OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Anesthesiology and Pain Medicine
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Peer Review Report for "Effectiveness of Spinal Analgesia for Labor Pain Compared with Epidural Analgesia"

Author(s): Javad Rahmati, Mohammadali Shahriari, Ali Shahriari, Masoomeh Nataj, Zeinab Shabani, Vihan Moodi

Review Timeline:

Submit Date: 29 Jan 2021
Revised Date: 17 Mar 2021
Accepted Date: 4 Apr 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0)

16 Feb 2021

Dear AE,
This manuscript has well designed, but it needs some explanations and corrections that should be done by the authors. I'm mentioning below each category with few examples.
• Abstract:
- There is a paradox in Bupivacaine dosage in this part with material and method part (3.75 mg vs 2.5 mg). It should be corrected
• Result part:
- In table 1 cervical dilatation in the spinal group should be corrected (5.40. ±5?)
- There is a paradox between the P-value of pruritis in table2 and this part. (003 vs 0.1) please correct it
- Explain and compare between a number of patients who were administrated rescue dosages in both groups
- Explain and compare between the dosage of rescue therapy (pethidine and epidural intermittent bolus) in both groups
- The duration of analgesia was determined as the time after neuraxial block until the VAS score rises ≥ 5, please explain about rescue therapy in VAS >4 and this definition
• Discussion part:

- Add and compare the mean duration of analgesia in spinal and epidural groups in Elkhateeb(7) and Tarek Abdelearr(9) articles
Thanks.

REFEREE: Reviewer | **Revision** (0) 17 Feb 2021

Dear AE,
Manuscript has several errors of different categories that are mentioned below and should be addressed by the authors:
1. In abstract the drug dose in spinal group was different from the dose as mentioned in intervention parts
2. There are some typing and vocabulary errors
3. As epidural placement has catheter and need for extra doses, the unawareness of nurse who responsible for data collecting is somehow impossible
4. As procedure done at cervical dilation 5-6 cm, duration of labor was 107-117min in spinal and epidural groups respectively, which is lower than mean duration of analgesia in both groups, and as postpartum pain differ from prelabor phase, so what is the reason to choose this size and same size of cervical dilation in both nullipara and multipara for start intervention? And how the pain score assessment show increase in postpartum (as VAS>5 used for determining analgesia ends)?
5. For pain control rescue therapy the administration of meperidine was done at VAS score 4 which is lower than analgesia score 5 that has been chosen for analgesia duration endpoint
Thanks.

REFEREE: Reviewer | **Revision** (0) 19 Feb 2021

Dear AE,
Here are my comments for the authors:
- The dose of spinal bupivacaine in the abstract part is different from the dose of bupivacaine in the intervention part.
- Why did the authors select meperidine i.m. as a rescue therapy while they could take it intravenously?
- Were there any failures in performing the spinal or epidural analgesia?
- Consort chart should be added to the text
- There is one sentence in the result part about 3 cases who had spinal analgesia: “ VAS scores of 5 or 6 after 180 min, but none of them requested additional analgesia”. How could the authors explain the cases with the VAS scores of more than 4 without any needs to rescue therapy?
Thanks.

REFEREE: Associate Editor | **Revision** (0) 19 Feb 2021

Dear EIC,
With regards and appreciation for sending the manuscript under the title of: "Effectiveness of Spinal Analgesia for Labor Pain Compared with Epidural Analgesia" to be reviewed. I think the topic was interesting and it was carefully designed. But, according to the

reviewers' comments, the submitted manuscript needs major revision.
Thanks.

