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Quinlivan R, Martinuzzi A, Schoser B. Pharmacological and nutritional treatment for McArdle disease (Glycogen Storage Disease type V). *Cochrane Database of Systematic Reviews* 2014, Issue 11. Art. No.: CD003458. DOI: 10.1002/14651858.CD003458.pub5.

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[Intervention Review]

Pharmacological and nutritional treatment for McArdle disease (Glycogen Storage Disease type V)

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Editorial group: Cochrane Neuromuscular Group. **Publication status and date:** New search for studies and content updated (no change to conclusions), published in Issue 11, 2014.

Citation: Quinlivan R, Martinuzzi A, Schoser B. Pharmacological and nutritional treatment for McArdle disease (Glycogen Storage Disease type V). *Cochrane Database of Systematic Reviews* 2014, Issue 11. Art. No.: CD003458. DOI: 10.1002/14651858.CD003458.pub5.

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ABSTRACT

Background

McArdle disease (Glycogen Storage Disease type V) is caused by an absence of muscle phosphorylase leading to exercise intolerance, myoglobinuria rhabdomyolysis and acute renal failure. This is an update of a review first published in 2004.

Objectives

To review systematically the evidence from randomised controlled trials (RCTs) of pharmacological or nutritional treatments for improving exercise performance and quality of life in McArdle disease.

Search methods

We searched the Cochrane Neuromuscular Disease Group Specialized Register, CENTRAL, MEDLINE and EMBASE on 11 August 2014.

Selection criteria

We included RCTs (including cross-over studies) and quasi-RCTs. We included unblinded open trials and individual patient studies in the discussion. Interventions included any pharmacological agent or nutritional supplement. Primary outcome measures included any objective assessment of exercise endurance (for example aerobic capacity (VO₂) max, walking speed, muscle force or power and fatigability). Secondary outcome measures included metabolic changes (such as reduced plasma creatine kinase and a reduction in the frequency of myoglobinuria), subjective measures (including quality of life scores and indices of disability) and serious adverse events.

Data collection and analysis

Three review authors checked the titles and abstracts identified by the search and reviewed the manuscripts. Two review authors independently assessed the risk of bias of relevant studies, with comments from a third author. Two authors extracted data onto a specially designed form.

Main results

We identified 31 studies, and 13 fulfilled the criteria for inclusion. We described trials that were not eligible for the review in the Discussion. The included studies involved a total of 85 participants, but the number in each individual trial was small; the largest treatment trial included 19 participants and the smallest study included only one participant. There was no benefit with: D-ribose, glucagon, verapamil,

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vitamin B₆, branched chain amino acids, dantrolene sodium, and high-dose creatine. Minimal subjective benefit was found with low dose creatine and ramipril only for patients with a polymorphism known as the D/D angiotensin converting enzyme (ACE) phenotype. A carbohydrate-rich diet resulted in better exercise performance compared with a protein-rich diet. Two studies of oral sucrose given at different times and in different amounts before exercise showed an improvement in exercise performance. Four studies reported adverse effects. Oral ribose caused diarrhoea and symptoms suggestive of hypoglycaemia including light-headedness and hunger. In one study, branched chain amino acids caused a deterioration of functional outcomes. Dantrolene was reported to cause a number of adverse effects including tiredness, somnolence, dizziness and muscle weakness. Low dose creatine (60 mg/kg/day) did not cause side-effects but high-dose creatine (150 mg/kg/day) worsened the symptoms of myalgia.

Authors' conclusions

Although there was low quality evidence of improvement in some parameters with creatine, oral sucrose, ramipril and a carbohydrate-rich diet, none was sufficiently strong to indicate significant clinical benefit.

PLAIN LANGUAGE SUMMARY

Drug and nutritional treatment for McArdle disease

Review question

We reviewed the evidence about the effects of drug and nutritional treatment for McArdle disease.

Background

McArdle disease (also known as glycogen storage disease type V) is a disorder affecting muscle metabolism. The condition is caused by the lack of an enzyme called muscle phosphorylase. This results in an inability to break down glycogen 'fuel' stores. McArdle disease leads to pain and fatigue with strenuous exercise. Sometimes severe muscle damage develops and occasionally this results in acute reversible kidney failure.

Study characteristics

After a wide search, we identified 13 randomised studies that included 85 participants with McArdle disease. This is an update of a review first published in 2004. We found no new trials at this update.

Key results and quality of the evidence

The review found no benefit compared with placebo with the following treatments: D-ribose, glucagon, verapamil, vitamin B_6 , oral branched chain amino acids, dantrolene sodium, high-dose creatine and ramipril. Low dose creatine and ramipril produced minimal benefit for patients who also have the D/D angiotensin converting enzyme (ACE) phenotype. Taking low dose creatine supplements had a minor benefit in improving exercise tolerance in a small number of people with the condition. Taking a sugary drink before planned strenuous exercise can improve performance but this treatment is not practical for day-to-day living. A diet rich in carbohydrate may be superior to a diet rich in protein. Adverse effects were reported in four studies. Oral ribose caused symptoms suggestive of a low blood sugar including light-headedness, hunger and diarrhoea. One study of branched chain amino acids resulted in a deterioration in participants. Dantrolene was reported to cause a number of side-effects including tiredness, sleepiness, dizziness and muscle weakness. Low dose creatine (60 mg/kg/day) did not cause any side-effects but high-dose creatine (150 mg/kg/day) worsened the symptoms of muscle pain. The quality of these studies was low due to the small number of participants; the largest number in one trial was 19 and one trial had only one participant.

The evidence is current to August 2014.