Immediate ischemic preconditioning based on somatosensory evoked potentials seems to prevent spinal cord injury following descending thoracic aorta cross-clamping

Ivan S. Bonillo Contreras[a], Luiz Felipe P. Moreira[a,*], Gerson Ballester[b],
Bernardo A. de Mônaco[b], Carmem Lúcia P. Lancellotti[c], Altamiro R. Dias[a], Sérgio A. Oliveira[a]

[a]Cardiothoracic Surgery, Heart Institute (Incor) Division, University of São Paulo Medical School, São Paulo, SP, Brazil
[b]Experimental and Functional Neurosurgery Laboratory, University of São Paulo Medical School, São Paulo, SP, Brazil
[c]Department of Pathology, Santa Casa School of Medicine, São Paulo, SP, Brazil

Abstract

Objective: Delayed ischemic preconditioning has demonstrated neuroprotective effects in spinal cord ischemia. We investigated the effects of immediate ischemic preconditioning based on somatosensory evoked potentials monitoring in a model of spinal cord injury due descending thoracic aorta occlusion in dogs. **Methods**: Twenty-one dogs were submitted to spinal cord ischemia induced by descending thoracic aorta cross-clamping for 45 min. Control group underwent only the aortic cross-clamping ($n=7$), group A underwent one cycle of ischemic preconditioning ($n=7$) and group B underwent three equal cycles of ischemic preconditioning ($n=7$), immediately before the aortic cross-clamping. Ischemic preconditioning cycles were determined by somatosensory evoked potentials monitoring. Neurologic evaluation was performed according to the Tarlov score at 72 h of follow-up. The animals were then sacrificed and the spinal cord harvested for histopathology. **Results**: Aortic pressures before and after the occluded segment were similar in the three groups. Ischemic preconditioning periods corresponded to a mean ischemic time of 3 ± 1 min and a mean recovery time of 7 ± 2 min. Severe paraplegia was observed in three animals in Control group, in four in group A and in none in group B. Tarlov scores of group B were significantly better in comparison to the Control group ($P=0.036$). Histopathologic examination showed severe neuronal necrosis in the thoracic and lumbar gray matter in animals who presented paraplegia. **Conclusions**: Immediate repetitive ischemic preconditioning based on somatosensory evoked potentials monitoring seems to protect spinal cord during descending aorta cross-clamping, reducing paraplegia incidence.
© 2005 Elsevier B.V. All rights reserved.

Keywords: Aortic aneurysm; Spinal cord; Paraplegia; Ischemic preconditioning; Evoked potential

1. Introduction

Major causes of spinal cord injury during thoracoabdominal aortic surgery are the duration and degree of ischemia, the failure to re-establish blood flow to the spinal cord after the repair, and a biochemically mediated reperfusion injury. For several years, numerous methods have been attempted to prevent this complication. With the surgical adjuncts of distal aortic perfusion and cerebrospinal fluid drainage [1,2], the probability of neurological deficits decreased considerably. Nevertheless, acute spinal cord ischemia resulting in paraplegia or paraparesis remains a frequent possibility in the treatment of extent thoracoabdominal aortic aneurysms despite these protective strategies. This complication has also been reported even after endovascular repair of these aneurysms [3].

Since the advent of ischemic preconditioning in the myocardium, more and more attention has been paid to the effects of this phenomenon in the spinal cord. Some authors have demonstrated the improvement of ischemic tolerance of the motor neurons several hours after brief periods of ischemic pretreatment in different animal species [4-7]. On the other hand, the immediate effects of ischemic preconditioning on the spinal cord are controversial [8-12]. The ischemic times required to induce preconditioning are species-specific and organ system specific, and the overall incongruity of the spinal cord's vascular anatomy makes it virtually impossible to determine, with any degree of certainty, the correct ischemic and reperfusion times that need to be involved in this process. In this regard, the sensitivity of somatosensory evoked potentials (SSEP) monitoring to the interruption of spinal cord perfusion has led this method as an effective tool for the intraoperative assessment of spinal cord function and viability [13].

---

* Corresponding author. Address: Division of Surgery, Heart Institute (Incor), University of São Paulo Medical School, Av. Dr. Enéas Carvalho Aguiar, 44, 2 Level, Block 2, Room 13, 05403-000 São Paulo, SP, Brazil. Tel.: +55 11 30695075; fax: +55 11 30695318.

