THYROTOXIC PERIODIC PARALYSIS, β_2-ADRENERGIC BRONCHODILATOR, AND INSULIN—AN INTERESTING INTERPLAY

To the editor: The article by Yeh and colleagues[1] is indeed interesting. The occurrence of hypokalemia was attributed to the effects of a β_2-adrenergic bronchodilator on the membrane-bound sodium potassium adenosine triphosphatase pump, resulting in a skewed distribution of potassium and producing an extracellular to intracellular shift. This potassium shift resulted in thyrotoxic periodic paralysis (TPP). In addition to an increased adrenergic response, patients with TPP have hyperinsulinemia during acute attacks with an exaggerated insulin response to an oral glucose challenge, compared to thyrotoxic patients without TPP. This further supports the idea that insulin plays a pivotal role in the pathogenesis of hypokalemia in TPP.[2] Salbutamol induces hyperglycemia by promoting glycogenolysis.[3] This effect is observed even after inhalation and is dose dependent. The elevated serum insulin levels are ascribed either to direct stimulation of islet cells or to the rising serum glucose. Although the insulin rise tends to peak sooner than the glucose rise, it is inadequate for the observed rise in glucose, resulting in persistent hyperglycemia. An increase in insulin and glucose results in a larger shift of potassium into the intracellular space. Carbohydrate-rich meals and sweet snacks are known triggers of hypokalemic periodic paralysis, which supports this observation.[4] Sympathetic stimulation of insulin release provides additional rationale for using nonselective β-blockers to treat acute hypokalemia and paralytic attacks of TPP. Interestingly, diabetic ketoacidosis has been reported where β_2-agonists are used to terminate premature labour.[5] In addition to β_2-adrenergic bronchodilators, insulin-dependent factors may play an important role in the pathogenesis of TPP. From the perspective of patient safety, prescribers must remember the adverse effects of hyperglycemia and hyperinsulinemia when prescribing or using any form of β_2-agonists.

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References

1. Yeh FC, Chiang WF, Wang CC, Lin SH. Thyrotoxic periodic paralysis triggered by β2-adrenergic bronchodilators. *CJEM* 2013;15:1-5.
2. Lee KO, Taylor EA, Oh VM, et al. Hyperinsulinaemia in thyrotoxic hypokalaemic periodic paralysis. *Lancet* 1991; 337:1063-4, doi:10.1016/0140-6736(91)91710-C.
3. Haffner CA, Kendall MJ. Metabolic effects of β2-agonists. *J Clin Pharm Ther* 1992;17:155-64, doi:10.1111/j.1365-2710.1992.tb01285.x.
4. Chang CC, Cheng CJ, Sung CC, et al. A 10-year analysis of thyrotoxic periodic paralysis in 135 patients: focus on symptomatology and precipitants. *Eur J Endocrinol* 2013;169:529-36, doi:10.1530/EJE-13-0381.
5. Thomas D, Gill B, Brown P, Stubbs W. Salbutamol-induced diabetic ketoacidosis. *Br Med J* 1977;2:438, doi:10.1136/bmj.2.6084.438.

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