Reviewer's report

Title: Catecholamine reversal: a case report on unexpected hypotension

Version: 1 Date: 27 Jan 2017

Reviewer: Hori Hariyanto

Reviewer's report:

Dear dr Yohei Okada,

Thankyou for your revised manuscript. I have reviewed the added materials; however, there are still some data sets missing in this paper.

1. On the original review comments, I have requested the vital signs which include heart rate, blood pressure, respiratory rate, capillary refill time, body temperature and urine output. Since you have his cardiac output, cardiac index and SVR measurements, it would be helpful to list them as well on a daily basis. Please complete them by making a table.

2. If your patient was clinically stable on day 2, what hesitated you to transfer him to the general ward up to day 5 of his care? This was unanswered from the previous comment. Please elaborate.

3. You mentioned that continuous hemofiltration was performed due to his metabolic acidosis and elevated lactate level, please list his serial lactate level and upon what basis was hemofiltration terminated?

4. Here are the comments on some of the references that you listed:

   a). Reference #2 reported on the use of BOTH alpha and beta blockade and the concomitant use of adrenaline. In your case, risperidone is reported to have an alpha blocking effect; NONE on beta-1 nor beta-2 receptors. Therefore, if noradrenaline and dopamine works by binding strongly to alpha-1 receptors with minimal effect on beta-1 and almost negligible effect on beta-2 receptors1, how can it cause unopposed stimulation through B2 vasodilatory effect?

   Yes, adrenaline does have a high affinity for beta-2 receptors and have been known to contribute to hypotension; however, how do you explain the possible mechanism of noradrenaline in causing hypotension? It would be helpful to elaborate more on the proposed mechanism by which 'Noradrenaline' may cause hypotension through published reports from other papers/research.

   b). Reference #4 is a report of antipsychotic overdose and even recommends the use of norepinephrine for hypotension, based on the drugs mechanism of action. There are multiple
reports on risperidone overdose with an ingested dose ranging from 1mg-240mg, and their reported side effects. 2,3 Perhaps it might be true that concomitant noradrenaline usage with alpha blockade may cause unexpected hypotension. Please find the supporting evidence.

c). Reference #7 is a report on hypotension and beta-1 blockade using carvedilol. This reference is not applicable for your case report which solely acts on alpha blockade, due to risperidone. It has no effect on beta blockade; hence, the use of dobutamine in your case would not cause unopposed B2 stimulation which may have caused the hypotension.

d). Reference #8 is a paper on specific molecular models of receptors and how to improve their binding affinity. Can you elaborate on how this evidence supports your statement on hypotension during dobutamine infusion and beta-blockade?

Overall, this paper may bring light to the possibility that noradrenaline may have caused refractory hypotension through mechanisms that you still need to explore. I suggest you review and revise the content of your paper. Multiple journals have published several cases of risperidone and antipsychotic agents overdose alongside its management; hence this is not the first case on refractory hypotension due to effects on alpha blockade. The references are too few with some being outdated as far back as 1964 and based on small scale animal models.

Additionally, it would be helpful if this case report was written in a flowing and eloquent manner instead of reporting information piece by piece.

Here are some of the references that I came across while searching for risperidone overdose:


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