E-mail address: dcimoreira@incor.usp.br (L.F.P. Moreira).

Accordingly, the purpose of this study is to investigate the effects of immediate ischemic preconditioning based on SSEP monitoring in a model of spinal cord injury due to descending thoracic aorta occlusion in dogs.

2. Materials and methods

The Scientific and Ethic Committee of the Heart Institute (Incor), University of São Paulo Medical School approved the experimental protocol. All animal care was performed in compliance with the 'European Convention on Animal Care'.

Twenty-one adult mongrel dogs weighting from 15 to 25 kg were randomly assigned to three different groups according to the ischemic preconditioning protocols. Control group was only submitted to a period of 45 min of aortic occlusion ($n=7$), group A underwent one cycle of ischemic preconditioning ($n=7$) and group B underwent three equal cycles of ischemic preconditioning ($n=7$), immediately before the period of aortic occlusion.

2.1. Animal preparation

The dogs were anesthetized with intravenous pentobarbital sodium (30 mg/kg) and paralyzed with pancuronium bromide (0.3 mg/kg). The trachea was intubated and the lungs were ventilated with 100% oxygen. Respiratory settings included a tidal volume of 12 ml/kg, and a respiratory rate to maintain the partial tension of oxygen at more than 100 mmHg and the partial tension of carbon dioxide between 35 and 45 mmHg, as measured by arterial blood gas analysis. The electrocardiogram was recorded using needle electrodes and a rectal temperature probe was inserted. Under sterile conditions, the left jugular vein was catheterized for intravenous administration of complementary anesthetic drugs, fluids and cefalotin (15 mg/kg). Catheters were also inserted into the left carotid artery and right femoral artery to record the arterial pressures proximal and distal to aortic cross-clamping. All pressures were continuously monitored with a pressure transducer. To monitor SSEP, two subcutaneous electrodes were placed in the right leg, at the region corresponding to the right tibial nerve. One silver lead was inserted into the midline interspinous ligament to be in contact with the spinal cord lamina at the L1–2 levels, and a reference subcutaneous electrode was also placed at the cranium basis.

In the right lateral position, a left thoracotomy in the sixth intercostal space was performed. The aorta was isolated distal to the left subclavian artery and close to the diaphragm. After anticoagulation with heparin (100 U/kg), the aorta was cross-clamped distal to the left subclavian artery and nearby the diaphragm to perform the ischemic preconditioning stages and to induce spinal cord ischemia for 45 min. After unclamping the aorta, 1 mg/kg of protamine was administered. Sodium bicarbonate was also infused to restore the acid–base status. After 1 h of reperfusion, all the animals were hemodynamically stable. All the catheters were removed, the chest was closed in layers, and anesthesia was discontinued. When the dog was breathing spontaneously, the trachea was extubated.

2.2. SSEP monitoring and ischemic preconditioning protocol

Detection of the conduction pathways by SSEP was performed by the stimulation of the right leg. SSEP were recorded in a unipolar fashion with a Medelec Saphire 4ME evoked potential instrument (Medelec, USA). The stimuli used were pulses of 0.1 ms duration and 4–7 mA intensity delivered at 10 Hz. A number of 256 repetitions were averaged. The SSEP were recorded before the initial aortic occlusion, and every minute during the first ischemic preconditioning cycle and for 1 h after the final reperfusion of the aorta.

Ischemic preconditioning periods were determined by SSEP monitoring. Initial aortic occlusion was maintained until the time when N1 wave amplitude in SSEP decreased at less than 60% of its original value (Fig. 1). The ischemic period was followed by aortic reperfusion for a time that was sustained until the return of N1 wave amplitude to the preischemic level. For the dogs in Group A, these periods corresponded to the single ischemic preconditioning cycle. Three equal cycles according to the first ischemic preconditioning cycle were sequentially performed in Group B, immediately before the extended aortic occlusion.

The SSEP recovery time was determined by the SSEP monitoring for 1 h after the final unclamping of the aorta. It corresponded to the time necessary to the return of N1 wave amplitude to the preischemic level.