REFEREE: Reviewer | **Revision (0)**

11 Mar 2021

Dear AE,
I read with interest this manuscript and my suggestions are as follows for the authors.
- IRCT code was not correct and not available on the IRCT website. Please mention the correct code number.
- Is it reasonable to prescribe the same dose of Fentanyl (50 mcg) in both methods?
- For increasing the quality of this article, consider and add below 21 references:
* Imani F, Lotfi S, Aminisaman J, Shahmohamadi A, Ahmadi A. Comparison of Spinal Versus Epidural Analgesia for Vaginal Delivery: A Randomized Double Blinded Clinical Trial. Anesth Pain Med. 2021;11(1):e108335.
* Almassinokiani F, Ahani N, Akbari P, Rahimzadeh P, Akbari H, et al. Comparative Analgesic Effects of Intradermal and Subdermal Injection of Sterile Water on Active Labor Pain, Anesth Pain Med. 2020;10(2):e99867.
* Derakhshan P, Imani F, Koleini Z S, Barati A. Comparison of Adding Sufentanil and Low-Dose Epinephrine to Bupivacaine in Spinal Anesthesia: A Randomized, Double-Blind, Clinical Trial, Anesth Pain Med. 2018;8(5):e69600
* Fathi M, Imani F, Joudi M, Gudarzi V. Comparison of the Effects of Ringer`s Lactate and Hydroxyethyl Starch on Hemodynamic Parameter After Spinal Anesthesia: A Randomized Clinical Trial. Anesth Pain Med. 2013;2(3):127-33.
* Imani F, Entezary SR, Alebouyeh MR, Parhizgar S. The maternal and neonatal effects of adding tramadol to 2% lidocaine in epidural anesthesia for cesarean section. Anesth Pain Med. 2011;1(1):25-9.
* Gousheh MR, Akhondzade R, Asl Aghahoseini H, Olapour A, Rashidi M. The Effects of Pre-Spinal Anesthesia Administration of Crystalloid and Colloid Solutions on Hypotension in Elective Cesarean Section, Anesth Pain Med. 2018;8(4):e69446.
* Chandra S, Nugroho AM, Agus H, Susilo AP. How Low Can We Go? A Double-Blinded Randomized Controlled Trial to Compare Bupivacaine 5 mg and Bupivacaine 7.5 mg for Spinal Anesthesia in Cesarean Delivery in Indonesian Population, Anesth Pain Med. 2019;9(2):e91275.
Nugroho AM, Sugiarto A, Chandra S, Lembahmanah L, Septica RI, et al. A Comparative Study of Fractionated Versus Single Dose Injection for Spinal Anesthesia During Cesarean Section in Patients with Pregnancy-Induced Hypertension, Anesth Pain Med. 2019;9(1):e85115.
* Shafeinia A, Ghaed MA, Nikoubakht N. The Effect of Phenylephrine Infusion on Maternal Hemodynamic Changes During Spinal Anesthesia for Cesarean Delivery, Anesth Pain Med. 2020;10(1):e99094.
* Olapour A, Akhondzadeh R, Rashidi M, Gousheh M, Homayoon R. Comparing the Effect of Bupivacaine and Ropivacaine in Cesarean Delivery with Spinal Anesthesia, Anesth Pain Med. 2020;10(1):e94155.
* Javaherforooshzadeh F, Pipelzadeh MR, Akhondzadeh R, Adarvishi S, Alghozat M. Effect of Sequential Compression Device on Hemodynamic Changes After Spinal Anesthesia for Caesarean Section: A Randomized Controlled Trial, Anesth Pain Med. 2020;10(5):e104705.

Nikooseresht M, Seifrabiei MA, Hajian P, Khamooshi S. A Clinical Trial on the Effects of Different Regimens of Phenylephrine on Maternal Hemodynamic After Spinal Anesthesia for Cesarean Section, Anesth Pain Med. 2020;10(4):e58048.

Sincerely yours

REFEREE: Associate Editor | **Revision (**0**)**

11 Mar 2021

Dear EIC,

This article needs some corrections.

Regards

REFEREE: EIC | **Revision (**0**)**

11 Mar 2021

Dear Author,

The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.

Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

In the name of God

Dear Editor in-chief

The Journal of : Anesth Pain Med

Thank you most sincerely for your kind consideration and giving us the opportunity to revise our paper entitled entitle " **Effectiveness of Spinal Analgesia for Labor Pain Compared with Epidural Analgesia**. ID: 113350

Here I am submitting the answers to the comments of the honorable reviewers and also the revised version of the paper that was changed according to the precious comments of the reviewers as you had requested. We hope they are to your satisfaction and that of the reviewers.
Following, we provide the answers and the changes made to the paper.

Reviewer # 1

Dear Sir/Madam,

Thank you so much for your precious time and valuable comments.

comment : 1. In abstract the drug dose in spinal group was different from the dose was mentioned in intervention parts.

Correction: Thanks for your valuable comment, the manuscript were corrected as the reviewer suggested and the new changes were highlighted in the manuscript. (lines 6 of abstract)

2. There are some typing and vocabulary errors

Correction: The manuscript was reviewed by a native person for the typing and vocabulary errors and corrected as the reviewer had recommended. The new changes were highlighted yellow in the manuscript.

3. As epidural placement has catheter and need for extra doses, the unawareness of nurse who responsible for data collecting is somehow impossible

Answer ; A nurse who responsible for collecting the relevant data was unaware of the type of intervention and she was only responsible for collecting the relevant data in certain periods . Then data was transferred to the anesthesiologist and the drug was administered via the epidural catheter by the anesthesiologist. In similar studies, a nurse who was responsible to

compare spinal groups and epidural groups was considered blinded to the participants division. As the study cited below:

.

