Response letter

Response to the comments from Reviewer 2

Dear Reviewer #2:

We really appreciate your valuable comments.

"1) Introduction The aim of the study should be described. Lines 84-86 belong to the Patients and Methods section of the manuscript and should be removed."

Response:

The aim of the study is presenting our experience on the use of this incorporated prophylactic strategy for PDPH after ADP. We have added this as you suggested. Please see "Introduction section: lines 83-85, page 4". Lines 84-86 have not been migrated according to Guidelines and Requirements For Revision from WJCC. Please see "Introduction section: lines 91-94, page 4".

"2) Patients and Methods The authors state that Ethical approval was obtained for information retrieval from the medical records. The question is did they obtain relevant approval before applying this technique? (Epidural infusion of HES). Did these patients have a formal neurologic examination for detecting neurologic deficits? Did they employ a formal evaluation of pain and headache? For example a VAS evaluation?"

Response:

Over the recent five years, we have been trying to find a simple and non-invasive prophylactic strategy for PDPH after ADP with a large-bore epidural needle in obstetric population at our hospital. A variety of prophylactic strategies have been tested, including epidural infusion of HES. We provided patients with a detailed explanation of the possibility of PDPH and the possible consequences of various prophylactic strategies. Whether to employ prophylactic measures or not and which measures to employ were at the patients' sole discretion. Over a one-year study period in this case series, 40 ADPs were reported. Of them, only 20 ADP parturients agreed to receive this incorporated prophylactic strategy (epidural analgesia followed by epidural HES) with

written consent. We really appreciate these patients for their confidence in our anesthesia care and commitment to helping promote advance in obstetric medicine.
These patients did not have a formal neurologic examination for detecting neurologic deficits. The presence of any neurologic deficits (nuchal rigidity, mental status change, motor deficit, paresthesia) was determined with physical examination by the research personnel in charge of follow-up while patients being in the hospital. After discharge, identification of any neurologic deficits depended on patients' self-reporting.
For evaluation of pain and headache, a numeric rating scale was employed ranging from 0 to 10, where 0 represents no pain and 10 represents the worst pain imaginable. We have supplemented this detailed description for headache assessment in the manuscript as you suggested. Please see "Outcome and follow-up section: lines 161-162, page 6".

"3) Discussion The sentence "However, the prophylactic benefit … in closing the dural defect" (Lines 176-179) is confusing and somewhere contradictive. The sentence "Since the case series … studies of this nature"(Lines 202-203) needs also clarification. "

Response:

We have amended "Lines 176-179" to "some ADP parturients developed a PDPH several hours after catheter removal (noted in our clinical practice)" as you suggested. Please see "Discussion section: lines 219-220, page 8".
"Lines 202-203" has been clarified as you suggested. They are amended as "The case series examined in this report was from a single center, which limits the generalizability of the results reported in our paper to a broader circumstance. Furthermore, there is a high chance of selection bias inherent in observational retrospective studies of this nature, given that the decision to employ this incorporated prophylactic strategy is made by parturients themselves." Please see "Discussion section: lines 250-255, page 9".

"4) Other points Please pay attention to : "We first reported" (Abstract and throught the manuscript), epidural placement (line 94), this is still a lack of reliable evidence (line 155). CSEA (line 195) should be given in full. Overall, linguistic editing will imprve the manuscript. "

Response:

We have amended these as you suggested. Also, we asked for linguistic editing from Elsevier Language Editing Service to improve the manuscript.

Response to the comments from Reviewer #3

Dear Reviewer #3,

We really appreciate your critical comments.

"1. Can the study type be clarified (prospective / retrospective)?"

Response:

We have clarified the study type as retrospective as you suggested. Please see "Introduction section: line 85, page 4."

"2. The other details - duration of study, inclusion / exclusion criteria, individual case follow up details are not included."

Response:

We have added the details including duration of study, inclusion/exclusion criteria, and follow-up as you suggested. Please see "Introduction section: lines 86-91, page 4" and "Outcome and follow-up section: lines 160-166, pages 7".

"3. What is the incidence of accidental dural puncture in the author's series?"

During a one-year period from October 2019 to September 2020, a total of 5439 patients have received epidural procedures during labor and delivery at our hospital, of which 40 ADPs were reported. The incidence of ADP was 0.74%. We have indicated this in the manuscript. Please see "Introduction section: lines 86-88, page 4".

"4. When a planned intervention was undertaken, why was it not compared with a control group?"

Response:

Due to the regulatory policies of COVID-19 Isolation and Quarantine, we were short of enough staff to follow up all obstetric patients with ADP during the study period. There were many missing data related to PDPH in the medical records of those patients who did not receive the incorporated prophylactic strategy. Thus, we did not perform a comparison between the incorporated prophylactic strategy and a control group.

