Studies must be carried out to determine whether exercise slows the onset of type 1 diabetes in children and adults

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Rates of type 1 diabetes—the autoimmune form of the condition that often begins in childhood and eventually results in lifelong dependency on insulin—are increasing in almost all nations worldwide. However, while it appears possible from research in other forms of diabetes that physical exercise could slow the progression of this disease, there have been no studies to date that explore this in patients with type 1 diabetes. In a paper published in *Diabetologia* (the journal of the European Association for the Study of Diabetes) researchers argue that such trials must be carried out to potentially benefit the millions of people affected by type 1 diabetes worldwide.

In the UK, approximately 0.3% of the population (or 1 in 300 to 350 people) is affected by type 1 diabetes. It is characterised by immune-mediated destruction of insulin-producing beta cells in the pancreas. It is mostly diagnosed during childhood or young adulthood. Eventually, the body can no longer produce enough insulin to adequately deal with increases in blood sugar, meaning the person must at some point begin injecting insulin and continue doing so for the rest of their life. "However, significant beta cell function is usually still present at the time of diagnosis of type 1 diabetes, and preservation of this function has important clinical benefits," says paper co-author Dr Parth Narendran, of the Institute of Biomedical Research, The Medical School, University of Birmingham, UK. "The last 30 years have seen a number of largely unsuccessful trials for beta cell preservation, and with therapies that have

potential for harm. There is a need to explore new more tolerable approaches to preserving beta cell function, and ones that can be implemented on a large clinical scale. Exercise could be an ideal example of such an approach," he adds.

Research has shown that preserving beta cell function reduces rates of complications including retinopathy (that can lead to blindness) and neuropathy (pain and numbness related to impaired nerve function), as well as decreasing the chances of hypoglycaemia (episodes of dangerously low blood sugar that can be fatal).

In this paper, the authors discuss the evidence to back new large-scale trials of exercise in type 1 diabetes. Physical exercise elicits marked elevations in circulating levels of key molecules such as growth hormone (GH), insulin-like growth factor (IGF)-1, glucagon-like peptide (GLP)-1, interleukin 6 (IL-6), and interleukin-1 receptor agonist (IL-1ra), all of which are thought to have a preserving effect on beta cell mass. Furthermore, exercise decreases levels of harmful inflammatory molecules such as leptin and tumour necrosis factor-alpha, that can promote an immune response leading to the cycle of cell death that kills beta cells. Exercise also helps to normalise plasma glucose and blood fats in both diabetic and pre-diabetic individuals, factors that when chronically elevated are known to cause beta cell death.

They also discuss the evidence from non-human studies in rats, showing that exercise can increase beta cell mass and also increase the amount of insulin produced per beta cell when the total number of cells is decreasing. Regarding evidence from humans, the authors discuss a number of differing studies, including the STRRIDE study from Sweden showing that moderate exercise in middle-aged, overweight people improved beta cell function. They also cite the improvements in insulin sensitivity and blood glucose control seen in many patients with type 2 diabetes who exercise.

In addition, there is evidence from other autoimmune diseases, such as Graves Thyroid disease, psoriasis and multiple sclerosis, that exercise can have a beneficial effect on the cells that are under autoimmune attack.

The authors say: "There is little disagreement that physical exercise has health benefits in type 1 diabetes, and that it should be encouraged as part of routine management. Exercise promotes fitness, reduces insulin requirements and blood fats, improves blood vessel function and well-being, and reduces insulin resistance, cardiovascular disease and mortality in patients with type 1 diabetes. However, exercise is associated with increased risk of hypoglycaemia and increased fluctuations in glucose levels that may explain why it does not always improve blood sugar control in patients."

They continue: "Studies have clearly shown that many people with type 1 diabetes do not undertake enough exercise, and that exercise is not actively promoted nor supported at the time of diagnosis with type 1 diabetes*. The reasons for this are multifactorial, complex, and include anxieties relating to hypoglycaemia and patients' loss of control over their diabetes. However if trials of exercise are shown to salvage residual beta cell function, there would be a strong argument to promote exercise much earlier in the natural history of this condition, and to develop strategies to encourage and support patients at this time. As a therapy, its attraction lies not only in the many health benefits exercise provides, but also because it can be carried out alone, or as a combination therapy for beta cell preservation in type 1 diabetes."

They conclude: "We are currently undertaking a preliminary pilot study of exercise in patients with type 1 diabetes. With this information we hope we and others will be able to move forward to design and conduct large scale trials of exercise to preserve beta cell function in new onset type 1 diabetes. This will need to be tied into other mechanistic studies,

as well as studies of exercise motivation and adherence."

Provided by Diabetologia