

Dec 12, 2013.

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6977-review.doc).

Title: Pathophysiology, diagnosis, and treatment of intermittent claudication in patients with lumbar canal stenosis

Author: Shigeru Kobayashi

Thank you for the referees' comments concerning our manuscript. We are pleased to note the favorable comments of the referees in their opening sentences. We have studied their comments carefully and have made corrections which we hope meet with their approval. I wish to express my appreciation to you and to the referees for suggesting how best to improve our papers. I hope that the revised manuscript is now acceptable for publication.

I am sending a copy of my revision. This copy of revision had performed to be highlighted by underlined to indicate revisions from original submission.

Yours sincerely,

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Reviewer: 1

Is it a review or original article? I have found over-developed part of citing other publications and the main part of the text is only in two paragraphs on the page 15. What exactly the autor would like to convey? That the PGF does not work in a narrow stenosis and it is shown in a small group of patients or he wants to report about up-to-date knowledge in lumbar stenosis problem? But there is a difference in pathophysiology in nerv root compression in the disc herniation cases and the chronic lumbar stenosis ones. I recommend complete revision of the text to highlight the main benefit or aim of the study itself not to express widely accepted theories. The language should be revised by a native speaker to prevent uncertainties and some less skillful formulation

RESPONSE: The referee's comments were most helpful and gave us a better perspective of our work. This is a review article. I have reviewed about the pathophysiology, diagnosis, and treatment of lumbar canal stenosis associated with intermittent claudication in this article. This article have checked by a native speaker "Dr.Adam Meir" in University Collage London Hospital .

Reviewer: 2

The authors are to be congratulated on a very well written article that includes an extensive review of the literature and the potential circulatory disturbance that could play an important role in the mechanism of intermittent claudication in patients with lumbar canal stenosis.

RESPONSE: Thanks a lot.

Reviewer: 3

This is a thorough review of the literature on the subject of nerve root compression and pathophysiology of neurogenic intermittent claudication related to spinal canal stenosis. I suggest that the authors consider to include in their review the work of Shirasaka M which pertinent to the reported subject of study. Shirasaka M et al (BMC

Musculoskeletal Disorders, 2008) have studied that the PGE1 derivate improved blood flow in the arteries but did not induce blood stasis in the veins. Their results suggested that the PGE1 derivate might be a potential therapeutic agent, as it improved blood flow in the nerve roots in a canine model of chronic cauda equina compression. These results are in harmony with what is concluded in this paper. Shirasaka M, Takayama B, Sekiguchi M, Konno S, Kikuchi S. Vasodilative effects of prostaglandin E1 derivate on arteries of nerve roots in a canine model of a chronically compressed cauda equina. BMC Musculoskelet Disord. 2008 Apr 8;9:41. doi: 10.1186/1471-2474-9-41. PMID:18394203 Please insert year of publication at reference 42 (2008).

RESPONSE: Thank you for your nice suggestion. I have added a Shirasaka's paper.

80. Shirasaka M, Takayama B, Sekiguchi M, Konno S, Kikuchi S. Vasodilative effects of prostaglandin E1 derivate on arteries of nerve roots in a canine model of a chronically compressed cauda equina. BMC Musculoskelet Disord. 2008 Apr 8;9:41. doi: 10.1186/1471-2474-9-41. PMID:18394203

AR Meir, SK Kobayashi, JCT Fairbank, JPG Urban. "The effects of cell density on GAG synthesis and metabolism of chondrocytes and disc cells in alginate beads". JBJS B 2003;84-B Issue SUPP_I, 93.