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[Intervention Review]

Growth hormone therapy for people with thalassaemia

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ABSTRACT

Background

Thalassaemia is a recessively-inherited blood disorder that leads to anaemia of varying severity. In those affected by the more severe forms, regular blood transfusions are required which may lead to iron overload. Accumulated iron from blood transfusions may be deposited in vital organs including the heart, liver and endocrine organs such as the pituitary glands which can affect growth hormone production. Growth hormone deficiency is one of the factors that can lead to short stature, a common complication in people with thalassaemia. Growth hormone replacement therapy has been used in children with thalassaemia who have short stature and growth hormone deficiency.

Objectives

To assess the benefits and safety of growth hormone therapy in people with thalassaemia.

Search methods

We searched the Cochrane Haemoglobinopathies Trials Register, compiled from electronic database searches and handsearching of journals and conference abstract books. We also searched the reference lists of relevant articles, reviews and clinical trial registries. Our database and trial registry searches are current to 10 August 2017 and 08 August 2017, respectively.

Selection criteria

Randomised and quasi-randomised controlled trials comparing the use of growth hormone therapy to placebo or standard care in people with thalassaemia of any type or severity.

Data collection and analysis

Two authors independently selected trials for inclusion. Data extraction and assessment of risk of bias were also conducted independently by two authors. The quality of the evidence was assessed using GRADE criteria.

Main results

One parallel trial conducted in Turkey was included. The trial recruited 20 children with homozygous beta thalassaemia who had short stature; 10 children received growth hormone therapy administered subcutaneously on a daily basis at a dose of 0.7 IU/kg per week and 10 children received standard care. The overall risk of bias in this trial was low except for the selection criteria and attrition bias which were unclear. The quality of the evidence for all major outcomes was moderate, the main concern was imprecision of the estimates due to the small sample size leading to wide confidence intervals. Final height (cm) (the review's pre-specified primary outcome) and change

in height were not assessed in the included trial. The trial reported no clear difference between groups in height standard deviation (SD) score after one year, mean difference (MD) -0.09 (95% confidence interval (CI) -0.33 to 0.15 (moderate quality evidence). However, modest improvements appeared to be observed in the following key outcomes in children receiving growth hormone therapy compared to control (moderate quality evidence): change between baseline and final visit in height SD score, MD 0.26 (95% CI 0.13 to 0.39); height velocity, MD 2.28 cm/year (95% CI 1.76 to 2.80); height velocity SD score, MD 3.31 (95% CI 2.43 to 4.19); and change in height velocity SD score between baseline and final visit, MD 3.41 (95% CI 2.45 to 4.37). No adverse effects of treatment were reported in either group; however, while there was no clear difference between groups in the oral glucose tolerance test at one year, fasting blood glucose was significantly higher in the growth hormone therapy group compared to control, although both results were still within the normal range, MD 6.67 mg/dL (95% CI 2.66 to 10.68). There were no data beyond the one-year trial period.

Authors' conclusions

A small single trial contributed evidence of moderate quality that the use of growth hormone for a year may improve height velocity of children with thalassaemia although height SD score in the treatment group was similar to the control group. There are no randomised controlled trials in adults or trials that address the use of growth hormone therapy over a longer period and assess its effect on final height and quality of life. The optimal dosage of growth hormone and the ideal time to start this therapy remain uncertain. Large well-designed randomised controlled trials over a longer period with sufficient duration of follow up are needed.

PLAIN LANGUAGE SUMMARY

Growth hormone therapy for people with thalassaemia

Review question

We reviewed the evidence about the effect of treating people with thalassaemia with growth hormones.

Background

Thalassaemia is an inherited blood disorder that causes anaemia of varying severity. People who have the more severe forms of thalassaemia need regular blood transfusions from early childhood resulting in excess iron accumulating in vital organs such as the heart, liver and hormone-secreting glands (endocrine glands). One of the glands at risk is the pituitary gland which secretes growth hormone which in turn regulates the growth and function of the human body. If the production of growth hormone is disrupted by iron deposition, the affected children may not grow very tall.

Short stature is very common amongst people with thalassaemia. It may be caused by various factors including problems with growth hormone or other hormones, insufficient blood transfusions or poor nutrition. Synthetic growth hormone is one way of treating short stature in thalassaemia, especially in children with defective growth hormone production. This usually involves an injection of growth hormone under the skin (subcutaneously) several days a week over a period of time. However, it is unclear whether the use of synthetic growth hormone provides any consistent or clear benefits to people with thalassaemia.

Search date

The evidence is current to 08 August 2017.

Study characteristics

We found only one small trial for our review. It included 20 children with beta thalassaemia who were considerably shorter than they should be based on growth charts. Ten of the children were randomly selected to receive daily growth hormone treatment in addition to their usual (standard) treatment and the other 10 children just had their usual treatment. Investigators recorded the height of the children and did blood tests every three months. The trial was conducted over a one-year period.

Key results

Height velocity is the rate at which a child grows taller and is calculated by measuring the difference in height over a period of time (usually measured as cm per year). In this review, the children who received growth hormone for one year had a higher height velocity (on average 2.28 cm per year more) compared to those who did not receive growth hormone. In other words, those given growth hormone grew modestly faster than those not on growth hormone. The height of a child may also be scored based on standard charts of the population (height standard deviation scores). Using this measurement, children treated with growth hormone had similar scores to those not on growth hormone at the end of one year. None of the 20 children suffered from any side effects. Although, while there was no clear difference between groups in the oral glucose tolerance test at one year, those children on growth hormone therapy had higher fasting blood glucose levels, but these were still within the normal range. The trial did not provide information beyond the one-year period, hence we do not know if the adult height of the children in the trial was affected by growth hormone therapy in any way.

There were no trials in people with thalassaemia which examined the effects of growth hormone therapy over a longer period, at different dosages or in different age groups; neither were there any trials studying the effect of growth hormone therapy on adult height or general well-being (quality of life).

Quality of the evidence

Overall, we considered the quality of evidence for the outcomes described above (short-term growth and side effects) to be moderate, but we had a major concern that there was only a small number of participants.

Conclusions

Based on moderate quality evidence from one small trial, the use of growth hormone may modestly improve some measures of growth. However, there was no information on final height or quality of life. More trials are needed before a clear conclusion can be drawn on the overall benefits and risks of using growth hormone in people with thalassaemia.