Bezafibrate as treatment in males for Barth syndrome: CARDIOMAN, a double-blind, placebo-controlled crossover RCT

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Plain language summary

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Plain language summary

Barth syndrome is a rare genetic syndrome with mutations in the tafazzin gene causing long-term effects in several organ systems, leading to significant lifelong comorbidities and a reduced quality of life. Barth syndrome shows an X-linked inheritance, hence it is almost exclusively present in males. Tafazzin gene mutations impair overall cell energy metabolism, and affected individuals show compromise of the immune system with a high risk for life-threatening infections, as well as cardiac dysfunction and cardiomyopathy, muscle and general fatigue, and generally reduced mobility also leading to psychological challenges and dysfunction. Currently, specific medical therapies are limited to symptomatic treatment, and drug therapies targeting the causative mitochondrial energy disturbance are urgently needed. This randomised controlled trial explored the use of oral bezafibrate, a licensed drug that can improve cell energy metabolism. Eleven male patients received either bezafibrate or a placebo for 4 months. Exercise capacity by cardiopulmonary exercise testing on a cycle ergometer, as the primary outcome measurement, as well as cardiac function by echocardiography and magnetic resonance imaging, and cellular anatomy and function by in vitro assays and microscopy, were measured before and after this 4-month period. Bezafibrate did not significantly improve exercise capacity, cardiac function or the cellular metabolism, although several cardiac function parameters showed slight improvements with bezafibrate treatment. No significant adverse effects were recorded. The limitations of the trial were its low participant number and the relatively short duration of the drug treatment phase. The trial did prove that complex randomised controlled drug trials are feasible in people with rare diseases. Adherence was good, with parents reporting few difficulties with pill swallowing. The qualitative interviews also found that the study was acceptable to participants and the burden of participating not too onerous. We hope the research can provide a template for future studies.

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