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RESEARCH ARTICLE

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CASE REPORT: QUETIAPINE-INDUCED TRANSIENT ELEVATION OF ACTIVATED PARTIAL THROMBOPLASTIN TIME

*¹Ismail Mohamed Omar Elghuwael and ²Wan Ariffin Abdullah

¹International Islamic university Malaysia (IIUM), Kulliyah of Medicine, Malaysia, Kuantan 25200

²MAHSA University, Faculty of Medicine, Malaysia, Selangor, 42610

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*Corresponding author: *Andréia Santana Bezerra*

ABSTRACT

We report a case of 3-year old Pakistani boy who was previously well and brought to the hospital because of an accidental ingestion of quetiapine 8 hours before admission. No gastric lavage or activated charcoal done because of late presentation. He developed headache, excessive drinking and sleepiness few hours post ingestion but his symptoms resolved before arrival. His laboratory work up (Full blood count, blood urea and serum electrolytes, liver function test and coagulation profile) showed only an elevated activated Partial Thromboplastin Time (APTT). The patient was discharged after 24 hours. We checked APTT weekly. Even though, he remained well clinically his APTT continued to be high until after 1.5 months of ingestion when repeated APTT was normalized. Review at literature reported many anti-psychotics including quetiapine can cause an elevation of Prothrombin Time (PT) and APTT and low platelet count in adult patients taking them regularly [6], drug overdose can cause APTT elevation as well [4]. We conclude that this 3 years old child has quetiapine-induced transient elevation of APTT.

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INTRODUCTION

Acute Poisoning in children is still an important public health problem and represents a frequent cause of admission in emergency units. Drugs and corrosive agents are the most frequent agents causing Poisoning [9]. Quetiapine is an antipsychotic medicine that is used to treat schizophrenia and bipolar disorders in patients over 13 and 10 years old respectively. It is also used together with antidepressants to treat major depressive disorder in adults. Though it is frequently involved in poisonings, the evidence for paediatric poisonings is scant and case based [10]. Greater than 100mg in a child <12 years may be associated with severe toxicity. Management includes standard supportive care and Normal saline boluses for hypotension. There is no antidote [10]. Compared to other antipsychotics quetiapine has been reported to be relatively safer in overdose [5]. Catalano *et al* [2] reported quetiapine overdose in 15 years old child who ingested 1200 mg for suicide attempt and presented with tachycardia, agitation, hypotension, and unconsciousness.

Muller [7] reported suicide attempt in 32 years old man who attempted suicide and ingested very high dose (36 gm) presented collapsed and required intubation but despite that recovered without neurological sequelae. Statistically significant differences between patients on antipsychotics and control were observed $P < 0.01$ which indicate a state of prolongation in PT and APTT [6]. TY Chen *et al* [3] reported an enhanced bleeding tendency from warfarin in 74 years old man who is on quetiapine for schizophrenia and bipolar disorder, the article stated (our case is the first one whose PT/INR level went beyond the therapeutic window for warfarin, and prolonged aPTT was also noted). SN Gomez [4] reported 50 years old with overdose of quetiapine and enoxaprine for suicide attempt caused drowsiness and elevation of APTT. APTT measures the activity of intrinsic pathway of coagulation. It is the time needed for conversion of Prothrombin to Thrombin after adding phospholipid and surface activator to the blood sample. Thromboplastin is formed during this complex process. The test was originally

devised in 1953 and was called Partial Thromboplastin Time (PTT) in which only phospholipid was added with no surface activator [8]. Isolated elevation of PTT or APTT is a feature of Haemophilia A which is due to factor VIII deficiency and Haemophilia B which is due to factor IX deficiency. Normal value of APTT is 30 – 40 seconds [11].

Case presentation: On 31/12/2019 M who is 3 years old previously well and fully vaccinated Pakistani boy was brought by his mother due to an accidental ingestion of quetiapine which was prescribed by psychiatrist for regular use of the mother herself. Alleged 8 tablets were ingested in the morning time, one tablet is equivalent to 25mg active ingredient. The tablets were stored in a drawer. Post ingestion, the child ate and drank more than usual and started complaining of headache after 3.5 hours. The headache resolved after few hours and he became slightly sleepy. There was no abdominal pain or vomiting. On admission at 9 pm, he was afebrile and active as usual with no bladder or bowel problem. He was normotensive with slightly raised heart rate of 115 beats per minute but adequate Oxygen saturation. Peripheral perfusion was good and full systemic examination of respiratory, cardiovascular, gastrointestinal, nervous and lymphatic systems all were normal. His blood investigations showed normal full blood count, renal profile, liver function but elevated aPTT which is 70.9 seconds (normal range: 30 – 40), PT was normal but there was neither active bleeding nor bruises, petechiae or ecchymosis.