Comparison stage of vaginal delivery in painless labor with epidural & spinal analgesia

Alireza Kamali1, Samane Akbari1, Afsane Norouzi1, Maryam Shokrpour2

The study was conducted in a double-blind procedure and this was confirmed since the intern partner was responsible for completing the project questionnaires and the person who was responsible for the project statistical analysis was completely unaware of the study procedure and the studied groups. The anesthesiologist prepared the drugs and gave to the resident who performed the analgesic labor (spinal and epidural analgesia). The project intern partner who was responsible for complete the questionnaires as well as the person\ who was responsible for doing statistical analysis were blind toward the studied groups.

By the way the sentences of “A nurse who responsible for collecting the relevant data was unaware of the type of intervention” was corrected as the reviewer had recommended. The new changes were highlighted in the manuscript. (lines 14 of **Material and method)**

4. As procedure done at cervical dilation 5-6 cm, duration of labor was 107-117min in spinal and epidural groups respectively, which is lower than mean duration of analgesia in both groups, and as postpartum pain differ from prelabor phase, so what is the reason to choose this size and same size of cervical dilation in both nullipara and multipara for start intervention? And how the pain score assessment show increase in postpartum (as VAS>5 used for determining analgesia ends)?

Answer: The onset of active phase of labor , start from cervical dilatation 6 cm [Williams Obstetric Text Book 2019] and staring the analgesia before this time can protract the labor progression. Thus we choose cervical dilation 5-6 cm. In fact , the mean duration of labor was 107-117min in spinal and epidural groups respectively and the mean duration of labor differs from the entire duration of labor in each individual, and we needed analgesia for the entire time of labor of each patients, and the duration of analgesia was measured only in patients who was in the phase of labor. So the mean duration of analgesia calculated in this way can be longer than the mean duration of labor

5. For pain control rescue therapy the administration of meperidine was done at VAS score 4 which is lower than analgesia score 5 that has been chosen for analgesia duration endpoint

Answer: In our maniscript, we mentioned :meperidine was administrated when the pain score was above 4. The manuscript was corrected as the reviewer had recommended and the new changes were highlighted in the manuscript. (lines 11 of intervention)

Reviewer 2:

Dear Sir/Madam,

Thank you most sincerely for your precious time and valuable comments.

Reviewer Comment For Author:
This manuscript has well designed, but it needs some explanations and corrections. I'm mentioning below each category with few examples.
• Abstract:
- There is paradox in Bupivacaine dosage in this part with material and method part (3.75 mg vs 2.5 mg) . It should be corrected

Correction : Thanks for your valuable comment, the manuscript were corrected as the reviewer suggested and the new changes were highlighted in the manuscript. (lines 6 of abstract)

• Result part:
- In table 1 cervical dilatation in spinal group should be corrected (5.40. ±5?)

Correction : Thanks for your valuable comment, the manuscript were corrected as the reviewer suggested and the new changes were highlighted in the manuscript. 5.40. ±0.5 (Table 1)

- There is paradox between P value of pruritis in table2 and this part. (003 vs 0.1) please correct it

Correction : Thanks for your valuable comment, the manuscript were corrected as the reviewer suggested and the new changes were highlighted in the manuscript. (lines 28 of result)

- Explain and compare between number of patients who were administrated rescue dosages in both groups
- Explain and compare between dosage of rescue therapy (pethidine and epidural intermittent bolus) in both groups

Correction: The manuscript was corrected as the reviewer had recommended and the new changes were added and highlighted in the manuscript. (lines 21-23 of result and Table 3)

- The duration of analgesia was determined as the time after neuraxial block until the VAS score rises ≥ 5, please explain about rescue therapy in VAS >4 and this definition

Correction : In our manuscript , we mentioned :meperidine was administrated when the pain score was above 4 that is the same ≥ 5. The manuscript was corrected as the reviewer had recommended and the new changes were highlighted in the manuscript. (lines 11 of intervention)

• Discussion part:
- Add and compare the mean duration of analgesia in spinal and epidural groups in Elkhateeb(7) and Tarek Abdelearr(9) articles

Correction: The manuscript was corrected as the reviewer had recommended and the new changes were highlighted in the manuscript. (lines 10 , 11 and 31 , 32 of Discussion)

The duration of sensory block was longer (123.21 ± 8.06 min) in **spinal** group versus (103.0 ± 12.62 min) in epidural group.

Duration of sensory block was longer (120.4 ± 15.6 vs 103.2 ± 18.3 min, $p < 0.001$) in S group compared to E group.

