Summary and conclusions.
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The aims of the study described in this thesis were: 1. to establish reference values for muscle force, functional ability, calf circumference and echogenitcity of muscle tissue; 2. to assess disease severity in ambulant DMD patients by using these reference values; 3. to determine the effects of prednisone therapy on muscle function and muscle force in DMD patients.

In chapter 1, the general introduction, the clinical, pathophysiological and genetic characteristics of DMD are described. It ends with giving an outline of the thesis. In chapter 2, we provide quantitative reference values for maximum isometric muscle force obtained by hand-held dynamometry in 270 normal children. These values were measured in 11 different muscle groups. Reference values were given for each individual muscle group as well as for summed scores for arm and leg muscles and proximal and distal localised muscle groups. There appears to be no difference in maximum muscle force between boys and girls until the age of 14 years. Thereafter boys become significantly stronger for most tested muscle groups. We conclude that these reference values can be used to assess the extent of possible muscle weakness in individual muscle groups, to determine distribution patterns of muscle weakness and to evaluate disease progression and the effects of therapy in any disease that causes muscle weakness. In chapter 3, we describe normal values for timed functional tests (running 9m and rising up from the floor to a standing position) in 123 healthy children. In addition we applied these values and the reference values for muscle force in 16 ambulant DMD patients. Healthy children become quicker with age in executing these timed tests whereas, DMD patients become slower. Compared to healthy children muscle force is significantly reduced in DMD patients. A small reduction of muscle force is accompanied by a large reduction of muscle function in ambulant DMD patients. We conclude that timed functional testing changes more than muscle force and can therefore, be used as an additional parameter to determine the extent of disease progression and to evaluate the effects of therapy in ambulant DMD patients. In chapter 4, we describe the extent of calf enlargement in DMD patients compared to healthy boys. Although calf enlargement is said to be a classical feature in DMD patients, the magnitude of calf enlargement is unknown. Circumferences of the calf and upper and lower extremities were quantified in 59 healthy children. These values were compared with those of 19 ambulant DMD patients. Calf circumference was significantly increased in the group of DMD patients. However, in individual patients calf enlargement can be feigned by a discrepancy between calf circumference and circumference of the upper leg and arm muscules as part of a generalised muscle atrophy. In chapter 5, we describe reference values of biceps and quadriceps muscle dimension.
and muscle aspect in healthy children. These values were applied to evaluate their additional value in children with proven neuromuscular disorders.

By using density analysis healthy children and children with neuromuscular disorders can be distinguished. However, to distinguish between different types of neuromuscular disorders in children detailed aspect analysis is necessary.

In chapter 6, we review the literature about the use of steroids in DMD. A search for trials in DMD was carried out in Clinical Evidence (BMJ Publishers), metaregister RCTs (Biomed Central), Cochrane Library, Embase from 1974 to 2004 and a ‘second opinion search’ in Medline. Twenty articles, which reported the effects of deflazacort, oxandrolone, prednisone or prednisolone, were analysed. On the basis of this review, short-term intermittent prednisone treatment can be justified in DMD patients, since it has a beneficial effect on muscle function and muscle force in DMD. The long-term beneficial effect on altering disease course however, remains unclear and it is unknown to what extent long-term side effects will be present.

In chapter 7, we present the results of a randomised controlled trial of intermittent prednisone therapy in ambulant DMD patients. Prednisone (0,75 mg/kg/d) or a placebo was given for 6 months during the first 10 days of each month. After a wash-out period of 2 months, patients received the other regime for further 6 months. In these patients, the increase in time needed to run 9 m and to climb 4 standard-size stairs was significantly lower during the prednisone period compared to that during the placebo period. This was paralleled by an increase in total muscle force as well as proximal-and arm muscle force during the prednisone period. Although the number of side-effects was larger in the prednisone period, the quality of life did not change significantly during this period.

Conclusions

1. This thesis provides an extensive set of quantitative normal values for different parameters related to the neuromuscular system, which can be used to determine the extent of disease severity in any disease that affects these parameters and to evaluate the effects of therapy.

2. Intermittent prednisone therapy, 0,75 mg/kg/d during the first 10 days of each month, slows down disease progression on the short-term in ambulant Duchenne muscular dystrophy patients.

3. Short-term (6 months) intermittent prednisone therapy does give some side effects in ambulant Duchenne muscular dystrophy patients, but does not affect the quality of life.