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Beta-blocker Rebound Phenomenon in an Adolescent with Graves' Disease

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Dear Editor,

Graves' disease is the most common cause of hyperthyroidism in children (1). The most common complaints at admission are palpitation, sweating, tremor, and irritability (2). Beta-blockers such as propranolol (0.5-2 mg/kg/day) are mostly used for adrenergic symptoms of children with Graves' disease until euthyroidism is achieved (3).

Sudden withdrawal of beta-blocker drugs in adults can lead to unwanted effects such as tachycardia, arterial hypertension, angina pectoris, and an increase in heart failure symptoms. These symptoms and signs following sudden cessation of beta-blockers are called the "beta-blocker rebound phenomenon", also known as beta-blocker withdrawal syndrome (4). Adult patients may exhibit hypertension, headache, palpitation, sweating, and chest pain. These symptoms occur within the first few days after discontinuation of the drug (4). In adults with underlying overt or occult ischemic heart disease, this phenomenon may cause major complications. Moreover, an exacerbation of migraine headache attack may develop in patients withdrawn from beta-blocker therapy (5). Although the optimal prevention methods for the beta-blocker rebound phenomenon are not known, sudden discontinuation of long-term propranolol therapy (longer than 3 months) should be avoided to prevent rebound effects in the adult population (4,6). The daily dose of propranolol in adults with propranolol withdrawal syndrome is 160-320 mg and a lower propranolol dose is less likely to lead to this phenomenon (4,5,6,7).

A 17-year-old female patient presented with complaints of palpitation, irritability, and weight loss. Physical examination revealed a weight of 0.2 standard deviation score (SDS), height of -1.0 SDS, body mass index of 1.0 SDS, heart rate 164/min, arterial blood pressure 120/80 mmHg, goiter, and fine tremor. Laboratory test results were as follows: free thyroxine (fT4) 4.9 ng/dL (N: 0.7-1.48), free triiodothyronine (fT3) 16.5 pmol/L (N: 3.0-9.0), thyroid-stimulating hormone (TSH) 0.01 uIU/mL (N: 0.35-4.94) and anti-thyroglobulin 5.1 IU/mL (N: <4.1). Thyroid ultrasonography showed an enlarged thyroid gland (volume 16.9 mL, 4.8 SDS), hypoechoic heterogeneous thyroid echotexture, and hypervascularity. The patient was diagnosed with Graves' disease and methimazole 20 mg/day (0.33 mg/kg/day), propranolol 80 mg/day (1.3 mg/kg/day) treatments were started. The dose of methimazole was reduced and propranolol was discontinued on the 16th day. One day after the discontinuation of propranolol, the patient developed severe headache, palpitation, and malaise. Physical examination at that time revealed systemic hypertension (arterial blood pressure 140/90 mmHg) with normal systemic findings. Serum levels of thyroid hormones were as follows: fT3 4.68 pg/mL (N: 1.71-3.71), fT4 1.27 ng/dL (N: 0.7-1.48), TSH 0.001 uIU/mL (N: 0.35-4.94). All the complaints spontaneously disappeared within 24 hours. The patient was normotensive and physical examination findings were normal after 24 hours. Typical findings and spontaneous regression of symptoms suggested that this attack may be due to beta-blocker withdrawal but there are no data regarding the incidence and characteristics of withdrawal reactions in children receiving relatively low dose propranolol for a short period.

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In conclusion, the beta-blocker rebound phenomenon may occur in adolescents with Graves' disease who are treated with short-term and relatively low-dose propranolol and whose treatment is rapidly discontinued. Although the clinical significance of this situation in adolescents without underlying ischemic heart disease or migraine is not known, it may lead to discomfort and a decrease in the quality of life of the patient. It is not known whether tapering, rather than rapid, discontinuation of propranolol in adolescents with Graves' disease will prevent this condition. However, pediatric endocrinologists must be aware of beta-blocker rebound to inform their patients about it.

Ethics

Peer-review: Internally peer-reviewed.

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References

1. Léger J, Carel JC. Hyperthyroidism in childhood: causes, when and how to treat. J Clin Res Pediatr Endocrinol 2013;5(Suppl 1):50-56.
2. Aldemir Sönmez A, Erbaş İM, Acar S, Demir K, Bober E, Abacı A. Evaluation of clinical characteristics and treatment outcomes of Graves' disease in children and adolescents. Trends in Pediatrics 2021;2:18-27.
3. Mooij CF, Cheetham TD, Verburg FA, Eckstein A, Pearce SH, Léger J, van Trotsenburg ASP. 2022 European Thyroid Association Guideline for the management of pediatric Graves' disease. Eur Thyroid J 2022;11:e210073.
4. Koracevic G, Micic S, Stojanovic M, Tomasevic M, Kostic T, Velickovic Radovanovic R, Lovic D, Djordjevic D, Randjelovic M, Koracevic M, Ristic Z. Beta blocker rebound phenomenon is important, but we do not know its definition, incidence or optimal prevention strategies. Hypertens Res 2020;43:591-596. Epub 2020 May 7
5. Frishman WH. Beta-adrenergic blocker withdrawal. Am J Cardiol 1987;59:26-32.
6. Nattel S, Rangno RE, Van Loon G. Mechanism of propranolol withdrawal phenomena. Circulation 1979;59:1158-1164.
7. Rangno RE, Nattel S, Lutterodt A. Prevention of propranolol withdrawal mechanism by prolonged small dose propranolol schedule. Am J Cardiol 1982;49:828-833.