2.3. Neurologic evaluation

Neurologic status was assessed on the third postoperative day by an independent observer using the modified Tarlov score [14]. A score of 0–4 was assigned to each animal as follows: grade 0, spastic paraplegia with no movement of the hind limbs; grade 1, spastic paraplegia with slight movement of the hind limbs; grade 2, good movement of the hind limbs, but unable to stand; grade 3, able to stand, but unable to walk normally; and grade 4, complete recovery.
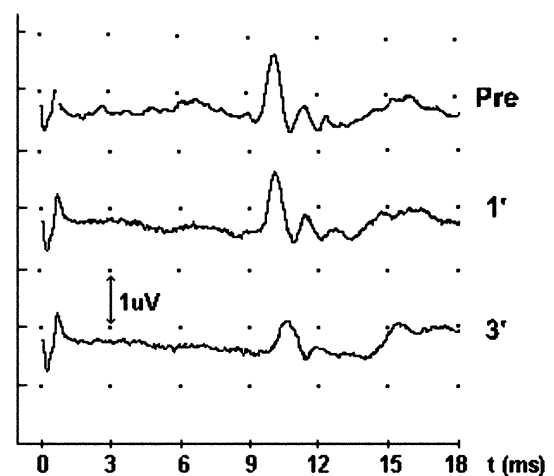

Fig. 1. Recordings of the somatosensory evoked potentials during the first aortic occlusion in the ischemic preconditioning cycle.

2.4. Histopathologic study

All dogs were submitted to euthanasia 72 h after the end of the experiment with an overdose intravenous injection of sodium pentobarbital. The lower thoracic and lumbar spinal cords were fixed in a 10% formalin solution for 120 h and subsequently embedded in paraffin. Serial transverse sections (8 μm) of lower thoracic (T9–T12) and lumbar (L1–L3) spinal cord segments were obtained from each animal and stained with hematoxylin and eosin. An experienced pathologist unaware of the dog's neurologic outcome examined each slice for evidence of cellular necrosis and presence inflammatory cells. Histopathologic changes of the gray matter were graded in the worst samples as follows: grade 3, severe necrosis corresponding to more than one half of the gray matter area; grade 2, mild to moderate necrosis corresponding to less than one half of the gray matter area; grade 1, presence of moderate to high grade of inflammatory cells infiltrate; grade 0, normal histologic appearance.

2.5. Statistical analysis

Physiologic data are presented as the mean ± the standard deviation. Neurologic outcomes, SSEP recovery times and histopathologic scores are expressed as the median and percentiles. The overall group differences regarding physiological variables were compared by single factor analysis of variance, followed by the Tukey procedure. Multiple group differences of neurologic outcomes, SSEP recovery times and histopathologic scores were analyzed using the Kruskal–Wallis procedure, followed by the Mann–Whitney U test with Bonferroni corrections for preconditioning groups' comparison to the Control. The Spearman rank correlation test was used to analyze the relationship between the SSEP recovery times and the neurologic outcome. A P value of less than 0.05 was considered significant as determined with SPSS for Windows, version 10.0 (SPSS, Inc., Chicago, IL).

3. Results

There were no significant differences between the three groups with regard to dogs' weight, and about rectal temperatures, hemoglobin, hematocrit and blood gas analysis during the experimental procedure. No significant differences were also seen between the groups with regard to proximal and distal aortic pressures at baseline, during the aortic cross-clamping and at the reperfusion period (Table 1).
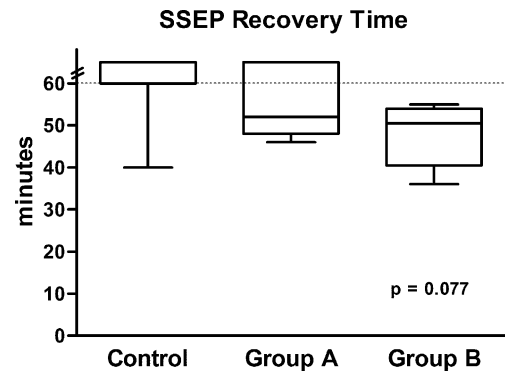

Fig. 2. Plots of the median and quartiles of the somatosensory evoked potential recovery times up to 1 h after spinal cord ischemic induction in the control and ischemic preconditioning groups (Group A, one cycle; Group B, three cycles). Statistical analysis with Kruskal-Wallis test.

