

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Diabetes

**ESPS manuscript NO:** 26956

**Title:** Effect of pioglitazone on nerve conduction velocity of the median nerve in the carpal tunnel in type 2 diabetes patients

**Reviewer's code:** 00004982

**Reviewer's country:** Japan

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-05-03 14:36

**Date reviewed:** 2016-05-14 16:56

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

## COMMENTS TO AUTHORS

The authors examined the effects of pioglitazone on terminal latency and amplitude of motor and sensory components of left median nerve spanning the wrist and covering carpal tunnel. Pioglitazone-group had poorer amplitude in sensory median nerve vs non-Pioglitazone. There was improvement of terminal latency in sensory ulnar nerve for Pioglitazone group. Pioglitazone has beneficial effect on nerve electrophysiology which was nullified when the nerve was exposed to compressive neuropathy. The findings are interesting. I have several concerns as follows. 1. It would be better to add an information that the medical treatment than pioglitazone in the present study. 2. It would be better to add a molecular mechanism of pioglitazone on nerve electrophysiology. 3. It would be better to add a limitation that the number of patients is low.

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**Name of journal:** World Journal of Diabetes

**ESPS manuscript NO:** 26956

**Title:** Effect of pioglitazone on nerve conduction velocity of the median nerve in the carpal tunnel in type 2 diabetes patients

**Reviewer's code:** 01213075

**Reviewer's country:** Taiwan

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-05-03 14:36

**Date reviewed:** 2016-05-15 20:14

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

**SUMMARY:** This clinical study aimed to measure the terminal latency and amplitude of motor and sensory components of left median nerve spanning the wrist and covering carpal tunnel. The authors assessed the patients with diabetes as either pioglitazone or non-pioglitazone group (14 in each group), and conducted electrophysiological testing by nerve conduction velocity (NCV) at baseline and 3 months. The results showed that at 3 months, pioglitazone-group had poorer amplitude in sensory median nerve than non-pioglitazone group ( $p=0.002$ ). The non-pioglitazone group showed improvement in amplitude in the sensory median nerve ( $p=0.01$ ) and amplitude in motor median nerve; and worsening of terminal latency of in motor ulnar nerve( $p=0.043$ ). There was improvement of terminal latency in sensory ulnar nerve for Pioglitazone group ( $p=0.038$ ). The authors concluded that pioglitazone pharmacotherapy confers higher risk of compressive neuropathy. The ulnar nerve showed better electrophysiological parameters in pioglitazone group, although the glycemic control was similar to those not receiving pioglitazone. Pioglitazone has beneficial effect on nerve electrophysiology which was nullified when the nerve was exposed to compressive neuropathy.

COMMENT: The authors reported a new data on the effect of pioglitazone on NCV of the median nerve in the carpal tunnel in type-2 diabetes patients. From the data shown, the authors concluded that non-pioglitazone group showed improvement in amplitude in the sensory and motor median nerve; and worsening of terminal latency of motor ulnar nerve. Pioglitazone group showed improvement of terminal latency in sensory ulnar nerve. Therefore, pioglitazone has beneficial effect on nerve electrophysiology. However, the beneficial effect is nullified by the higher risk of compressive neuropathy conferred. Therefore, the data in this manuscript showed some new data of effects of pioglitazone on the nerve electrophysiology of type 2 DM patients. However, the data seemed somewhat conflicting. Some parameters improved whereas the others deteriorated after treatment with pioglitazone. The nerve electrophysiology data seemed different between median nerve and ulnar nerve, may be between sensory nerve and motor nerve. Therefore the authors may need to study more cases and the mechanism to clarify the real effects of the pioglitazone before being considered to be published in the ESPS. Specific comments: 1. The manuscript focused on the effect of pioglitazone on NCV of the median nerve in the carpal tunnel in type-2 diabetes patients. Therefore, the patients selected should have similar background. The DM duration was longer in non- pioglitazone although no statistical difference was found. The clinical symptoms and blood sugar data should be compared. The indications for use of pioglitazone also needed to be mentioned. 2. The authors may need to explain the protocol of NCV study in more detail. Did these NCV data correspond to the clinical symptoms? How about the time course of the neuropathy? Is NCV study at 3 months optimal for every patient? 3. In Figures 1, 2, and 4 legends, 3 weeks should be 3 months. 4. Some animal studies on the neural effects of pioglitazone can be included for discussion. For example, Jin HY1, Lee KA, Wu JZ, Baek HS, Park TS, The neuroprotective benefit from pioglitazone (PIO) addition on the alpha lipoic acid (ALA)-based treatment in experimental diabetic rats. *Endocrine*. 2014 Dec;47(3):772-82. doi: 10.1007/s12020-014-0198-x. Epub 2014 Feb 18. 5. The possible mechanism should be discussed. Does it work through control of glucose metabolism or another pathway?

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**Name of journal:** World Journal of Diabetes

**ESPS manuscript NO:** 26956

**Title:** Effect of pioglitazone on nerve conduction velocity of the median nerve in the carpal tunnel in type 2 diabetes patients

**Reviewer's code:** 00036318

**Reviewer's country:** Greece

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-05-03 14:36

**Date reviewed:** 2016-05-16 00:43

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
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		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

This is an interesting and well-performed study that reports novel findings regarding the effects of pioglitazone on peripheral nerves and on carpal tunnel syndrome pathogenesis in patients with type 2 diabetes mellitus. The methods are appropriate and the results are clearly presented. I would however suggest that the authors add that the use of pioglitazone is rather limited in patients with type 2 diabetes due to its adverse effects including edema, heart failure, bone fractures and the possible risk for bladder cancer.