

CRD summary
This review assessed the effects of corticosteroids in boys with Duchenne dystrophy. It concluded that prednisone can improve muscle strength and function and pulmonary function, and that deflazacort also provides similar benefits. This conclusion was supported by the results presented; however, poor reporting of review methods and study details make it difficult to confirm the reliability of the authors' conclusions.

Authors' objectives
To evaluate the effects of corticosteroid treatment in boys with Duchenne dystrophy (DD).

Searching
The sources searched included MEDLINE (1966 to 2004) and Current Contents. The search terms were reported and no language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Inclusion criteria were not specified in terms of the study design. Randomised controlled trials (RCTs), open trials and case reports were included.

Specific interventions included in the review
Although inclusion criteria for the interventions were not explicitly reported, it was clear that studies of corticosteroid treatment were eligible for inclusion. Regimens evaluated in the primary studies included: 0.3 to 1.5 mg/kg per day prednisone/prednisolone; 1.25 to 5 mg/kg prednisone/prednisolone on alternate days; deflazacort 0.9 to 1 mg/kg per day; or deflazacort 2 mg/kg on alternate days. The duration of treatment ranged from 6 weeks to 14 years.

Participants included in the review
Although inclusion criteria for the participants were not explicitly reported, it was clear that studies of boys with DD were eligible for inclusion. The age of the boys in the included studies ranged from 3 to 19.4 years.

Outcomes assessed in the review
Inclusion criteria were not specified in terms of the outcomes. The review assessed a variety of outcomes including muscle strength, 24-hour urinary excretion of creatinine, muscle function, loss of ambulation, pulmonary function, forced vital capacity (FVC) and side-effects.

How were decisions on the relevance of primary studies made?
Individual members of the committee selected the studies.

Assessment of study quality
Individual members of the committee assessed validity. The studies were graded using the hierarchy of study design described by the Quality Standards Subcommittee of the American Academy for Neurology. Class I studies were RCTs in a representative population with masked outcome assessments with clearly defined inclusion criteria, primary outcomes, comparable treatment groups at baseline (or suitable statistical adjustments made) and that accounted for drop-outs. Class II studies were prospective matched group cohort studies with masked outcome assessment and poorer quality RCTs. Class III included all other controlled studies in a representative population with independent outcome
assessment. Class IV studies included uncontrolled studies, case series, case reports and expert opinion.

**Data extraction**
Individual members of the committee extracted the data from the studies. The data extraction tables were available on the Neurology website (accessed 21/04/2007), but a journal subscription may be required for access.

**Methods of synthesis**

- **How were the studies combined?**
  The studies were grouped by corticosteroid regimen, study design and outcome and combined in a narrative, with accompanying tables. The level of evidence for corticosteroids was graded using a hierarchy of evidence described by the Quality Standards Subcommittee of the American Academy for Neurology.

- **How were differences between studies investigated?**
  Some differences were accounted for in the grouping of the studies for the narrative synthesis, but there was no formal assessment or discussion of differences between the studies.

**Results of the review**

Twenty-five reports of 23 studies were included (n=868); 2 studies were extensions of other studies. There were 7 double-blind RCTs evaluating prednisone/prednisolone (n=276; sample size ranged from 14 to 103), 2 double-blind RCTs evaluating deflazacort (n=56), 11 open trials or case reports of prednisone (n=278; sample size ranged from 1 to 103), 3 double-blind RCTs comparing prednisone and deflazacort (n=172), and 2 retrospective reports comparing deflazacort and no treatment (reported as historical controls) (n=86).

**Prednisone/prednisolone.**

Seven RCTs demonstrated beneficial effects of prednisone, with 0.75 mg/kg per day being the optimal dose for boys aged 5 to 15 years. The results from the 11 open trials and case reports were consistent with the RCT results.

- **Muscle strength and function:** 4 RCTs reported improvements in muscle strength (average muscle score over 34 muscle groups, or kg weights lifted) with prednisone treatment, with maximum benefits observed after 3 months. The increase in muscle strength was significantly greater with 0.75 mg/kg per day compared with 0.03 mg/kg per day in 2 studies. One of these studies also reported on muscle function and found that the time to climb four stairs, travel 9 metres, or arise from supine to standing significantly improved at 6 months (p<0.005) in boys taking prednisolone (0.75 or 1.5 mg/kg per day) compared with placebo. However, an extension to one of these studies also reported that alternate day prednisolone (1.25 or 2.5 mg/kg) was associated with a decline in previous gains observed for strength and muscle function from daily prednisolone 0.75 or 1.5 mg/kg. The other RCT of alternate day prednisolone (5.0 mg/kg) found less deterioration in ambulation at 36 months compared with placebo (6 out of 7 on corticosteroids continued walking versus 7 out of 7 on placebo who stopped walking).