During the ischemic preconditioning stages, the times of ischemic induction and of reperfusion based on SSEP monitoring were similar in group A and B. The times for N1 wave to decrease below 60% were 2.7 ± 0.6 min (range, 2–4 min) and 2.6 ± 0.5 min (range, 2–3 min) in group A and B, respectively. Normalization of N1 wave during aortic reperfusion after the first period of ischemic induction occurred in 6.4 ± 1.5 min in group A (range, 4–8 min) and in 7.5 ± 1.6 min in group B (range, 5–10 min). During the other two cycles of ischemic preconditioning performed in Group B, there was no significant changes of N1 wave in all the experiments.

Plots of the SSEP recovery times during the final reperfusion period are depicted in Fig. 2. Most animals in Control group did not recover normal SSEP during the first hour after the unclamping of the aorta, while all dogs in group B and most of the dogs in group A recovered normal SSEP during this period. Nevertheless, the differences between the SSEP recovery times among the three groups were not statistically significant.

The results of the neurologic assessment performed 72 h after the experimental procedure are presented in Table 2. Severe paraplegia was observed in three dogs in Control group, in five in group A and in none in group B. The overall difference between the Tarlov scores of the three groups was statistically significant ($P=0.023$). The neurologic outcome of group B was significantly better in comparison to the Control group ($P=0.036$), while it was similar to the Control group for dogs in group A ($P=0.310$). Fig. 3 shows the existence of a significant correlation between the SSEP recovery times during the final aortic reperfusion period and the neurologic outcome at 72 h of follow-up.

There was no statistically significant difference between the histopathologic scores of the Control and the two preconditioning groups ($P=0.229$), as presented in

Table 1
Proximal and distal mean arterial blood pressure (mmHg)

	Baseline		Aortic cross-clamping	
	Proximal	Distal	Proximal	Distal
Control group	117 ± 14	118 ± 13	121 ± 14	12 ± 6
Group A	111 ± 20	110 ± 18	116 ± 9	16 ± 6
Group B	111 ± 10	110 ± 9	119 ± 12	13 ± 5
P value	0.687	0.347	0.457	0.370

Values are expressed in mean ± standard deviation. Statistical analysis with one-way analysis of variance.

Table 2
Tarlov scores at 72 h after spinal cord ischemic induction

	Normal (4)	Weak (2–3)	Paralysis (0–1)
Control group	3	1	3
Group A	2	0	5
Group B	7	0	0

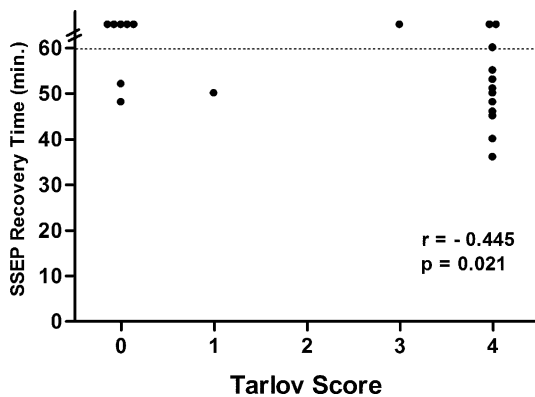Statistical analysis with Kruskal-Wallis test ($P=0.023$).

Fig. 3. Correlation between the somatosensory evoked potential (SSEP) recovery times and the Tarlov score of all the studied animals. Statistical analysis with Spearman correlation test.

Table 3. However, the incidence of severe necrosis corresponding to more than one half of the gray matter area in the thoracic and lumbar sections of the spinal cord occurred only in two animals in Control group and in one in group A. Furthermore, normal histological appearance of the spinal cord was found in only two dogs in Control group, while it was found in four and five animals in group A and B, respectively. Existence of meningic hemorrhage was finally observed in two of the four dogs with normal spinal cord histology in group A.

4. Discussion

The present investigation shows that some degree of ischemic tolerance of the spinal cord to prolonged aortic occlusion can be achieved by immediate ischemic preconditioning, when this process is based on the adequate monitoring of the functional effects of the ischemia and reperfusion phases. This observation represents an important step to add ischemic preconditioning as a neuroprotective strategy in thoracoabdominal aortic surgery, as delayed preconditioning of the human spinal cord would be impractical.

