



An Approved Treatment in Periodic Paralysis: Diclorphenamide

Periyodik Paralizilerde Onaylanmış Bir Tedavi Seçeneği: Diklorfenamid

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Periodic paralysis (PP) are autosomal inherited muscle diseases that are directly associated with changes in serum potassium levels. Classified as channelopathies, PP are often triggered by exercise. Hyperkalemic periodic paralysis (HYP) is associated with mutations in *SCN4A* gene, and hypokalemic periodic paralysis (HOP) is associated with mutations in a calcium channel gene called *CACNA1S* and a sodium channel gene called *SCN4A*. PP becomes symptomatic in the first decade of life. The frequency of attacks in this group of diseases, which present with attacks, can be reduced by carbonic anhydrase inhibitors (acetazolamide and diclorphenamide) or potassium-sparing diuretics (1). Sansone et al. (2) showed in their randomized, multi-center, double-blind, placebo-controlled trial that diclorphenamide can be used in the treatment of PP with an evidence level of class 1. Forty-four patients with HYP and 21 with HOP were included in the trial. Two randomized, double-blind, placebo-controlled trials lasted 9 weeks, followed by a 1-year extension phase in which all participants received dichlorphenamide (DCP). The median attack rate, frequency of severe attacks, and the duration of attacks were lower in patients with HYP on DCP. The median attack rate was also lower in patients with HOP on DCP compared with placebo, but without reaching statistical significance. There were

no significant effects of DCP on muscle strength or muscle mass in either trial. The most common adverse events were paresthesia, confusion, cognitive decline, and kidney stones. The median attack rate and frequency of severe attacks were increased in one patient with HOP on DCP with the NaV1.4pR222W mutation who had not previously used a carbonic anhydrase inhibitor; DCP treatment was stopped and the patient was excluded from the trial. The main shortcomings of these trials mentioned by the authors were the lack of comparison between DCP and acetazolamide and the limited number of participants, which precluded analysis by genetic subgroup. Finally, the Food and Drug Administration approved the use of DCP in HYP and HOP in August 2015.

Ethics

Peer-review: Internal peer-reviewed.

References

1. Statland JM, Barohn RJ. Muscle channelopathies: the nondystrophic myotonias and periodic paralyses. *Continuum (Minneapolis, Minn)* 2013;19:1598-1614.
2. Sansone VA, Burge J, McDermott MP, Smith PC, Herr B, Tawil R, Pandya S, Kissel J, Ciafaloni E, Shieh P, Ralph JW, Amato A, Cannon SC, Trivedi J, Barohn R, Crum B, Mitumoto H, Pestronk A, Meola G, Conwit R, Hanna MG, Griggs RC. Muscle study group. Randomized, placebo-controlled trials of dichlorphenamide in periodic paralysis. *Neurology* 2016;86:1408-1416.

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