Archives de Pédiatrie 31 (2024) 410–418

Contents lists available at ScienceDirect

Archives de pédiatrie

journal homepage: www.elsevier.com/locate/arcped

Practice guidelines

Choice of compound, dosage, and management of side effects for long-term corticosteroid treatment in Duchenne muscular dystrophy: Guidelines from the Neuromuscular Commission of the French Society of Pediatric Neurology

ARTICLE INFO

Keywords:
Duchenne muscular dystrophy
Glucocorticoids
Drug therapy

ABSTRACT

The French Society of Pediatric Neurology and the FILNEMUS network created a working group on corticosteroid therapy in children with Duchenne muscular dystrophy in order to analyze the literature review and current French practices. The aim of this work was to produce guidelines regarding treatment initiation, pre-therapeutic interventions, choice between available compounds, and treatment monitoring (dosage, duration, and discontinuation). The treatment side effects and their management are also detailed: osteoporosis, endocrinological anomaly (growth delay, weight gain, pubertal delay), cataract, arterial hypertension, behavioral disorders, management of immunosuppression and vaccines, and management of gastrointestinal and metabolic complications.

Background and objectives of the guidelines

The management of Duchenne muscular dystrophy (DMD) requires a multidisciplinary approach to address the needs of patients affected by this severe progressive neuromuscular disease. Whereas genetic therapies are under investigation in clinical studies, DMD treatment is still mainly symptomatic and includes rehabilitation, orthopedic devices and surgery, ventilatory support, cardiological follow-up, and preventive treatment of cardiomyopathy. Physiotherapy and treatment with corticosteroids remain the mainstays of DMD care [1]. Long-term glucocorticoid therapy has been shown to prolong the ability to walk, increase the median age at loss of mobility milestones by 2.1–4.4 years [2], reduce the requirement for scoliosis-related spinal surgery, improve cardiorespiratory capacity [3], delay the need for noninvasive ventilation [4], and increase the life expectancy [2,3] and the quality of life of patients [4].

In France, children with neuromuscular diseases are monitored in reference centers that organize care (three coordinating reference centers, 26 constituent centers, and 38 centers of competence) for almost 2000 adult and pediatric patients with DMD. In these centers, children are cared for during day hospitalizations and benefit from multidisciplinary consultations (neurological, physical medicine and rehabilitation, respiratory, cardiological, and orthopedic), which facilitates the communication between specialists. These referent centers are coordinated by the Neuromuscular Commission of the French Society of Pediatric Neurology (*Société Française de Neurologie Pédiatrique*, NC-SFNP) and the French Network of Neuromuscular Diseases (FILNEMUS network). NC-SFNP–FILNEMUS was mandated to create disease-specific registries and set up multidisciplinary consultation meetings dealing with diagnoses, follow-up of clinical trials, and innovative treatments.

Within the NC-SFNP–FILNEMUS, a Corticosteroids and DMD Working Group was created in June 2020 in order to evaluate French practices regarding corticosteroid management in children with DMD.

To this end, in November 2020 a questionnaire was addressed to prescribing physicians of French reference centers. Although international care recommendations are proposed [1,3–7], the questionnaire highlighted that practices are not homogeneous between neuromuscular centers in France. While there was a high degree of agreement on prescribing corticosteroids to patients with DMD, treatment management and follow-up in the case of side effects remained heterogeneous.

The aim of the present project was to provide guidelines based on a literature review to assist practitioners involved in DMD patient management, particularly practitioners from reference centers, for corticosteroid prescription and follow-up of children with DMD (choice of compound, dosage, and management of side effects), as well as to assist in their discussions with patients and their families.

Methods

Within the NC-SFNP–FILNEMUS, the Corticosteroids and DMD Working Group was created in June 2020 and is composed of 10 pediatricians experienced in DMD patient care from six reference centers. In order to propose detailed guidelines, small subgroups worked on the following main topics: corticosteroid treatment initiation, follow-up examinations, dosage adaptation, discontinuation protocol, and screening and management of side effects.

Each subgroup carried out a literature review to produce a subspecialized report. If guidelines were available for a topic, a summary of these guidelines was mainly used to produce the subspecialized report. If they were not available, a proposed guideline was produced based on

https://doi.org/10.1016/j.arcped.2024.05.003
Received 20 December 2023; Accepted 26 May 2024
Available online 27 September 2024

published evidence, and in the case of a lack of published evidence, consensus-based opinion of best practice of care was used to produce the subspecialized report.

All reports were then combined into a single document that was addressed to all the members of the work group for proofreading and validation. The finalized text was submitted to the NC-SFNP–FILNEMUS in July 2021. The non-consensual points were discussed until a consensus was reached. All members of the neuromuscular commission were invited by electronic mail to comment on, accept, or reject this final version of the manuscript. These French guidelines were translated into English in 2022.

Part 1: guidelines for the long-term use of corticosteroid therapy in the context of pediatric DMD

International guidelines had been published regarding the long-term use of corticosteroid therapy in the context of pediatric DMD. Hence, we propose a summary of these guidelines on the various aspects of managing patients on corticosteroid therapy.(Table 1)

Benefits of corticosteroid treatment

Corticosteroids are recommended for the chronic treatment of pediatric DMD patients (international consensus). Two compounds are used: prednisone/prednisolone (0.75 mg/kg/day) and deflazacort (0.9 mg/kg/day) [1].