Ischemic preconditioning is the process whereby a sublethal ischemic stress enhances the tolerance of the tissue to a subsequent ischemic insult. This process involves endogenous cellular protective mechanisms, that include an early and a late phase of protection [15]. Although several authors have previously demonstrated the delayed protection seen with brief periods of ischemic induction on the spinal cord [4-7], the acute effects of immediate ischemic preconditioning on that organ have been controversial. Some studies have shown significant impact of previous periods of

Table 3
Histopathologic data

	Grade 0	Grade 1	Grade 2	Grade 3
Control group	2	1	2	2
Group A	4	0	2	1
Group B	5	0	2	0

Statistical analysis with Kruskal–Wallis test ($P=0.229$).

ischemic induction some minutes before prolonged aortic occlusion in the prevention of spinal cord injury [9,12]. Nevertheless, other authors failed to demonstrate the same effect with the use of shorter ischemic periods and intervals in similar animal species [11].

Residual blood flow in the spinal cord during the aortic occlusion may vary between animal species and from animal to animal [16], situation also suggested by the low incidence of spinal cord dysfunction in this experimental study after the ischemic induction in the control group. Therefore, as determinations of proper duration of ischemia and of adequate duration of reperfusion, before the subsequent ischemic induction, are thought to be the key factors for acquisition of immediate and delayed ischemic tolerance, it is mandatory to monitor spinal cord function and viability during both the ischemic and reperfusion periods. In this regard, determination of SSEP provides helpful diagnostic data about the status of spinal cord function [13]. Variations of either amplitude and or latency of the predominant signal peak, in comparison with baseline values, are decisive in diagnosing spinal cord ischemia. Deterioration of the N1 signal component is indicative of diminishing posterior and lateral spinal column sensory conduction, indicating compromised spinal cord perfusion [13,17]. During an ischemic process, we can also see the sequential disappearance of the component waves of SSEP, which return in reverse order after reperfusion [18]. According to spinal cord vascular anatomy, different types of SSEP responses have been identified and used to indicate the necessity of prophylactic measures to attenuate spinal cord ischemia [13].

In this experimental model, we used the decrease of N1 wave signal amplitude of SSEP to define the ischemic duration for preconditioning. This choice was based on its sensitivity to regional hypoperfusion and on the fact that prolonged spinal cord ischemia would result in total signal degradation, indicating a total absence of conduction. The time for N3 and N4 waves in SSEP to disappear may also define appropriated intervals to induce ischemic tolerance, as proposed by Matsumoto et al. [4]. It appears that N1 and N2 waves are presynaptic components, while the contrasting behavior of N3 and N4 waves suggests a postsynaptic origin [18].

Besides the proper duration of ischemic preconditioning, the adequate duration of the reperfusion time, before a subsequent deleterious event, need to allow the complete recover of the sublethal injury determined by the ischemic induction. In this regard, the recover of N1 component wave amplitude of SSEP to preischemic levels in the present study indicates the complete normalization of the conduction pathways.

How many cycles of sublethal ischemic stress should be used to induce ischemic tolerance has also been controversial. Based on the experience with the myocardium [15], we tested the effectiveness of one and three cycles of ischemia followed by reperfusion as the conditions for ischemic preconditioning. Although only the repetitive ischemic preconditioning process was efficient to prevent neurological deficit after descending aorta cross-clamping in the present study, we cannot assume that it was more effective than one single cycle. The high incidence of neurologic deficits with one cycle of ischemic preconditioning

was associated with the occurrence of meningic hemorrhage in two of those experiments, precluding definitive conclusions about its value.

Looking for the lack of neuroprotection by ischemic preconditioning in some previous studies, one can speculate that it might be explained by the insufficient duration of ischemic pretreatment or the inadequate time window between the pretreatment and the subsequent insult. Cheng et al. showed that the later waves of SSEP are more sensitive to ischemia and disappear concomitantly with the decrease of N1 wave amplitude more than 6 min after the induction of spinal cord ischemia in rabbits [18]. Using similar animal species, de Haan et al. [19] and Ueno et al. [11] did not demonstrate induction of spinal cord ischemic tolerance with short periods of sudlethal stress, while Matsumoto et al. [4], Munyao et al. [6] and Sakurai et al. [7] successfully used longer periods of ischemic preconditioning. On the other hand, the response of SSEP to spinal cord ischemic induction seems to be more precocious in dogs [17], justifying the use of short periods of aortic cross-clamping in the preconditioning cycles in the present experimental protocol.

