Author’s response to reviews

Title: Efficacy of Iloprost and Montelukast Combination on Spinal Cord Ischemia/Reperfusion Injury in a Rat Model

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Author’s response to reviews: see over
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Author's response to reviews: see over
Thank you for consideration of our manuscript for publication in your journal. We have reviewed the above manuscript according to your reviewer’s comments.

Reviewer # 2 (Dr Evvah Karakilic)

MINOR COMMENTS:

1. spelling mistakes: For example page,5; line 8

"For evaluation of sensory function, the placing/stepping reflex was assesment based on" correct form is : "assessment"

   • Done. Other spelling errors were also corrected in the text.

Reviewer # 3 (Dr Hakan Ozhan)

1. Some changes for better reading and understanding should be necessary such as;

   ---Effectiveness of Iloprost and Montelukast Combination on Spinal Cord; ……

   ("Efficacy of…")
The tissue level of HSP-70 was found to be similar among the 3 groups, however, MPO level was found to be significantly higher in the control group than in the sham group or in the study group (p=0.007). The IL-6 receptor level was found to be significantly lower in the sham group than in the control group or in the study group (p=0.005). (HSP-70 was highest and MPO level was lowest in the control group (p=0.007 and p=0.005; respectively).

In Abstract and Results sections; was changed to: The tissue level of HSP-70 was found to be similar among the 3 groups, however, MPO was highest and IL-6 receptor level was lowest in the control group (p=0.007 and p=0.005; respectively).

Several grammatical errors such as; evaluted, assessment, tha sham group

Who has done the hematologic and neurological assessment? Were they blinded to the study groups?

Yes, the observers were blinded to the study groups (Associated sentences were added to the text and highlighted)

After reperfusion, two of the study authors who are blinded to the groups of the animals have evaluated the hindlimb motor function at 6, 12, 24, and 48 hours.

Histopathological assessment was performed by a study author, who is blinded to the groups of the animals.
3. Although the authors have put much effort in montelukast purification, absence of parenteral form is a clear limitation and should be added to the text.

• Done

Main limitation of the present study is preparation of the parenteral form of montelukast from oral tablets due to the absence of commercial parenteral form of this drug in our country.

4. The discussion should be written in-depth regarding montelukast and its potential mechanism on ischemia. Several recently published papers may be referred; such as “Effects of zileuton and montelukast in mouse experimental spinal cord injury; by Genovese et al and Montelukast inhibits caspase-3 activity and ameliorates oxidative damage in the spinal cord and urinary bladder of rats with spinal cord injury by Ersahin et al.

• Done

Previously, Ersahin et al. (31) showed that in a rat model of spinal cord injury montelukast has neuroprotective and antiapoptotic effects on the spinal cord and it also ameliorates bladder tissue damage. They suggest that these effects are mediated by the inhibition of lipid peroxidation, neutrophil accumulation, and pro-inflammatory cytokine release. In another experimental study Genovese et al. (32) also showed that montelukast can reduce the spinal cord inflammation and tissue injury, neutrophil infiltration, TNF-α, COX-2 and pERK1/2 expression, PGE₂ and LTB₄ production, and apoptosis.