Reply to the Article "Comparing Demographics, Clinical Presentation, Treatment and Outcome Between Sle Patients Treated in One Public and One Private Health System in Santa Fe, Argentina"☆

Réplica al artículo «Comparación de datos demográficos, presentación clínica, tratamiento y desenlace de pacientes lúpicos tratados en un centro público y otro privado de salud en Santa Fe, Argentina»

Dear Editor,

We thank you for the comments and suggestions made. We have carefully read the comments and we add that:

1. In the "Results" section, the progress time of patients until the first consultation (public or private) was defined and we would like to clarify that demographic data, activity by SLEDAI, physical examination and lab data were obtained in the first consultation. This data is clarified again in tables 1 and 2. Likewise, we explained that the outcome data of the patients were (obviously) taken at the last consultation.
2. In the "Results" section, it is explained that 116 patients were assisted in the public healthcare system and 43 in the private area. We also state that the same group of experts assisted both groups; therefore, it is incorrect to infer variability in the treatments, superposition or different periods of treatment.
3. No section of the article mentions that informed consent was required. On the contrary, it is explained that it was not necessary due to the anonymous and retrospective nature of the study.
4. The colleagues are confused about the question of the ethnic group, since this topic is not in the "Results" section, but in the "Discussion" section, and they are quotes from other authors. In addition, they are confused when they affirm it is data from our study, because we are mentioning data from Reveille et al.

We suggest a better reading of this work in order to make better suggestions.

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Consensus on the Use of Methotrexate Beyond the Clinical Recommendation: Adjusted Dose and Pharmacogenetics☆

Consenso sobre el uso de metotrexato más allá de la recomendación clínica: dosis ajustada y farmacogenética

Mr. Editor:

We have read with great interest the original document entitled "Recommendations on the use of methotrexate in rheumatoid arthritis: dose increase and reduction and routes of administration" published by Tornero Molina et al. in *Reumatología Clínica*.[1] First of all, we want to congratulate the authors of this eminently practical consensus, since it allows us to know in depth the experts' clinical practice in the handling of disease-modifying antirheumatic drugs (DMARD) in the treatment of rheumatoid arthritis (RA).

EULAR recommends to start treatment with DMARDs as soon as the diagnosis of RA is established.[2] Methotrexate (MTX) is the cornerstone of the treatment, which has 2 differentiated routes of administration. Consensus recommends the subcutaneous route of administration as a start in polymedicated patients, with overweight or obesity, under the suspicion of low adherence, depending on patient's preferences, with the purpose of reducing the dose to prevent gastrointestinal adverse effects and in active disease (DAS28 > 4). Moreover, the switch from the oral route to the subcutaneous route is posed as an option in cases of inefficiency, better cost-effectiveness profile and non-compliance with oral treatment. Consensus advises increases of 2.5–5 mg every 2–6 weeks depending on clinical severity, reaching a maximum dose of 25 mg.

Notwithstanding the usefulness of the document, we would like to provide 2 comments that we consider could be of special interest.

First, the average normal dose of MTX used in most studies is of 15 mg/week. Nevertheless, we consider calculating the MTX dose in accordance with the weight of the patient to be treated. The patient's weight, among other variables, indirectly intervenes in drug's plasma concentration, so it cannot be the same in 60 kg (132 pounds) patients as in 90 kg (198 pounds) patients. Possibly, a good approximation could be to adjust it to a dose of 0.2–0.3 mg/kg.

