Promethazine and Treatment Refractory Agitation in Clonidine Toxicity

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Background:Delirium is an acute and transient turmoil disorder in consciousness which is often caused by drugs.One of the adverse effects of clonidine is agitation. Clonidine is an agonist of α2-receptor which functionally overlaps with μ-receptor of opioids. Promethazine is H1-receptor antagonist and has antipsychotic properties. The necessary dose for initial control of agitation is 25-50 milligrams.

Case Presentation: A 27 year old man has been sent to emergency department following consumption of clonazepam 1 milligram, clonidine 0.1 milligram and alprazolam 0.5 milligram. Upon arrival at the toxicity emergency of the hospital, the patient's pulse rate suddenly dropped to 20 per min along with widening of QRS and increase of QTc as well as severe agitation. At the end of the second day due to continuous bradycardia pace maker was devised. The patient showed hallucination. In the third day, the patient's delirium increased. Due to no control of agitation by benzodiazepine, haloperidol, Promethazine 25 milligram was injected then slept after 5 minute.

Conclusion:In such patient with above restrictions, prescription of promethazine not only maintained blood pressure and caused no disorder in electrocardiogram, but also it immediately and certainly controlled patient's agitation.

Implication for health policy/practice/research/medical education:
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1. Introduction:

Delirium is an acute and transient turmoil disorder in consciousness which is often caused by drugs or multifactorial. It has no certain reason and has the potential of exposing the patient to risk (3-1).

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Medications such as benzodiazepines (midazolam, diazepam, lorazepam), atypical antipsychotic medications, sodium valproate, propofol, promethazine, etc. are used to control delirium (3-6). One of the adverse effects of clonidine is agitation. Clonidine is an agonist of α2-receptor which functionally overlaps with μ-receptor of opioids. Therefore, its manifestation is mostly similar to that of opioids. Furthermore, clonidine can produce metabolic acidosis. Its treatment is often supportive (2-5). Promethazine is one of the medications that use for control of agitation. It is H1-receptor antagonist and has anticholinergic and antipsychotic properties and is from phenothazine group. The necessary dose for initial control of agitation is 25-50 milligram (7-4). Promethazine and haloperidol are prescribed to be injected intramuscle. It controls severe agitations within 15 minutes and within the next 4 hours the patient needs less relevant medications (8).

2. Case presentation:

A 27 years old man (with the record of consuming opium and recent addiction treatment and consumption of clonidine) has been sent to emergency ward 2 hours ago following consumption of 20 tablets of clonazepam 1 milligram and 20 tablets of clonidine 0.1 milligram and 20 tablets of alprazolam 0.5 milligram . The patient suddenly lost his consciousness at home and became agitated and his consciousness did not increase after receiving 3 times naloxone 0.4 milligram intravenously by the emergency team in place. Upon arrival at the toxicity emergency of the hospital, the patient's pulse rate suddenly dropped to 20 per minute along with widening of QRS and increase of QTc and long PR in electrocardiogram as well as severe agitation with gloss cow coma scale (GCS) to a level of 9 out of 15 and a blood pressure of 130/70 mm and 10 breathes rate per minute. He was immediately injected atropine 0.5 milligram for three times and his heart rate reached 75 per minute and he was immediately taken to intensive care unit (ICU). Due to severe agitation and need to sedition, he was supported by mechanical breathing after receiving 150 milligram Thiopental Sodium and 15 milligram of midazolam. In atrial blood gas (ABG), respiratory acidosis and metabolic alkalosis was compensated. After 2 hours the patient's blood pressure dropped and reacted to 0.5 milligram atropine in continuous atropines. To avoid Atropinization, dopamine and then norepinephrine and glucagon were used. In urine screen test, morphine and benzodiazepine were positive. At the end of the second day, the patient was put under ex-tube and due to continuous bradycardia less than 50 per minute pace maker was devised for him. As gloss cow coma scale (GCS) rose to 14 out of 15, the patient showed visual and auditory hallucination and agitation which was put under treatment by haloperidol and bipridin and showed a good response. In the third day, the patient's agitation and hallucination increased and jabber and aggression were added to the above symptoms. Considering the patient's hypotension, he was prescribed with midazolam 5 milligram and haloperidol 0.5 milligram and an interval were considered for the medications to affect. After that, 10 milligram diazepam and haloperidol 0.5 milligram was prescribed for him. Due to no control and as ordered by a psychiatrist, promethazine 25 milligram was injected. The patient cooled down after injection of promethazine and slept after 5 minutes while his blood pressure did not drop. During agitation phase again the patient suffered from metabolic acidosis and compensated respiratory alkalosis. Finally, after receiving 25 milligram promethazine the patient's agitation and atrial blood gas (ABG), were removed and he was transferred to the

poisoning ward. On the eighth day, pace maker was removed and the patient was released after 9 days.

3. Discussion:

In the above case, there were several restricting factors in prescription of necessary medications to control agitation. Bradycardia along with wide QRS and long QTc causes restrictions in prescribing medications such as haloperidol. On the other hand, prescription of benzodiazepines such as midazolam was limited due to the intensification of patient's hypotension (3). In such patient with above restrictions, prescription of promethazine not only maintained blood pressure and caused no disorder in electrocardiogram, but also it immediately and certainly controlled patient's agitation and removed his autistic symptoms after complete consciousness. Metabolic acidosis and alkalosis of the patient which can be due to toxicity with clonidine was removed by removal of agitation (5). In such cases (treatment of refractory agitations), promethazine can be also considered.

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