − CSFP, the biologic significance of between-group differences in SCPP must be suspect. Alternatively, it is possible that a type II error occurred in the present study when measurement of DAP and CSFP were analyzed.

Esmolol, an intravenous beta adrenoreceptor blocker that acts within seconds of infusion, achieves peak blockade at 5 min,[18] has a half-life of only 9 min, and is devoid of vasodilator properties. Esmolol is broken down by red cell esterases and thus is not dependent on organ perfusion for elimination during aortic cross-clamping. Esmolol has been shown to decrease lactate production and preserve the ratio between endocardial and epicardial blood flow during acute coronary occlusion in dogs.[19] Thus, esmolol provides an alternative method of controlling proximal aortic hypertension during aortic cross-clamping. In this study, esmolol was as effective as sodium nitroprusside in controlling proximal hypertension, but in contrast to sodium nitroprusside, mean arterial pressures did not decrease significantly after clamp release. Esmolol infusion was associated with significantly greater DAP after 15 min of aortic cross-clamping when compared with nitroprusside infusion. Spinal cord perfusion pressure during esmolol infusion was similar to the control group and was significantly greater than during sodium nitroprusside infusion.

Paraplegia resulted in five of six animals in the sodium nitroprusside group, which represented a significantly worse outcome than that of survivors in the control group. It is of interest that the sixth animal became hypothermic peroperatively (34.7), always maintained a positive SCPP, and was noted to have a paraparesis 24 h after surgery. Decreased spinal cord metabolic rate secondary to hypothermia may have protected this animal from the effects of spinal cord ischemia. Neurologic outcome in the esmolol group was not significantly different from control. Four of five animals in the esmolol group were neurologically intact, and one was paraplegic 24 h after surgery. The one case of paraplegia occurred in the animal with SCPP less than 10 mmHg due to low DAP. Conclusions regarding neurologic outcome must be qualified, however. If animals in control and esmolol groups that died prior to assessment had survived with a neurologic deficit, there would have been no statistically significant difference in neurologic outcome between groups.

There were considerable differences when hemodynamic parameters of the two intervention groups were compared. When infused in association with aortic cross-clamping, esmolol resulted in marked left ventricular dysfunction with decreased CO and increased right and left ventricular filling pressures. This is in keeping with dose-dependent decreases in myocardial contractility known to occur with esmolol infusion.[20] These hemodynamic consequences may preclude its clinical use in patients with preexisting left ventricular dysfunction. Sodium nitroprusside, a potent vasodilator, controlled proximal hypertension by reducing left ventricular afterload and was associated with significantly higher COs than control or esmolol groups. Despite the difference in CO there was no apparent difference in tissue perfusion as assessed by hydrogen ion and bicarbonate concentrations, during and immediately after cross-clamping. This agrees with the observation of Gelman *et al.*[7] that tissue perfusion distal to aortic occlusion is pressure dependent.

In conclusion, proximal aortic hypertension during aortic cross-clamping was controlled effectively by either esmolol or sodium nitroprusside. However, in the esmolol group, SCPP was significantly greater than with sodium nitroprusside infusion. The adverse hemodynamic effects of esmolol infusion may limit use in patients with pre-existing left ventricular dysfunction.

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