Mutation analysis of the ALDH3A2 gene is a highly sensitive method of confirming the diagnosis of SLS.[4] More than 90 pathogenic variants of ALDH3A2 have been identified to date.[1] The diagnosis of SLS can be confirmed by measurement of enzyme activity in cultured skin fibroblasts or leukocytes.

There is no permanent cure for SLS and no specific therapy, so that a multidisciplinary approach is necessary.[3]

In conclusion, we report a new case of SLS caused by two novel mutations, supporting the rich mutational heterogeneity associated with this syndrome. High index of suspicion is necessary for the diagnosis of SLS, so that in a neonate or infant with congenital ichthyosis and neurological symptoms we must rule out this neurocutaneous disorder.

Conflict of interests

The authors declare no conflict of interest.

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E. García-Peris*, I. Latour-Álvarez, M. Pestana-Eliche, R. Sánchez

Department of Dermatology, Hospital Universitario de Canarias, Tenerife, Spain

*Corresponding author.
E-mail address: estelagperis@gmail.com (E. García-Peris).

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Split doses of Methotrexate in patients with moderate to severe Psoriasis

Dosis divididas de metotrexato en pacientes con psoriasis moderada a severa

Dear Editor,

Psoriasis is the most common inflammatory skin condition with a worldwide prevalence of 2%. Systemic or topical treatment is decided according to the severity of the disease.[1] For systemic treatment, Methotrexate (MTX) remains effective and medically accessible: it is widely used in hospitals in Latin America, where biological therapy is still limited for economic reasons.[2]

The article: ''Methotrexate in Moderate to Severe Psoriasis: Review of the Literature and Expert Recommendations''[3] outlines very important and interesting recommendations on the use of this drug in Psoriasis. However, one point that has not been taken into account is the split of MTX in two or three weekly doses, with the benefit of both efficacy and reduced side effects.

The benefits of fractional doses are listed below. As indicated in the article, MTX has significant gastrointestinal adverse effects that hinder its use, and increases with higher oral doses; but can be avoided or reduced with parenteral route, and with folates.[3] In addition, a divided dose of MTX is an alternative for reducing gastrointestinal side effects in patients with Psoriasis.[4] Second, with high MTX enteral doses, bioavailability decreases (for limiting absorption); therefore it is beneficial to divide MTX into smaller doses and thus increase its concentration systemically,[5] increasing efficiency without worsening adverse effects.[6]

Although MTX experience with divided doses for Psoriasis has been well known and accepted[7] for several decades,[8] it is based on a limited number of studies.[5,9] Thus, further experience with divided doses of MTX has been carried out in rheumatologic patients, but these are also limited.

Weinstein and Frost[9] first proposed the divided dose of MTX for Psoriasis in 1971. They showed that small doses of 2.5–7.5 mg of MTX given at intervals of 12 h for a total of three doses every week had an improvement from 75% to 100% in 26 patients with severe Psoriasis, with minimal adverse effects (nausea, oral ulcers and hives).

Chladek et al.[5] conducted a study that related the pharmacodynamics and pharmacokinetics of divided doses (2.5 mg and 5 mg three times a week) and weekly full doses (7.5 mg and 15 mg) of MTX with the Psoriasis Area Severity Index of 41 patients with severe disease. They concluded that split doses of MTX were associated with greater efficacy and lower risk of acute adverse effects during anti-psoriatic therapy.

In the rheumatology field, Dhaon et al.[6] randomly divided 135 patients with rheumatoid arthritis into three groups:

group 1 on split 7.5 mg doses of oral MTX two or three times weekly; group 2 on single 15–22.5 mg of oral MTX weekly; and group 3 on single intramuscular 15–22.5 mg dose of MTX weekly. Clinical efficacy of split and intramuscular doses was superior to single oral dose, but intramuscular administration lead to greater discomfort on patients. In addition, split doses group showed the lowest rates of gastrointestinal side effects, with higher levels of alopecia.

Pharmacokinetic studies demonstrate enhanced bioavailability of the drug with multiple dosing, supporting the clinical superiority of divided doses compared to single oral dose. Hoekstra et al.,[10] compared blood samples of 10 rheumatoid arthritis patients with fluorescence polarization immunoassay technique who received a single oral dose of 25–35 mg MTX, and after one week, divided two or three doses every 8 h. Bioavailability of split doses was 28% significantly higher than single doses and similar to that of subcutaneous doses, obtained from a previous study. The authors concluded that when high-dose of MTX is needed, the divided dose is an effective and comparable alternative to subcutaneous administration.

After demonstrating and bringing up the efficacy and safety of MTX split oral doses in patients with Psoriasis, it is important to remember that there are limitations and drawbacks in their use, mainly with delivery errors. Because patients must take three weekly doses of 2.5 mg or 5 mg, and MTX tablets are mainly available at 2.5 mg and 10 mg in this region, patients may accidentally fail in both: reducing or increasing the dose. However, in our experience this accident is very uncommon.

In conclusion, MTX remains as a first-line treatment for severe Psoriasis, and accessible in many Latin American countries. Enteral and parenteral weekly divided doses of MTX show similar efficacy and safety in several studies both in psoriatic and rheumatologic patients. Therefore, we should continue proposing low split oral doses in future guidelines and consensus, in comparison to the single oral dose, with the benefit of achieving greater adherence by reducing adverse effects, taking into account their limitations.

Conflict of interest

The authors declare no conflict of interest.

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M.J.M. Rodríguez-Zúñiga[a,b,*], F. Cortez-Franco[a], E. Qujiano-Gomero[a]

[a] *Servicio de Dermatología del Hospital Nacional Daniel Alcides Carrión, Callao, Peru*
[b] *Universidad Nacional Mayor de San Marcos, Lima, Peru*

[*] Corresponding author.
E-mail addresses: milton_rz@hotmail.com, mijomax@gmail.com (M.J.M. Rodríguez-Zúñiga).

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