- **Other outcomes:** one RCT reported that 24-hour urinary creatinine excretion was significantly increased after 6 months in boys taking prednisolone (0.75 or 1.5 mg/kg per day), consistent with an increase in muscle mass, but was significantly decreased in boys taking placebo. One RCT reported that FVC was significantly higher at 6 months in boys taking 0.75 mg/kg per day and also 1.5 mg/kg per day prednisolone compared with placebo.

**Deflazacort.**

Two RCTs reported that 1.0 mg/kg per day of deflazacort for 9 months and alternate day treatment with 2.9 mg/kg for 2 years increased muscle strength and function compared with placebo. Three RCTs, which were considered to be of
lower quality, compared deflazacort with prednisolone and reported similar effects for both regimens for slowing progression and improving strength and muscle function.

Side-effects: the side-effects were similar to those with prednisolone and were mainly weight gain and the development of cushingoid features. They were more frequent in longer term studies: 2 retrospective studies of 3 to 5 years’ duration assessing 0.9 mg/kg per day deflazacort reported cataracts, obesity or weight gain, and short stature.

Authors’ conclusions
Studies showed that prednisone improved muscle strength, timed muscle function and pulmonary function in boys with DD. Deflazacort provided similar results and can be used as an alternative. Patients taking corticosteroids should be monitored.

CRD commentary
The review addressed a clear question in terms of the participants and intervention, but inclusion criteria were not explicitly stated. Only two databases were named and this, along with the lack of specific attempts to identify unpublished studies, might have resulted in the omission of other relevant studies. Attempts were made to minimise language bias. The study selection, data extraction and assessment of validity were carried out by individual committee members, with no indication of how many people were involved or how any agreements were reached. This might have led to reviewer error and bias, but this review appeared to be a practice guideline rather than a traditional systematic review. Validity was assessed by considering aspects of study design, but full details of the validity of each study were not reported.

There was little information on the baseline characteristics of the participants, methods used to assess outcomes or individual study results, and this made it difficult to assess the comparability of the studies. The lack of clearly defined inclusion criteria for the outcomes increases the possibility of selective reporting of outcomes. Given the diversity of the studies, the narrative synthesis was appropriate and results from different study designs were given appropriate levels of emphasis. The conclusion appeared to be supported by the results presented; however, the poor reporting makes it difficult to confirm the reliability of the authors’ conclusions.

Implications of the review for practice and research
Practice: The authors stated that prednisone (0.75 mg/kg per day) should be offered as treatment to boys with DD. The dose could be tapered to as low as 0.3 mg/kg per day if side-effects require this. Patients on corticosteroids should be monitored for potential side-effects and benefits (such as timed function tests and loss of independent ambulation), and the risks and benefits of treatment should be discussed. Deflazacort (0.9 mg/kg per day) could be used as an alternative, where available, but patients should be monitored for asymptomatic cataracts and weight gain.

Research: The authors stated that double-blind RCTs are needed to compare prednisolone (0.75 mg/kg per day) with alternative regimens including higher-dose alternate-day treatment, intermittent treatment, high dose pulses on weekends and deflazacort. There is also a need to determine the effects of daily prednisolone on cardiac, gastrointestinal and cognitive functions in patients with DD; to assess the effects of different doses of prednisolone and deflazacort in younger children (aged 2 to 4 years) and their effects late in the course of DD; to determine the mechanism underlying the beneficial effect of corticosteroids using in vitro and animal studies; to evaluate quality of life in patients of all ages with DD; to examine the effects of long-term corticosteroid treatment on all aspects of DD; to examine the natural history of DD with respect to bone mass and bone density, and to assess the effects of calcium supplements and bisphosphonates on these parameters; and to determine the effects of dietary modification and exercise on the weight gain associated with corticosteroids.

Bibliographic details
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.