[課程-2]

審査の結果の要旨

氏名　パンティー ニルマル
Panthee Nirmal

Spinal cord injury remains a devastating complication after thoracic and thoracoabdominal aortic aneurysm (TAAA) repairs. Its incidence has been reported to range from 2 to 32 %. N-Methyl-D-Aspartate (NMDA) receptors have been shown to have an important role in mediating calcium mediated injury in neuronal tissue after a wide variety of insults, including ischemic. Memantine is a non-competitive antagonist of NMDA receptor. This study used oral memantine pretreatment for prevention of spinal cord injury and obtained following results:

1. Memantine pretreatment was protective against spinal cord injury as evidenced by higher modified Tarlov scores in memantine treated groups compared with the control group.
2. Memantine was protective against spinal cord injury at regimens of 60 mg per day for 7 days, 60 mg per day for 5 days, 30 mg per day for 5 days, and 30 mg per day for 3 days of oral pretreatment before surgery.
3. Serum level of memantine was similar in all the memantine groups. Modified Tarlov score of 5 (best protection against paraplegia) was obtained with a serum memantine level of 1.55-19.31 ng/ml.

4. Rabbits receiving memantine revealed a gradual decrease in amplitudes of motor evoked potential (MEP) waveforms before finally getting flat; and immediate reappearance of the waveforms after aortic declamping as opposed to control group which had almost immediate flattening of MEP after application of aortic clamp; and no reappearance of waveforms after aortic declamping. Median time to flat MEP after application of clamp was longer for memantine groups as opposed to control group. After declamping, MEP reappeared in majority of memantine treated rabbits as opposed to control rabbits. Mean values of percentage amplitude loss by the end of surgery from baseline values were significantly lower in memantine groups compared with control.
5. Majority of spinal cords were normal in memantine groups whereas majority of the cords in control group were severely ischemic.

Prevention of spinal cord injury requires a multimodality approach with a number of surgical adjuncts and pharmacological adjuncts, which include use of steroids, naloxone, and free radical scavengers. In this study, the applicant looked at another potential pharmacological adjunct using memantine oral pretreatment before planned surgery; and showed its effectiveness against spinal cord injury in a rabbit model of paraplegia. Memantine has already been approved for its clinical use in the treatment of moderate to severe Alzheimer's disease; and NMDA receptor blocking activity of memantine is being continuously explored for potential newer therapeutic applications since last several years. We believe that this research has opened a new possibility of use of oral pretreatment with memantine for combating

spinal cord injury following thoracic and thoracoabdominal aortic aneurysm surgery; and we recommend that this research be used as a dissertation.