CONCLUSIONS: Although risedronate did not reduce the severity of nausea and vomiting, it is likely to prevent muscle spasm caused by heavy exercise. Risedronate prevents hypercalcemia especially in subjects severely volume depleted. Hence, enhanced bone resorption causes exercise-induced hypercalcemia.

FP133 **RISEDRONATE PREVENTS EXERCISE-INDUCED HYPERCALCEMIA; A RANDOMIZED CONTROLLED TRIAL (RCT)**

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INTRODUCTION: In ERA-EDTA 2018, we reported that nausea or vomiting caused by heavy exercise was associated with post-exercise increased blood calcium levels, and that exercise-induced hypercalcemia was associated with enhanced bone resorption. We investigated the effect of risedronate sodium on nausea and vomiting caused by heavy exercise, and the causal relationship between bone resorption and exercise-induced hypercalcemia.

METHODS: We conducted a randomized, double-blind, placebo-controlled trial, enrolling 103 healthy trained male members of Japan Self-Defense Forces. The primary outcome was the severity of nausea and vomiting assessed by visual analogue scale during- or post-exercise. The secondary outcomes included severity of clinical symptoms associated with heatstroke, and post-exercise serum total calcium (tCa), tartrate-resistant acid phosphatase 5b (TRACP-5b) levels, which reflects the activity of osteoclasts, and eGFR. A risedronate sodium tablet 17.5mg or placebo was prescribed 3 and 10 days before heavy exercise lasting approximately 5 hours. Before and within 2 hours after the exercise, we collected laboratory data.

RESULTS: Mean (SD) age and eGFR were 26 (3) years old and 83 (13) mL/min/1.73m^2, respectively. The exercise decreased body weight by 5%. There were no significant differences between two groups in the primary outcome or post-exercise eGFR. However, post-exercise tCa and TRACP-5b were significantly lower in the risedronate group than in the placebo group [9.7 (0.5) vs. 9.9 (0.5) mg/dL (P=0.04), 323 (231-390) vs. 388 (312-477) mU/dL (P=0.001), respectively]. Similarly, the incidence of hypercalcemia defined as tCa$\geq$9.8 mg/dL (median value of all subjects) was significantly lower in the risedronate group than in the placebo group (42% vs. 60%, P$<$0.05). Especially in the patients who lost weight substantially, stronger treatment effect of risedronate on serum calcium levels was observed (P for interaction=0.002) (Figure). The incidence of muscle spasm tended to be lower in the risedronate group than in the placebo group (IRR=0.61; 95%CI: 0.33-1.12).