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PRESS RELEASE

Carnitine palmitoyltransferase II deficiency

Bezafibrate effective in the treatment of this mitochondrial myopathy

A team of researchers (CNRS laboratory on “Mitochondrial transporters and metabolism” housed at the University of Paris Descartes) and hospital doctors (CIC Necker, Hôpital Necker–enfants malades (AP-HP), Groupe hospitalier Pitié-Salpêtrière (AP-HP)), coordinated by Fatima Djouadi, a senior research officer at Inserm, and Jean-Paul Bonnefont, has just demonstrated the potential benefit of Bezafibrate, a product already widely used as a lipid-lowering drug, in the treatment of a metabolic myopathy: Carnitine Palmitoyltransferase II (CPT2) deficiency. This first clinical trial has demonstrated that treatment with bezafibrate for a period of six months stimulates the metabolic functions of the muscles and leads to an improvement in physical activity capacities and a reduction in muscle pain.

The study is available online, on the New England Journal of Medicine website. It was funded by the Association française contre les myopathies (AFM – French Association against Myopathies) using donations from Téléthon.

CPT2 deficiency is an autosomal recessive condition. It concerns a gene located on chromosome 1, the product of which is an enzyme present in all the tissues and located in the inner mitochondrial membrane. Mitochondria are essential for cells to function properly. Each of the body’s cells contains several hundred – or even thousands – of them, ensuring energy production in numerous tissues. CPT2 deficiency causes abnormal transfer of long-chain fatty acids (LCFA) from the cytoplasm of the cell to the mitochondrion, where they are oxidised. Since oxidation of fatty acids represents an energy source essential for the muscles to function properly, particularly in the event of prolonged exercise, CPT2 deficiency, in its moderate adult form, leads to an intolerance to exercise, muscle pain and muscle stiffness, along with a constant risk of muscle fibre destruction (rhabdomyolysis).

The team of researchers led by Fatima Djouadi and Jean Bastin had recently demonstrated that bezafibrate restored the capacity of the mitochondria to oxidise fatty acids in the myoblasts of patients suffering from the moderate form of CPT2 deficiency by stimulating expression of the mutated gene.

The clinical trial conducted therefore sought to assess the action of this medicinal product on the functional symptoms of patients with this moderate form of CPT2 deficiency. To this end, 6 adult patients were treated with bezafibrate for 6 months. In terms of laboratory tests, the efficacy of the treatment was verified by evaluating the capacity of the mitochondria to transform fatty acids into energy and by quantifying the levels of mRNA encoding CPT2 present in the muscles. The values increased for both these parameters.

In addition, following analysis of the questionnaires concerning the patients' quality of life, the researchers observed that there was a marked improvement in physical activity capacities and a reduction in muscle pain in all the patients treated.

Having demonstrated the therapeutic potential of bezafibrate, the researchers now aim to launch a European clinical trial designed to evaluate the efficacy of bezafibrate in CPT2 deficiency and in VLCAD (very long-chain acyl-coenzyme A dehydrogenase) deficiency, another form of mitochondrial myopathy with similar symptoms to that of CPT2 deficiency, in a larger cohort of patients. These studies are an essential phase to enable bezafibrate to ultimately obtain the status of orphan drug.

To find out more:

Bezafibrate for treatment of an inborn mitochondrial β -oxidation defect – Jean-Paul Bonnefont, Jean Bastin, Anthony Behin, Fatima Djouadi. *New England Journal of Medicine*, Volume 360:838-840, number 8.

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<http://content.nejm.org/cgi/content/extract/360/8/838>

To find out more about the disease:

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