safety and effectiveness of LDL-aphaeresis in Cerebrotendinous xanthomatosis.

CT2016/01

Introduction: Cerebrotendinous xanthomatosis (CTX) is an ultra-rare congenital disease which can cause important and severe neurological complications if not diagnosed and treated early. Chenodeoxycholic acid (CDCA) replacement therapy, whether or not in combination with HMG-CoA reductase inhibitors, is the standard therapy, though many patients diagnosed at adult age do not respond to the treatment or decide to stop it after a time, suffering a progressive neurological deterioration which can lead to death. LDL aphaeresis has been proposed as a possible alternative option for such patients.

Objectives: To assess the effectiveness and safety of LDL aphaeresis in the treatment of CTX.

Methods: A search of the scientific literature was conducted until June 2016, stipulating no time limit and covering computerised biomedical databases (PubMed, Embase, CRD, Cochrane, etc.). Due to the paucity of literature, for assessment purposes we considered all original studies published in scientific journals in Spanish, French, English, Portuguese or Italian, which furnished primary data on the effectiveness and safety of this procedure. The results were summarised in evidence tables and qualitatively synthesised.

Results: A total of four original studies were included. All were descriptive analyses of a single case or very small series. They included a total of 9 patients, with ages ranging from 24 to 54 years. The LDL aphaeresis procedure, in combination with QDCA and/or statins, was used in all cases. The maximum follow-up period was 14 months. One of the patients did not improve significantly, despite achieving normalisation of cholestanol levels. A slight improvement in neurological symptomatology was reported in the other three, though objective scales were not used for their evaluation. Only one patient, on whom LDL and HDL aphaeresis was performed, displayed substantial neurological improvement.

Discussion: The use of LDL aphaeresis is controversial, fundamentally because it is an invasive technique for which there is no proven clinical basis and practically no scientific evidence. Except for one case, all patients initiated LDL aphaeresis in conjunction with other treatments, and though the latter's differential effect could not be ascertained, the authors of these studies argue that the beneficial effect cannot be attributed to either CDCA or statins, since both are slow-acting.
Conclusions: Available scientific evidence on the effectiveness of LDL aphaeresis in CXT is practically nil and lacks clinical validity. The published information highlights the fact that currently there is no general agreement as regards a treatment guideline, and the few studies that do exist display contradictory results, with it not being clear whether LDL aphaeresis really serves to improve the neurological symptoms and/or slow disease progression.

Recommendations: The first-line treatment for CXT should be based on CDCA replacement therapy, alone or in combination with HMG-CoA reductase inhibitors. The use of LDL aphaeresis should be assessed with caution, and always in the context of a research study, with its application being restricted to highly selected patients. Bearing in mind the important degree of uncertainty

that exists, it is essential that a well-defined clinical follow-up protocol and objective efficacy criteria be drawn up.