

Hypogeusia as a side effect of leflunomide

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To the Editor.

Rheumatoid arthritis (RA) is a progressive, autoimmune disease associated with severe morbidity, functional changes, permanent disability and increased mortality¹.

In recent years, literature has shown a trend toward early initiation of aggressive treatment, using drugs that modify the course of the disease since the onset of clinical manifestations².

Because of the chronic nature of RA, Disease Modifying Antirheumatic Drugs (DMARDs) should be used for long periods, in monotherapy or in association.

Side effects of DMARDs are a major problem in the therapeutic control of RA.

To illustrate this statement, we can mention the therapeutic use of gold salts and D-penicillamine for decades in the control of RA. These drugs, however, are no longer frequently used due to their side effects, with morbidity and mortality incompatible with the therapeutic advances in the area of autoimmune diseases in recent decades.

Methotrexate can be cited as a drug that modified the natural history of RA, with high efficacy and safety.

However, methotrexate does not handle all cases of RA and some patients may present side effects or intolerance to the drug.

In such cases, clinical protocols to treat RA opt to introduce leflunomide as monotherapy or associated with other DMARDs³.

Appel da Silva et al⁴ described a case of ageusia and anosmia with the use of leflunomide in a 62 year old-patient with RA, after five months of medication. They reported that three months after drug discontinuation, the patient had a full recovery of gustatory and olfactory sensitivity.

We published in 2012 a retrospective study evaluating the side effects of leflunomide in 40 patients⁵.

The average follow-up of patients was 36.6 months. Side effects were observed in 26 patients (65%). The

most common side effects were increased frequency of daily bowel movements - 10 patients (25%) and hypogeusia - 4 patients (10%).

In these four patients, decreased taste sensitivity occurred early in the therapy with leflunomide. All patients had RA with positive rheumatoid factor, were aged 31, 57, 60 and 66 years, respectively, and all received the association with hydroxychloroquine sulfate.

In all patients leflunomide therapy was maintained and the hypogeusia receded at varying intervals of no longer than six months.

We recently treated a 52 year-old female patient with RA for two years and positive for rheumatoid factor. After receiving leflunomide for about 15 days, she developed ageusia and anosmia, which resolved after drug withdrawal. The patient refused to have the drug reintroduced, so we chose to use adalimumab.

According to Felix⁶, symptoms related to taste and smell are difficult to evaluate because there is confusion between "taste" and "savor", which are used interchangeably in most cases.

Furthermore, the investigation of changes in taste is difficult due to lack of standardized tests.

Taste is the sensation of salty, sweet, sour and bitter, whereas savor is the combination of sensations captured both by gustation and smell.

The author further states that the complete loss of taste is rare, since this sensation is transmitted by different cranial nerves (V, VII, IX, X).

Changes in taste can have several causes, the most common being the use of drugs, pregnancy and aging.

Although little reported in the literature, changes in taste and smell with the use of leflunomide may not be unusual and should be investigated by anamnesis of those patients using this DMARD.

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