Author's response to reviews

Title: Effectiveness of Intravenous lidocaine versus Intravenous morphine for patients with Renal Colic in the Emergency Department

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Author's response to reviews: see over
Dear reviewers,

Thank you for your thoughtful review of our manuscript. We take your concerns seriously and have addressed them to the best our abilities. We asked from one of our English literature academic staff to edit the manuscript. We address your comments point by point in Green and Red fonts as follow:

Review 1:

Q1: The authors report their prospective randomized trial for the treatment of renal colic. They evaluated the role of intravenous lidocaine vs morphine. According to EAU guidelines renal colic must be treat with NSAID as first line, as second line morphine and as third line spasmolytics. The authors didn’t use NSAID because are not available in their country but in their recent paper published in (J Med Case Reports. 2011; 5: 256) entitled “Parenteral lidocaine for treatment of intractable renal colic: a case series” they said..... All included patients previously underwent therapy with morphine and NSAIDs previously but were resistant to treatment..... Moreover The pharmacological dilution used didn’t allow a correct double blind trial infact in the lidocaine group more solution can be done. The max dose was not reported as well as the timing of repeating dose. In my opinion the manuscript don’t give as a useful contribution to the field.

Answer:

1. In the first article, the term used for NSAID applied to Suppository NSAID due to unavailability of any IV NSAID in our country; the route of medication administration however was not mentioned throughout the previously published article (J Med Case Reports. 2011; 5: 256). In the present article, we focused on not having IV NSAID in our country and therefore we attempted to look for a proper IV medication substitute i.e. Lidocaine considering its approved postoperative analgesic properties presented in the literature and also in our previous study case series. The excerpt from the discussion section containing the mentioned sentences has been highlited:

“Therefore, because in our country (Iran), intravenous nonsteroidal anti-inflammatory drugs are not available, we thought of an alternative intravenous drug, i.e. lidocaine, whose analgesic effects on various pains (postoperative, cancer and etc.) have been proven (3).”

2. All the processes of injection and filling in the questionnaires were performed by a third person who was an specialist (not involved in research project) and blinded to the injected drug as well as the patients groupings. Patients were blinded to the injected medications as well.

This sentence was corrected as following:
All the processes of injection and filling in the questionnaires were performed by another person who was an specialist (not involved in research project) and blinded to the injected drug as well as the patients groupings. Patients were blinded to the injected medications as well.

The following sentence was also added to the manuscript for further clarity:

The doses required for the administered medication were calculated by another colleague. Hence; neither the patients nor the administrator were aware of the medications used.

3. We did not have any repeated doses and our study was based on single shot and consequently the maximum dose for Lidocaine and morphine were the initial doses administered.

Review 2:

Q1) please cite the website where the trial is registered

The website used for registering the trial is as following:
Trial registration Clinical Trials IRCT138901042496N3
Funding International Clinical Trials Registry Platform (ICTRP)

Q2) please cite the sample size calculation and the randomization technique used (the citation of the web site randomization.com is largely insufficient)

The sample size was calculated based on the following formulas:

Considering pain incidence ratios of 29.3% and 12% for the control and intervention groups respectively, confidence interval of 0.05, power of 20% and loss probability of 20% throughout the follow-up period using the following formula, a sample size of 100 people were calculated:

\[ N = 2 \left( \frac{z_{1-\alpha/2} * z_{\beta}}{2} \right) 2 * \left( P * (1 - P) \right) / (p1 - p2)^2 \]

\[ P = (p1 + p2) / 2 \]
N = 86 + 15 ≠ 100

As the number of the patients with renal colic referring to the emergency department of Imam Reza Hospital is abundant, the sample size was considered as 120 people for both groups and a total number of 240.

Using the website of www.randomization.com 240 letters of A and B were evenly (120) produced and patients were allocated to one of the two groups of A (Group I) and B (Group II), in the order provided by the site.

Q₃) please specify how the colic pain is diagnosed (personally I think that the criteria of the hematuria is totally arbitrary)

thanks for your instructive guidance, the sentence was modified as following:
To provide the patients with required analgesia and to avoid any inconvenience regarding pain management, initial diagnosis was made based on clinical findings (unilateral abdominal pain radiating to the genitalia) associated with a positive urine analysis for Hematuria.

Q₄) please explain how subjects suffering from an acute colic pain could give their informed consent to a clinical trial that uses a potentially lethal drug; please explain also if in your country you can enroll patients aged less than 18 year without parental consent?

We did not comprehend clearly what you meant by “lethal drug”. If Lidocaine was meant, it should be mentioned that lidocaine is a medication approved by FDA which was used in its therapeutic ranges (Max 1.5 mg/kg) in the present study as single shot avoiding repeated doses to prevent toxic doses (more than 3 mg/kg).

Thanks for your concern in this regard, the figure 16 was typed as misprinting which was later replaced with 18 as it was earlier brought in the abstract. Thank you.

Q₅) please remove the graph about sex and age

The graphs mentioned were removed accordingly.

Q₆) please add a table with demographics characteristics and the p values about the comparisons of the groups.
The table mentioned was added accordingly(Table 1).

Q₇) please add a table with the results in term of pain reduction, stone spontaneous passage, frequency and distribution of side effects

The suggested tables(2,3) was added accordingly except for the spontaneous stone passage which was not studied in the present research.
Q₈) please in the abstract correct the description of the 95% CI, more than 95% CI = (60%, 69%), please write "95% CI 0.6-0.69"
The statistical data was corrected in the abstract.

Q₉) please edit all the references, some of them are inappropriate and some are incorrect.
The references were edited.

Looking to hear from you

Best regards

Authors