Reviewer 3:

Dear Sir/Madam,

Thank you most sincerely for your precious time and valuable comments.

With regards,
Here are my comments:

- The dose of spinal bupivacaine in the abstract part is different from the dose of bupivacaine in the intervention part.

Correction : Thanks for your valuable comment, the manuscript were corrected as the reviewer suggested and the new changes were highlighted in the manuscript. (lines 6 of abstract)

- Why did the authors select meperidine i.m. as a rescue therapy while they could take it intravenously?

Answer : As you know , Meperidine can be used Intra muscular or intravenously for labour analgesia . We use routinely Intra muscular meperidine in our labor room, because of safety for parturients and fetus .

- Were there any failures in performing the spinal or epidural analgesia?
Answer: As the procedures as done by an expert anesthesiologist, so no technical difficulty was seen in any patient. (line 3 of result)

- Consort chart should be added to the text
Answer ; Thanks for your valuable comment .Consort chart added to the text.

- There is one sentence in the result part about 3 cases who had spinal analgesia: " VAS scores of 5 or 6 after 180 min, but none of them requested additional analgesia". How could the authors explain the cases with the VAS scores of more than 4 without any needs to rescue therapy?

Pethidine administration must be depending on the patient condition and progress of delivery. And pethidine administration close to the delivery time may affect neonatal behavior and hinder breast feeding and KMC.

According to our proposal " If the pain intensity was ≥ 5 and the patient requested additional analgesia, 50 mg meperidine was administrated intramuscularly."(line 11,12 of intervention). In our study ,in the Spinal group, successful analgesia remained for 61 (95.31%) women for the entire labor duration. However, 3 (4.69%) women had VAS scores of 5 or 6 after 180 min (close to the delivery time) and none of them requested additional analgesia.

Similar article :

Single dose spinal analgesia: Is it a good alternative to epidural analgesia in controlling labour pain?

TarekAbdElBarr[a]

The duration of analgesia was defined as the time from the injection of the local anaesthetic solution until the patient requested additional analgesic dose.

Correction: however ,the manuscript was corrected as the reviewer had recommended and the new changes were highlighted in the manuscript. (lines 21 ,22 of result)

Reviewer 4:

Dear Sir/Madam,

Thank you most sincerely for your precious time and valuable comments.

Dear Editor in Chief
I read with interest this manuscript and mu suggestions are as follow.
IRCT code was not correct and not available at IRCT website. Please mention the correct code number.

Answer : IRCT registration number were checked : **IRCT20121006011020N14 and** Registration date is : **2020-11-03, 1399/08/13** . It is correct and available in IRCT website.

The link was added:.(https://en.irct.ir/trial/48305)

Is it reasonable to prescribe the same dose of the Fentanyl (50 mcg) in both methods?

Answer : Epidural analgesia for labor and delivery involves the injection of drugs into the lumbar epidural space. The injected agent gradually diffuses across the dura into the subarachnoid space, where it acts primarily on the spinal nerve roots and to a lesser .degree on the spinal cord and paravertebral nerves
In spinal analgesia, the analgesic agent is injected directly into the subarachnoid space, resulting in a more rapid onset of effect.

In spinal anesthesia for labour 25 µg dose of fentanyl lasts 60-90 minutes. The study investigating the dose response relation for intrathecal fentanyl showed that the maximal analgesic effect is achieved at about 25 µg fentanyl. Above this dose, the duration of action increases. Synergy has been noted between 25 µg of fentanyl and 2.5 mg of bupivacaine with analgesia lasting about 3 hours .we hypothesized that increasing the fentanyl dose to 50 µg with 2.5 mg bupivacaine can prolong the duration of analgesia. So, this dosage combination can be used at an early stage in appropriately-selected parturients.

Saad Elkhateeb and Ashraf Hamdy used 4 ml of bupivacaine (0.5%) +4 ml normal saline + 50 ug fentanyl in Epidural group;

Palmer et al. used 5-45 microg intrathecal fentanyl as part of a combined spinal-epidural technique.

Palmer CM, Cork RC, Hays R, Van Maren G, Alves D. The dose-response relation of intrathecal fentanyl for labor analgesia. The Journal of the American Society of Anesthesiologists. 1998 Feb 1;88(2):355-61.

