Clinical vignette: Clopidogrel overdose: a case report and literature review

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INTRODUCTION:

- Clopidogrel is an antiplatelet agent commonly prescribed for acute coronary, peripheral vascular disease, and prevention of thrombotic events. As it was among the highest of prescription drug sales in the US in 2011, hospitalists should be prepared to encounter and manage overdoses.

- Here we describe an unusual case of a clopidogrel overdose and the discovery that despite its frequent use, the literature is quite barren of case reports and discussion regarding the monitoring and management of potentially fatal hemorrhage.

CASE INFORMATION

HISTORY:

- A 54-year-old woman with hyperlipidemia and prior transient ischemic attack (TIA) two months prior presented to our hospital with vaginal bleeding and hematuria. Admitted to having intentionally overdosed on a study drug 12 hours earlier.

- She was diagnosed with possible TIA two months prior after presenting with right-sided weakness and dysarthria resolving after 4 hours. She was enrolled in the Platelet-Oriented Inhibition in New TIA (POINT) trial, a large ongoing, multi-centered, double-blind, randomized controlled study, which seeks to determine if clopidogrel prevents thrombotic events. As it was among the highest of prescription drug sales in the US in 2011, hospitalists should be prepared to encounter and manage overdoses.

- Consumed 30 study drug pills (placebo vs clopidogrel) following a domestic argument and binge drinking. She was also on aspirin 162 mg daily and atorvastatin. She denied blinded, randomized controlled study, which was clopidogrel.

- Platelet function assay was abnormal with prolongation of closure times above 300 sec.

- Platelet count of 245 x 10^3/mm^3 and normal hemoglobin and INR.

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HOSPITAL COURSE:

- On hospital day 3, the patient's vaginal bleeding resolved, her blood counts were stable, and she was discharged to Psychiatry.

- Our patient took 2,250 mg of clopidogrel, a higher dose than either the Kobacay or Claua cases and almost twice that of a "double loading dose" which can be used prior to angioplasty. Despite this, she was mildly symptomatic with vaginal bleeding and mild hematuria, but within 3 days of observation and conservative management, recovered completely.

DISCUSSION

- Clopidogrel is a thienopyridine which prevents ADP from binding to the P2Y_12 receptor; by doing so, it inhibits platelet activation and therefore, platelet aggregation. This inhibition is irreversible and lasts for the lifespan of platelets (7-10 days).

- Clopidogrel is a pro-drug with a half-life of 6 hours, but its active metabolite aggregation. This inhibition is irreversible and lasts for the lifespan of platelets (7-10 days).

CASE REPORTS

Case One:

- Kobacay et al (2006), Turkey
- 49 yo M, Suicide Attempt
- - Overdosed on 1,650 mg clopidogrel
- - Asymptomatic & No Bleeding
- - Normal vitals & lab results
- - Platelet Aggregation Tests over 7 days showed decreased aggregation fractions which recovered over the week.

Case Two:

- Claua et al (2009), Spain
- 49 yo F, Suicide Attempt
- - Overdosed on 1,975 mg clopidogrel
- - HR 101, BP 150/95, RR 22 O2
- - Hgb= 10.4 & Hct= 31
- - CT Chest: Pulmonary hemorrhage and hemothorax
- - Required thoracentesis (200mL) + transfusions
- - Recovered & discharged after 11 days

REFERENCES

- Kocabay et al (2006), Turkey
- Claua cases and almost twice that of a "double loading dose" which can be used prior to angioplasty. Despite this, she was mildly symptomatic with vaginal bleeding and mild hematuria, but within 3 days of observation and conservative management, recovered completely.

- Given its popularity, the lack of reported overdoses in the literature is surprising.

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CONCLUSIONS

- Clopidogrel is very commonly prescribed, ranked amongst the highest of prescription drug sales in 2011.

- Given its popularity, the lack of reported overdoses in the literature is surprising.

- There still remains very little guidance regarding management and monitoring of clopidogrel overdose.

From what we learned in our case and from the related literature review, we propose that in situations of clopidogrel overdose, a conservative approach be taken:

- Serial monitoring of blood counts
- Platelet & RBC transfusions, if needed
- Platelet testing/ functional monitoring is probably unnecessary in most cases