

PS2 – 032 : Proton pump inhibitors and vitamin K antagonists resistance: about an unknown interaction?



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BACKGROUND

Drug interactions with vitamine K antagonists (VKA) are expected. In France, Proton Pump Inhibitors (PPI) are widely prescribed and are often used as long-term treatments which raised concerns about long-term adverse effects and drug interactions. Well-known drug interactions with PPI are related to increase in gastric pH leading to VKA overdose. Recently, we were questioned about the possible etiology for low INR in a patient treated with fluindione and esomeprazole. A case of esomeprazole induced resistance to fluindione was already published and hepatic induction by PPI was considered to be implicated (1). We aimed to investigate about possible interactions between PPI and VKA, leading to lack of VKA efficacy.

METHODS

Using French Pharmacovigilance Database:

MedDRA terms

“Therapeutic and non-therapeutic effect” (HLGT)
“Coagulation and bleeding analysis” (HLT)

Drugs (« suspected » or « interacting »)

VKA:
fluindione, warfarine,
acenocoumarol



PPI:
omeprazole, esomeprazole, lansoprazole,
rabeprazole, pantoprazole

RESULTS

14 cases:

- Indandione derivatives mostly involved (12 cases with **fluindione**)
- PPI concerned: **omeprazole** and **esomeprazole** (6 and 7 cases respectively)
 - 1 case of thrombosis



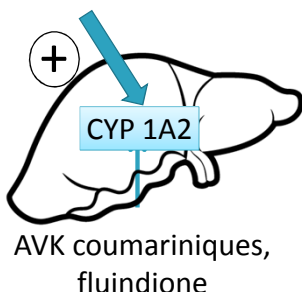
PPI was already prescribed and led to VKA resistance from the start of VKA drug (8 cases)



VKA resistance was observed between 2 to 15 days after starting PPI (4 cases)

DISCUSSION - CONCLUSION

Omeprazole, esomeprazole



Warfarine and fluindione are **CYP1A2** substrates and this cytochrome has been implicated in VKA resistance. A few data suggest that esomeprazole and omeprazole could induce hepatic cytochromes (in particular CYP1A2) (2). However, other VKA-resistance factors: genetic or environmental (tobacco), were not mentioned in any cases, although it could impact (3). These data suggest that concomitant prescription of PPI and VKA can explain VKA resistance. Even if it seems to be a **rare or underreported phenomenon**, we healthcare professionals should be informed.

REFERENCES

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