Research into the mechanisms of immediate spinal cord preconditioning is limited, but some studies suggest a role for an increase in spinal cord blood flow [11,20]. Ueno et al. [11] speculated that this effect may occur by the attenuation of postischemic capillary no-reflow and by a direct vasodilating action. Meanwhile, Fan and associates demonstrated that positive changes in spinal cord blood flow were associated with decreased concentrations of nor-epinephrine and activation of the A1 adenosine receptor some minutes after the induction of ischemic preconditioning in rabbits [20]. However, further studies are needed to adequately delineate the biochemistry of acute ischemic preconditioning in the spinal cord.

On the other hand, although several mechanisms have been proposed to explain the delayed protection seen with ischemic preconditioning [15], it is likely that changes in gene expression of protective proteins play an important role in the nervous system [21]. Recent studies have demonstrated the presence of enhanced levels of heat shock proteins 24 h or more after ischemic preconditioning of the spinal cord and that this fact was associated with the acquisition of ischemic tolerance to subsequent lethal ischemia [4,5,7]. Concomitantly, other authors have shown that the prior induction of the heat shock response in the whole animal may increase the content of stress proteins within the spinal cord and enhance the tolerance to ischemic effects of aortic occlusion [22,23]. It is hypothesized that in response to cellular stresses, heat shock proteins may allow denatured proteins to regain their conformation and facilitate the synthesis of new proteins.

The recover of the signal amplitude of the SSEP component waves after final aortic reperfusion has been correlated with the neurologic outcome in experimental [24] and clinical studies [25]. This fact was also observed in the present experience and is probably the result of a less important immediate compromise of the sensitive and motor pathways of the spinal cord. On the other hand, the existence of significant histopathologic changes in two animals submitted to repetitive ischemic preconditioning

without apparent functional compromise opens the possibility of a delayed development of paraparesis or paraplegia. This finding is consistent with the observations of Kakimoto et al. [8] that showed a surprising occurrence of delayed neurologic injury after ischemic preconditioning in a rat model of spinal cord damage.

The present study has some limitations. The number of studied animals was not sufficient to provide an adequate evaluation of possible differences in SSEP recovery times and histopathologic scores, as well as of the difference in neurological outcome observed between the uses of one or three cycles of ischemic preconditioning. In addition, the dogs were followed-up only for 72 h, situation that does not eliminate the possibility of delayed neurologic injury occurrence in those animals with some degree of histopathological damage. Nevertheless, we demonstrated that ischemic tolerance could be immediately achieved in the spinal cord against a clinically relevant ischemic insult, since ischemic preconditioning was based on the proper selection of induction times and intervals.

References

[1] Robertazzi RR, Acinapura AJ. The efficacy of left atrial to femoral artery bypass in the prevention of spinal cord ischemia during aortic surgery. Semin Thorac Cardiovasc Surg 1998;10:67-71.

[2] Coselli JS, Lemaire SA, Koksoy C, Schmittling ZC, Curling PE. Cerebrospinal fluid drainage reduces paraplegia after thoracoabdominal aortic aneurysm repair: results of a randomized clinical trial. J Vasc Surg 2002;35:631-9.

[3] Gravereaux EC, Faries PL, Burks JA, Latessa V, Spielvogel D, Hollier LH, Marin ML. Risk of spinal cord ischemia after endograft repair of thoracic aortic aneurysms. J Vasc Surg 2001;34:997-1003.

[4] Matsumoto M, Ohtake K, Wakamatsu H, Oka S, Kiyoshima T, Nakakimura K, Sakabe T. The time course of acquisition of ischemic tolerance and induction of heat shock protein 70 after a brief period of ischemia in the spinal cord in rabbits. Anesth Analg 2001;92:418-23.

[5] Matsuyama K, Chiba Y, Ihaya A, Kimura T, Tanigawa N, Muraoka R. Effect of spinal cord preconditioning on paraplegia during cross-clamping of the thoracic aorta. Ann Thorac Surg 1997;63:1315-20.

[6] Munyao N, Kaste M, Lindsberg PJ. Tolerization against loss of neuronal function after ischemia-reperfusion injury. Neuroreport 1998;9:321-5.

[7] Sakurai M, Hayashi T, Abe K, Aoki M, Sadahiro M, Tabayashi K. Enhancement of heat shock protein expression after transient ischemia in the preconditioned spinal cord of rabbits. J Vasc Surg 1998;27:720-5.

[8] Kakimoto M, Kawagushi M, Sakamoto T, Inoue S, Nakamura M, Konishi N. Evaluation of rapid ischemic preconditioning in a rabbit model of spinal cord ischemia. Anesthesiology 2004;99:1112-7.

