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Possible protective role of erythropoietin in vincristine-induced central toxicity in rat

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Aim: 1. To develop a rat model to study vincristine-induced SAIDH 2. To determine the possible role of erythropoietin in reducing the hyponatremia and survival rate associated with vincristine-induced SAIDH.

Methods: Rats were allocated into five groups (n=4-8 each). All groups were i.p. dosed 0.15 ug/Kg vincristine sulphate (VCR) for 15 days 6 days per week. Groups 2, 3 and 5 were administered either 40 U/Kg or 80 U/Kg erythropoietin i.p. along with the VCR. Groups 4 and 5 were administered 40 mg/Kg posaconazole (PSZ) orally starting the day of VCR administration. Rats' weights and survival rates were measured daily and their serum sodium and potassium levels were measured at days 0, 5, 9 and 15.

Results: No rats survived after day 12 of dosing. The VCR-induced SAIDH rat model showed 3.4% and 4.1% reduced sodium levels on days 5 & 9, respectively. Their serum potassium level showed no significant change on day 5 and 8% decrease on day 9. The rats exhibited weight reduction of 10% and 18% on days 5 and 9, respectively. Erythropoietin 40 U/Kg treated rats showed significantly less hyponatremia (0.6% decrease) and 24% increase in potassium levels on day 5. However, increasing the erythropoietin therapy duration beyond 5 days and/or dose (80 U/Kg treated groups) resulted in increased hyponatremia and demolished rats' survival. PSZ-VCR dosed rats and PSZ-VCR-erythropoietin dosed rats survived only for 4 days. Posaconazole-VCR treated groups showed increased VCR toxicity with ~12% increase in serum potassium levels, however, serum sodium levels showed no significant difference during the 4 days.

Conclusion: Initial rat model to study vincristine-induced SAIDH was developed. Co-administration of low dose erythropoietin (40 U/Kg) for short duration, ≤5 days, showed a potential benefit in reversing the VCR-induced hyponatremia however, we need to consider controlling the induced hyperkalemia. Human serum sodium, potassium and BUN levels for patients administered VCR alone or VCR along with erythropoietin in ALL treatment protocols needs to be studied to confirm such trends.

Biography

Malak Abouayana is a third-year undergraduate pharmacy student, Faculty of Pharmacy, Alexandria University.

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