In the quest for safer treatment for systemic lupus erythematosus

June 17 2014

The treatment of systemic lupus erythematosus has traditionally been based on glucocorticoids administered orally. Nevertheless, these drugs were known to cause serious side effects in the medium to long term. In order to determine whether a safety threshold exists in corticoid dose, the Hospital Universitario Cruces has conducted a study which has produced enlightening results. On the basis of these results and previous studies, the treatment currently being recommended for patients in the hospital limits the administering of glucocorticoids and favours the use of anti-malarial drugs as background treatment.

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. It can affect various organs, in particular, the skin, joints and kidneys although it displays great variability in extent and seriousness depending on the patient. Approximately nine out of every ten patients are female and it appears in one woman in every thousand.

As Dr Guillermo Ruiz-Irastorza, head of the Autoimmune Disease Research Unit of the Hospital Universitario Cruces, explained, traditionally lupus has been treated mostly with glucocorticoids (prednisone), despite the fact that its severe side effects have been known for years. "We doctors knew that administering high doses of prednisone in an ongoing way caused irreversible damage like osteoporosis, avascular necrosis of bone, diabetes or cataracts. However, the tendency was to accept these side effects as an inevitable price to pay in exchange for controlling the disease".

Yet recent studies by this same group indicate that lower doses of glucocorticoids could be just as effective. What is more, in more serious forms, pulsed therapy, in other words, the intermittent intravenous administering of high doses is highly effective and probably does not lead to so many adverse effects.

So the researchers at the Hospital Universitario Cruces decided to study the relation between treatment with prednisone administered orally over 4 years from the moment of diagnosis and the damage built up over the first 5 years. To complete the study, they also looked at the effect of another glucocorticoid, methylprednisolone, administered intravenously at high doses and intermittently, at the moments when the disease manifests itself with increased severity.

230 patients, 206 of whom were women, took part in the study. The average age when they were diagnosed with lupus was 35.75 years.

"We saw that by the end of the fourth year most of them, 80%, had been treated with prednisone at some point, and by the fifth year nearly 4 out of every 10, 37.8%, had developed damage," pointed out Dr Ruiz-Iraztorza. Significantly, the patients with damage had received higher doses of prednisone (10.4 mg/day as opposed to 6 mg/day in the patients without damage). In the specific study of the damage that could be directly attributed to the use of glucocorticoids, the results were similar, with average daily doses of 11 vs. 7 mg/day, respectively. And it does not stop there. As previous studies had suggested, they proved that the association with damage began with average doses of 7.5 mg/day. "In other words, above that dose, permanent side effects may appear." By contrast, pulsed methylprednisolone therapy was not associated with any kind of damage.

Anti-malarial drugs for treating lupus

The research carried out by the group at the Hospital Universitario Cruces has been published in the specialised journal *Rheumatology*. In fact, these results have confirmed that the guidelines used in the Auto-immune Disease unit of the Hospital Universitario Cruces for several years are good. Dr Ruiz-Irastorza stresses that the background treatment in patients with SLE has to be anti-malarial drugs, specifically hydroxychloroquine, since, as he maintains, "it has been proven that they are more effective in the long term than glucocorticoids for controlling lupus and, at the same time, they have far fewer side effects. The role of the latter needs to be restricted to managing periods during which the disease flares up."

"The beneficial effect of anti-malarial drugs on SLE was discovered by accident during the Second World War," explained the doctor. "In any case, as prolonged background treatment they were seen to be ideal for controlling lupus, even as a monotherapy in many patients with proven effects on long-time survival. So we reserve glucocorticoids to be administered when the disease flares up, and we know that in more serious cases we can administer pulsed methylprednisolone safely and effectively. For maintenance treatment, the prednisone dose must not exceed 5 mg/day so on occasions we have to add other immunosuppressive drugs. We believe that these combined guidelines that we use constitute a safer and more effective alternative for patients with SLE."

More information: The scientific paper referred to in this press release was published in the journal Rheumatology: Ruiz-Arruza I, Ugarte A, Cabezas-Rodriguez I, Medina J-A, Moran M-A, Ruiz-Irastorza G. "Glucocorticoids and irreversible damage in patients with systemic lupus erythematosus". *Rheumatology* 2014 (epub ahead of print).