[9] Sirin BH, Ortac R, Cerrahoglu M, Saribulbul O, Baltalarli A, Celebisoy N, Iskesen I, Rendeci O. Ischaemic preconditioning reduces spinal cord injury in transient ischaemia. Acta Cardiol 2002;57:279-85.

[10] Toumpoulis IK, Anagnostopoulos CE, Drossos GE, Malamou-Mitsi VD, Pappa LS, Katritsis DG. Early ischemic preconditioning without hypotension prevents spinal cord injury caused by descending thoracic aortic occlusion. J Thorac Cardiovasc Surg 2003;125:1030-6.

[11] Ueno T, Chao ZL, Okazaki Y, Itoh T. The impact of ischaemic preconditioning on spinal cord blood flow and paraplegia. Cardiovasc Surg 2001;9:575-9.

[12] Zvara DA, Colonna DM, Deal DD, Vernon JC, Gowda M, Lundell JC. Ischemic preconditioning reduces neurologic injury in a rat model of spinal cord ischemia. Ann Thorac Surg 1999;68:874-80.

[13] Robertazzi RR, Cunningham Jr JN. Monitoring of somatosensory evoked potentials: a primer on the intraoperative detection of spinal cord ischemia during aortic reconstructive surgery. Semin Thorac Cardiovasc Surg 1998;10:11-17.

[14] Nylander WA, Plunkett RJ, Hammon JW, Oldfield EH, Meacham WF. Thiopental modification of ischemic spinal cord injury in the dog. Ann Thorac Surg 1982;33:64–8.

[15] Hawaleshka A, Jacobsohn E. Ischaemic preconditioning: mechanisms and potential clinical applications. Can J Anaesth 1998;45:670–82.

[16] Acher CW, Wynn MM. Multifactoral nature of spinal cord circulation. Semin Thorac Cardiovasc Surg 1998;10:7–10.

[17] Laschinger JC, Cunningham Jr JN, Cooper MM, Baumann FG, Spencer FC. Monitoring of somatosensory evoked potentials during surgical procedures on the thoracoabdominal aorta. I. Relationship of aortic cross-clamp duration, changes in somatosensory evoked potentials, and incidence of neurologic dysfunction. J Thorac Cardiovasc Surg 1987; 94:260–5.

[18] Cheng MK, Robertson C, Grossman RG, Foltz R, Williams V. Neurological outcome correlated with spinal evoked potentials in a spinal cord ischemia model. J Neurosurg 1984;60:786–95.

[19] de Haan P, Vanicky I, Jacobs MJHM, Bakker O, Lips J, Meylaerts SAG, Kalkman CJ. Effect of ischemic pretreatment on heat shock protein 72, neurologic outcome, and histopathologic outcome in a rabbit model of spinal cord ischemia. J Thorac Cardiovasc Surg 2000;120:513–9.

[20] Fan T, Wang CC, Wang FM, Cheng F, Qiao H, Liu SL, Guo W, Xiang FY. Experimental study of the protection of ischemic preconditioning to spinal cord ischemia. Surg Neurol 1999;52:299–305.

[21] Lukacova N. The relevance of ischemic preconditioning and tolerance in the neuroprotectivity of ischemia-induced neuronal damage: an up-to-date review. Biologia 1999;54:29–34.

[22] Perdrizet GA, Lena CJ, Shapiro DS, Rewinski MJ. Preoperative stress conditioning prevents paralysis after experimental aortic surgery: increased heat shock protein content is associated with ischemic tolerance of the spinal cord. J Thorac Cardiovasc Surg 2002;124:162–70.

[23] Zhang P, Abraham VS, Kraft KRK, Rabchevsky AG, Scheff SW, Swain JA. Hyperthermic preconditioning protects against spinal cord ischemic injury. Ann Thorac Surg 2000;70:1490–5.

[24] Grabitz K, Freye E, Sandmann W. Somatosensory evoked potential, a prognostic tool for the recovery of motor function following malperfusion of the spinal cord: studies in dogs. J Clin Monit 1993;9:191–5.

[25] Yamamoto N, Takano H, Kitagawa H, Kawaguchi Y, Tsuji H, Uozaki Y. Monitoring for spinal cord ischemia by use of the evoked spinal cord potentials during aortic aneurysm surgery. J Vasc Surg 1994;20: 826–33.