"5. The first paragraph in discussion actually deals with the results and requires migration to the 'Results' section. "

Response:

We have migrated this part to the Introduction section according to your suggestion and Guidelines and Requirements For Revision from WJCC. Please see "Introduction section: lines 86-89, page 4" and "Outcome and follow-up section: lines 166-170, page 7".

"6. The group of 9 LSCS & 11 Vaginal delivery pts with different regimens of epidural infusion (dosage, duration) appears quite heterogenous to be grouped together. "

Response:

We agree with your concern about the heterogeneity of this case series. Given the less frequent incidence of ADP during epidural procedures in obstetric population, integrating CS and vaginal delivery patients would be an acceptable choice to assess the prophylactic effect of an intervention over a relatively short period. Existing literature assessing various prophylactic strategies on obstetric population enrolled labor and CS patients as a group.[1,2] In addition, in our case series, the incorporated prophylactic strategy employed in labor and CS patients was basically the same (epidural infusion 4 and 5 mL/hr for labor and CS patients, respectively, followed by 15 ml of HES), except for the duration of epidural infusion. As per standard care in our obstetric unit, patients who deliver vaginally are discharged home 48 h later and those undergoing cesarean section discharged 72 h later. We chose to have the epidural catheter in situ over 24 h for labor delivery and 48 h for CS so that this intervention would not interfere with patients' obstetric care.

References:

[1] Brinser Molly E,Seng David L,Mandell Gordon L et al. Neuraxial morphine after unintentional dural puncture is not associated with reduced postdural puncture headache in obstetric patients.[J] .J Clin Anesth, 2019, 52: 58-62.

[2] Riveros Perez Efrain,Sanchez Maria G,Rocuts Alexander et al. Use of a Triple Prophylactic Strategy to Prevent Post-dural Puncture Headache: An Observational Study.[J] .Cureus, 2020, 12: e7052.

"7. Is the conclusion justified in the absence of a control group?"

Response:

As you pointed out, there is yet no robust evidence of supporting the incorporated prophylactic strategy in the absence of a control group. In this case series, this strategy had a 100% success rate in preventing PDPH after ADP, compared with a success rate of approximately 50%-75% reported in the existing literature for various other prophylactic strategies. We have amended the conclusion as "This case series of twenty parturients described an incorporated strategy that might have great efficacy in preventing PDPH after ADP with a 16-gauge Tuohy needle". Please see "Conclusion section: lines 259-261, page 10."

"8. Have the safety concerns of using HES adequately addressed? [Intensive Care Med. 2017 Oct;43(10):1526-1528. Is the literature inconclusive about the harm of HES?]"

Response:

We have supplemented information about the safety of HES use provided by Dr Schetz's paper [Intensive Care Med. 2017 Oct;43(10):1526-1528] in the manuscript as you suggested. Please see "Discussion section: lines 241-247, page 9".

Response to the comments from Reviewer #4

Dear Reviewer #4**,**

Your valuable comments to our manuscript are well appreciated.

"1- Do you use this technique of injecting starch fluid in the epidural space routinely at your institution? "

Response:

We do not use this technique of injecting HES in the epidural space routinely, because the safety of epidural administration of HES has not been confirmed. We provide obstetric patients who experience ADP during epidural procedures a detailed explanation of the possibility of PDPH and its possible consequences, as well as various prophylactic strategies including epidural HES. Patients choose whether to employ prophylactic measures or not and which measure to use at their discretion.

"2- Do you use in non-obstetric cases too? If you have experience with non-obstetric cases, I think you should add them to your series. "

Response:

By now, we have not yet used this incorporated prophylactic strategy in non-obstetric cases, because the incidences of PDPH after ADP in non-obstetric population (such as orthopedic patients) are relatively low, compared with that in obstetric patients. We do not have any experience with non-obstetric cases, and we are expecting to employ this strategy in broader patient groups at our hospital.

Response to the Editorial Office's comments and suggestions

Dear Science Editor,

We really appreciate your kind comment and hard work on our manuscript.

"(1) I found the title was more than 18 words. The title should be no more than 18 words; (2) I found the "Case Presentation" did not meet our requirements. Please re-write the "Case Presentation" section, and add "FINAL DIAGNOSIS" section to the main text, according to the Guidelines and Requirements for Manuscript Revision."

Response:

We have amended the manuscript as you suggested.

Dear Company editor-in-chief,

Your critical comments help improve our manuscript.

"Before final acceptance, the author(s) must add a table/figure to the manuscript. However, the quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company."

Response:

We have added a table to the manuscript as you suggested. Linguistic editing of the manuscript has been performed by Elsevier Language Editing Service. Please see the attached English Language Certificate.