Further history is no family history of bleeding tendency, he was circumcised at age of 6 months with no marked bleeding post-circumcision. Management was mainly observation for hemodynamics which were kept stable without need of fluid boluses. The advice of management was taken from national poisoning centre. His APTT was repeated next day after discharge and was still high (63.6 seconds) without any bleeding tendency noticeable by history or physical examination, even on the day of follow up he fell down and his head hit the floor without any bruising. On follow up after one week, APTT was 72.2 seconds. On second week, factor VIII and factor IX assay was done and both were normal, factor VIII 52.3% (normal range: 50 – 150) and factor IX 69.9% (normal range: 65 – 150)

After around 1.5 month from the incident, repeat APTT was normal, 39.5 seconds.

DISCUSSION

Common symptoms and signs of quetiapine toxicity include Central Nervous System (CNS) depression, hypotension and tachycardia [10]. Transient elevation of APTT after exposure to quetiapine [6],[7],[3],[1] was not emphasized adequately in the literature. Prolong result was observed in APTT in patient on long time usage of psychotropic drug[1]. statistically significant difference were observed $P < 0.01$ which indicate a state of prolongation in PT and APTT [6]. TY Chen *et al* [3] reported an enhanced bleeding tendency from warfarin in 74 years old man who was on quetiapine for schizophrenia and bipolar disorder, the article stated (Our case is the first on whose PT/INR level went beyond the therapeutic window for warfarin, and prolonged APTT was also noted). The prolonged PT/INR is explained by warfarin while prolonged APTT is related to quetiapine because warfarin works on extrinsic pathway which affect PT rather than APTT. We

suspect drug-related elevation of APTT as the patient did not have bleeding post-circumcision. During all his venipuncture, no prolonged bleeding or hematoma was noted. Family history of bleeding disorders was negative too. Most important, factor VIII and factor IX were normal and the child is not for testing factor XII and XI as increased APTT was only transient (Figure 1).

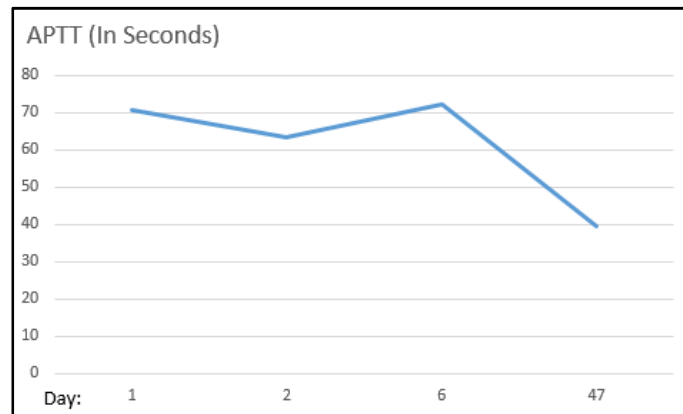


Figure.1 APTT after accidental ingestion of Quetiapine by the child

Learning points /Conclusion

- Any patient with an accidental drug ingestion/drug overdose, basic tests like blood urea and serum electrolytes, liver function test and coagulation profile should be done even if the patient is asymptomatic.
- Always check side effects commonest of drug taken and check side effects with poisoning centre/google, so that any abnormalities can be expected.
- In this patient, the side effects of the drug were checked and high APTT was there from day 1 as possible side effect, hence we are not alarmed by increased APTT as there was no history of bleeding tendency.

However factor VIII and factor IX levels were done because:

- Their deficiency is the most common cause of inherited bleeding disorder in boys.
- We expected increased APTT to normalize by 1 week but it persisted longer with no clear cut point of normalization found in literature.

Accidental drug ingestion is common in children; proper storage place and container are important.

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