Another issue we find worth mentioning is the introduction of MTX pharmacogenetics in the clinical practice of RA. Several polymorphisms that can predict favourable response and toxicity to the drug have been defined, getting us closer to the concept of personalised medicine in the treatment with MTX.[3] In the last decade, there have been descriptions of allelic variations in genes that participate in the folates metabolic pathway, either at transmembrane transportation level or at intracellular level, which are associated to the lack of response to MTX or MTX toxicity.[4] Our collaboration group's previous experiences with other drugs, such as azathioprine, have allowed us to adjust the drug dose

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depending on the existing enzyme level.[5,6] More recently, after analysing 27 genetic variations in the dihydrofolate reductase (DHFR), thymidylate synthase (TYMS), methylenetetrahydrofolate reductase (MTHFR), 5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase (ATIC) and cyclin D1 (CCND1) genes, we reached the conclusion that variants in the MTHFR and DHFR genes might be considered as pharmacogenetic markers of response in patients with RA, and ATIC gene variants might be considered as toxicity markers.[7]

Nevertheless, we cannot fail to mention that pharmacogenetics has addressed the search for MTX toxicity and response predictors to MTX in a dissimilar manner. The different studies that have been published do not show coherent results, either due to the clinical heterogeneity of the sample, due to the differences in the way they define efficiency and toxicity, or due to the small size of the sample.[8]

Thus, we considered that, once the most frequent variables allowing us to predict beforehand favourable drug response or possible drug toxicity have been confirmed, the pharmacogenetic study should be routine to optimise the most efficient route of administration and dose. This consideration opens the door, in a not too distant future, to a personalised medicine for each patient that could be extended with the study of different therapeutic targets.[9]

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Rhabdomiolysis Secondary to Physical Activity and Simultaneous Electrostimulation. A Case Report☆

Rabdomiólisis secundaria a la realización de actividad física y electroestimulación simultánea: reporte de un caso

Mr. Editor:

We have recently assessed a 33-year-old female patient, an aerobic athlete who practises 180 min of swimming and 30 km (18.6 miles) of trotting per week, and who complained about proximal weakness and pain in lower limbs associated with noticeable volume increase in both thighs, of one day of evolution. Patient did not have any medical history of interest and was not taking any medication. The day before, she had used, for the first time, an electrostimulation device on the painful area while performing her regular exercises, which involved running on a treadmill for 30 min. The device consisted of short pants with electrodes for muscle stimulation of both glutei. The program used by the patient had a frequency of 50 Hz in accordance with the manufacturer's data sheet. The patient presented pain on palpation in quadriceps and lateral heads of triceps brachii and she showed proximal weakness that conditioned her pace. From the analytical point of view, she showed normal renal function, creatine phosphokinase (CPK) of 64,150 U/l, lactate dehydrogenase (LDH) 616 mg/dl, glutamate pyruvate transaminase (GPT) 640 UI/l, glutamate-oxalacetate transaminase (GOT) 1050 UI/l and myoglobinuria ++/+++. She was treated with overhydration and bed rest for 3 days, after which the pain ceased significantly; the thighs volume was reduced, the myoglobinuria disappeared and the CPK descended to 1222 U/l. Two months later, all analytes were normalised and the patient went back to her regular sport activity without presenting new symptoms until after 6 months from the episode. Approximately 3 months after the episode, she had an electromyography done which did not identify a pattern compatible with neuropathy or myopathy. A lactate test was performed with normal results.

Post-exercise rhabdomyolysis is a process that can present itself in healthy subjects or in patients with metabolic muscular diseases. It is characterised by a lysis of the musculoskeletal striated fibre after physical exertion that manifests itself clinically as the triad of myalgia, weakness and choluria.[1–3] Its management is mainly support-oriented, and it consists of athletic rest and overhydrating to prevent renal failure secondary to myoglobinemia.[4,5] In scientific literature, there is only one case of rhabdomyolysis associated with the use of an electrostimulation device in a young male patient who was exposed to such device for several weeks.[6] Electrostimulation devices allow the performance of passive physical exercise through electrodes that generate isometric contractions in specific muscle areas.[7] These devices are available for domestic use and at gymnasiums since their popularity lies on the promise of physical conditioning without the need of performing voluntary physical exertion. Our patient was exposed to electrostimulation once, which is a fact that stands out when comparing her case with the one described in 2004 by Guarascio et al.[6] However, our patient performed her regular aerobic routine while carrying the electrostimulation device in both thighs. The complete analytical normalisation, the electromyographic study, the normality in the lactate test and the reincorporation to regular physical activity reasonably rule out that the patient suffers from any

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