Reviewer's report

Title: Regulation of urinary bladder function by protein kinase C in physiology and pathophysiology

Version: 1 Date: 20 Sep 2015

Reviewer: R. Lombardo

Reviewer's report:

The authors aim to describe in this review the involvement of PKC in the physiology and pathophysiology of the bladder. The authors clearly state the objective of their study. The overall content of the review is very interesting and innovative however even if the article has been reorganized, the whole methodology is to be reviewed: the structure of the article and the abstract should reflect the standards of this journal. (see guide for authors section).

Methods:

This section should be written according to the international standards and should describe the strategy used to do the revision of the literature. The actual section is brief and do not include which key words have been used and which databases have been searched.

Results:


Discussion

This section in the former article includes the major findings of the review. The paragraphs are well written and the reader easily follows and understands the different roles of PKC in the regulation of urinary bladder function. However I would have a few remarks:

- 'Modulation of DSM excitability and ion channel activity by PKC': The relationship between VGCC and PKC is not very clear and should be better described, in fact the figure 3 seems to show no real connection between PKC and VGCC . Figure 3 should be included as a reference at the end of the paragraph with a line of conclusion summarizing the relationship between ion channels and PKC. (minor)

- 'Link between muscarinic receptors and PKC signaling in the control of detrusor contractility': The paragraph very clearly elucidates the important role of PKC in the maintenance of detrusor contraction and the lesser role in the peak contraction.
- 'Role of PKC in regulation of spontaneous contractions in the urinary bladder': Very clear paragraph.

- 'Effects of calcium on PKC activity': Very well explained'

- 'Functional modulation of bladder innervation by PKC': The very scarce evidence on this area as stated by the authors make this paragraph of low interest and I would briefly summarise this information in the new discussion section. The paragraph should be deleted. (minor)

- PKC signaling in the human bladder: This new paragraph is well written and summarizes the available evidence on the role of PKC on human bladder.

- 'Regulation of bladder function by PKC under pathophysiological conditions': From the former paragraph it clearly appears that regulation of PKC is associated with both PBOO and DO. However the paragraph is a little confusing. It is not very clear if animals with DO have lower or higher levels of PKC as the first and the second paragraph seem to affirm the opposite: See page 12 lines 6-10 'inhibition of PKC{…}characterized by an increase in non-voiding contractions(DO)' and see page 12 lines 22-26' High levels of PKC stimulation {…} associated with enhanced nerve-mediated contractions'. The authors should better clarify this point. (minor)

- Do the authors think of any human clinical applicability of the PKC activators for patients with DO and frequency(minor).

- Is there any evidence on the role of PKC in detrusor underactivity?(minor)

Conclusions
This section should be reorganized. The second paragraph should be included in the discussion. The first paragraph is well written and represents the Conclusions section.

Limitations
A paragraph including the limitations of the former review should be included.

Abstract and Title
Title: clearly states the main topic of the article.

Abstract: The abstract is missing the results section and a phrase in the background section giving the aim of the study should be added.

Writing
Well written, easy to read.
Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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