The manuscript was corrected as the reviewer had recommended and the new changes were highlighted in the manuscript. (lines 14-19 of Disscussion)

For increasing the quality of this article, consider and add below 21 references: Imani F, Lotfi S, Aminisaman J, Shahmohamadi A, Ahmadi A. Comparison of Spinal Versus

Epidural Analgesia for Vaginal Delivery: A Randomized Double Blinded Clinical Trial. Anesth Pain Med. 2021;11(1):e108335.
Almassinokiani F, Ahani N, Akbari P, Rahimzadeh P, Akbari H, et al. Comparative Analgesic Effects of Intradermal and Subdermal Injection of Sterile Water on Active Labor Pain, Anesth Pain Med. 2020;10(2):e99867.
Derakhshan P, Imani F, Koleini Z S, Barati A. Comparison of Adding Sufentanil and Low-Dose Epinephrine to Bupivacaine in Spinal Anesthesia: A Randomized, Double-Blind, Clinical Trial, Anesth Pain Med. 2018;8(5):e69600
Fathi M, Imani F, Joudi M, Gudarzi V. Comparison the Effects of Ringer`s Lactate and Hydroxyethyl Starch on Hemodynamic Parameter After Spinal Anesthesia: A Randomized Clinical Trial. Anesth Pain Med. 2013;2(3):127-33.
Imani F, Entezary SR, Alebouyeh MR, Parhizgar S. The maternal and neonatal effects of adding tramadol to 2% lidocaine in epidural anesthesia for cesarean section. Anesth Pain Med. 2011;1(1):25-9.
Gousheh MR, Akhondzade R, Asl Aghahoseini H, Olapour A, Rashidi M. The Effects of Pre-Spinal Anesthesia Administration of Crystalloid and Colloid Solutions on Hypotension in Elective Cesarean Section, Anesth Pain Med. 2018;8(4):e69446.
Chandra S, Nugroho AM, Agus H, Susilo AP. How Low Can We Go? A Double-Blinded Randomized Controlled Trial to Compare Bupivacaine 5 mg and Bupivacaine 7.5 mg for Spinal Anesthesia in Cesarean Delivery in Indonesian Population, Anesth Pain Med. 2019;9(2):e91275.
Nugroho AM, Sugiarto A, Chandra S, Lembahmanah L, Septica RI, et al. A Comparative Study of Fractionated Versus Single Dose Injection for Spinal Anesthesia During Cesarean Section in Patients with Pregnancy-Induced Hypertension, Anesth Pain Med. 2019;9(1):e85115.
Shafeinia A, Ghaed MA, Nikoubakht N. The Effect of Phenylephrine Infusion on Maternal Hemodynamic Changes During Spinal Anesthesia for Cesarean Delivery, Anesth Pain Med. 2020;10(1):e99094.
Olapour A, Akhondzadeh R, Rashidi M, Gousheh M, Homayoon R. Comparing the Effect of Bupivacaine and Ropivacaine in Cesarean Delivery with Spinal Anesthesia, Anesth Pain Med. 2020;10(1):e94155.
Javaherforooshzadeh F, Pipelzadeh MR, Akhondzadeh R, Adarvishi S, Alghozat M. Effect of Sequential Compression Device on Hemodynamic Changes After Spinal Anesthesia for Caesarean Section: A Randomized Controlled Trial, Anesth Pain Med. 2020;10(5):e104705.
Nikooseresht M, Seifrabiei MA, Hajian P, Khamooshi S. A Clinical Trial on the

Answer ; Thanks for your valuable comment . These references were added .

Again I would like to thank you most sincerely for your kind consideration and for the precious comments that helped us a lot in enhancing the quality of our paper.

Yours Sincerely

Comment- The true conclusion of this study could be this sentence which has been mentioned in the manuscript: “Mannitol infusion affects faster and earlier for the treatment of PDPH than Acetaminophen-caffeine capsule”. According to the results of this study, there is no evidence for another sentence which has been included in the conclusion “Acetaminophen-caffeine could be a better choice for late headaches because of oral administration”. So it should be withdrawn from the conclusion

Correction: The conclusion was corrected as the reviewer had recommended and this sentence “Acetaminophen-caffeine could be a better choice for late headaches because of oral administration” was withdrawn from the conclusion.

Again I would like to thank you most sincerely for your kind consideration and for the precious comments that helped us a lot in enhancing the quality of our paper.

Yours Sincerely

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) — 4 Apr 2021

Dear AE,
Thank you for inviting me to review the revised manuscript ID#113350. The majority of requested items were corrected, but there are two minor problems, which can be corrected during publishing process as below:
1- The correct IRCT code is IRCT20121006011020N13.
2- References should be written as Vancouver style
Sincerely yours

REFEREE: Associate Editor | **Revision** (1) — 4 Apr 2021

Dear EIC,
Based on reviewers' comments this revised format can be considered for publishing, but note to consider brief corrections recommended by the reviewer.
Regards

REFEREE: EIC | **Revision** (1) — 4 Apr 2021

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.