Indapamide-induced (acute hypokalaemic) rhabdomyolysis

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Background

Indapamide is a non-thiazide diuretic, indicated for essential hypertension treatment. In the routine signal detection process of Uppsala Monitoring Centre (UMC) rhabdomyolysis associated with indapamide was identified as a validated signal due to its high vigiRank score [1], and case report of hypokalaemic rhabdomyolysis in the literature [2-4].

Aim

To assess the causality and any possible risk factors with the association between rhabdomyolysis and the use of indapamide.

Methods

vigiRank is a data-driven predictive model for emerging safety signals. In addition to disproportionate reporting patterns, it also accounts for the completeness, recency, and geographic spread of individual case reporting, as well as the availability of case narratives [1].

Clinical review of reports with rhabdomyolysis associated with indapamide included in VigiBase up to April 2019 was performed. Duplicates were excluded.

Results

VigiBase contained 26 unique cases reporting rhabdomyolysis with indapamide as suspected or interacting medicine, 15 females and 11 males. Indapamide dose was known in 14 cases: 1-2.5mg daily in 12 patients and 5mg daily in 2 patients.

In 12 cases, hypokalaemia was a co-reported event, indapamide being the only suspected drug in 7 cases. The time from indapamide start to the events onset ranged 3 days to 21 months among the 6 cases where this information is available (3d, 4d, 15d, 3w, 18m and 21m). Positive dechallenge was mentioned in 7 of the 12 cases.

In 2 cases, liquorice (containing glycyrrhizin and being used in traditional Asian medicine for its anti-inflammatory properties) was added to the long-term indapamide treatment before hypokalaemia and rhabdomyolysis were reported. Severe hypokalaemia and hypokalaemic muscular weakness due to liquorice consumption have been reported previously [5].

Hyponatremia was a co-reported event in 6 cases (with co-reported hypokalaemia in 4 cases, without hypokalaemia in 2 cases where fall and syncope/collapse were reported).

Among the cases without hypokalaemia or hyponatremia, multiple co-suspected or concomitant medicines (including statins, ezetimibe, fenofibrate or gemfibrozil, n=4) were reported.

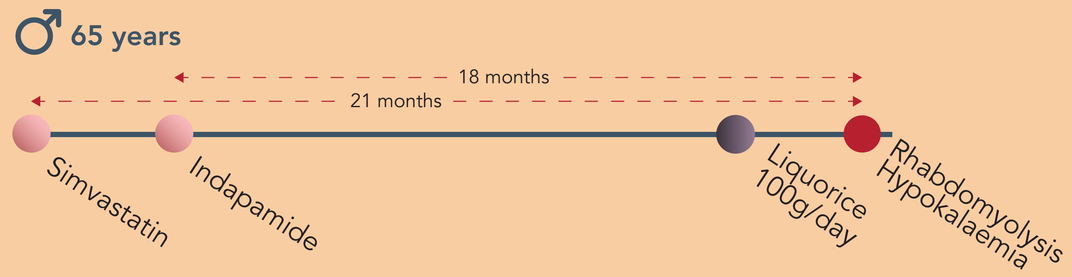
Conclusion

Hypokalaemia is a known adverse reaction of indapamide. Rhabdomyolysis caused by severe hypokalaemia has been reported [2]. The reported temporal relationship including positive dechallenge in our reviewed cases and the plausible mechanism support a causal relation between indapamide and rhabdomyolysis. In addition to indapamide-induced hypokalaemia, there were also other risk factors (e.g. fall, concomitant drugs with risk of hypokalaemia or muscle injury). Healthcare professionals should be aware of this risk.

Liquorice: trick or treat?

The FDA has previously warned for overconsumption of black liquorice, since it contains the compound glycyrrhizin, which is the sweetening compound derived from liquorice root. Glycyrrhizin can cause potassium levels in the body to fall. When that happens, some people experience abnormal heart rhythms, as well as high blood pressure, oedema (swelling), lethargy, and congestive heart failure.

https://www.fda.gov/consumers/consumer-updates/black-licorice-trick-or-treat



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