A Cochrane review [6] reported the benefits of short-term (2 years) corticosteroid treatment on strength and muscle function in placebo-controlled studies, notwithstanding the moderate methodological quality of these studies. These data have been confirmed in a 2016 review by Gloss et al. [3], which reported an improvement in survival and muscle strength, a delay in the loss of walking (ranging from 1.4 to 2.5 years) and in the development of cardiomyopathy and scoliosis, and an improvement in respiratory function.

These observations have been confirmed by a long-term follow-up duration study showing that the median age of loss of ambulation was 10 years in patients treated for less than 1 year and 13.4 years in those treated for more than 1 year. Moreover, patients treated for more than 1 year displayed loss of upper extremity functionality (by 2.8–8 years) and prolonged survival compared with patients treated for less than 1 year [2]. Barber et al. also reported a delay in the occurrence of heart disease [8], and Pane et al. an improvement in the long-term progression of the disease, by delaying the loss of upper limb function [9].

Treatment initiation

Few studies have correlated the age of corticosteroid treatment initiation with the clinical course. As loss of walking occurs in 30% of patients before the age of 10 years and in 90% before the age of 15 years, an early initiation of treatment (before substantial physical decline) has been recommended. The mean age for loss of walking is 9.5 years if the treatment has been administered for less than 3 years, and 12.3 years if it has been administered for more than 3 years [1,10,11].

There is no clear international consensus regarding the optimal moment for treatment initiation, and this decision is based on age, motor function progression, and side-effect-related risk factors [1]. Some studies show that an early initiation (<5 years) of corticosteroid treatment seems to be associated with early cardiomyopathy, lower forced vital capacity values, and a higher risk for adverse events such as fractures [12].

The criteria leading to treatment initiation include a confirmed DMD diagnosis, the ability for patients and their family to follow the instructions and the monitoring specific to the prescription of corticosteroids, and the family non-opposition to the treatment.

International recommendations suggest initiating treatment before substantial physical decline, and a plateau often occurs between 4 and 6 years of age: There is no medical evidence supporting corticosteroid treatment initiation before the age of 4 years.

If possible, two functional motor evaluations should be performed before the introduction of corticosteroids in order to determine the clinical progression profile. In the case of late diagnosis and stability or in the case of deterioration already observed by the patient's family, it is recommended to initiate the treatment without further delay.

It should be noted that treatment initiation is possible at any age, even after the loss of walking or during adulthood. Some adults may benefit from treatment as it may have a positive effect on respiratory function or swallowing, but they must be vigilant of the risk of side effects, which requires increased monitoring [7].

Pretherapeutic interventions

Before treatment initiation and throughout the follow-up, functional motor assessments are performed, such as the Motor Function Measure (MFM 20 or 32) [13,14] or the 6-min walk test [15] to determine the clinical progression profile (improvement, stability, deterioration) (Fig. 1).

The pretherapeutic analyses should consist of a clinical examination; the determination of blood pressure, weight, height, dietary calcium intake (the GRIO questionnaire at http://www.grio.org/espace-gp/calcul-apport-calcique-quotidien.php can be used); and measurement of complete blood count, blood calcium, glucose and phosphorus levels, fasting blood glucose, blood proteins, vitamin 25 OH D_3 levels, and calcium/creatinine urinary ratio. Additionally, vaccinations must be updated. Also, an ophthalmological examination should determine the

Table 1
Key points for prescription and efficacy of long-term corticosteroid therapy in patients with DMD.

- *Prednisone/prednisolone 0.75 mg/kg/day or deflazacort 0.9 mg/kg/day*
- *Administered in the morning with breakfast*
- *Adapted to tolerance and efficacy*
- *Benefit–risk balance of each compound: deflazacort is more difficult to obtain in France, leads to a smaller final height, and is associated with a higher risk of cataract but creates less weight gain*
- *Initiation in the motor plateau phase between 4 and 6 years*
- *Information for families regarding side effects, dietary rules, instructions to never stop the treatment abruptly and not to give nonsteroidal anti-inflammatory drugs*
- *Treatment prescription after family agreement, examination, laboratory and ophthalmological check-ups, bone densitometry, and vaccinations*
- *Introduced preferably at the therapeutic target dose (gradual introduction in the case of behavioral problems)*
- *Maintenance of a daily dose appropriate for weight (maximum 30–40 mg prednisone/day)*
- *Minimum effective dose: 0.33 mg/kg/day for prednisone/prednisolone*
- *Assessment of efficacy: interviews and functional tests (MFM and 6MWT at least)*
- *Assessment of tolerance: regular clinical monitoring (weight, height, BMI, BP, puberty), laboratory monitoring (vitamin D levels, kalemia, glycosuria/glycemia), radiological monitoring (full-spine X-ray in profile, at least every 2 years), and annual ophthalmological examination*
- *Daily dose is superior in terms of efficacy but alternative dose shows less delay in height growth*
- *Discontinuation of corticosteroid therapy can be indicated in the case of major side effects; decrease in dose should be progressive to prevent acute adrenal insufficiency*

DMD: Duchenne muscular dystrophy; MFM: motor function measure; BMI: body mass index; 6MWT: 6-min walk test; BP: blood pressure.

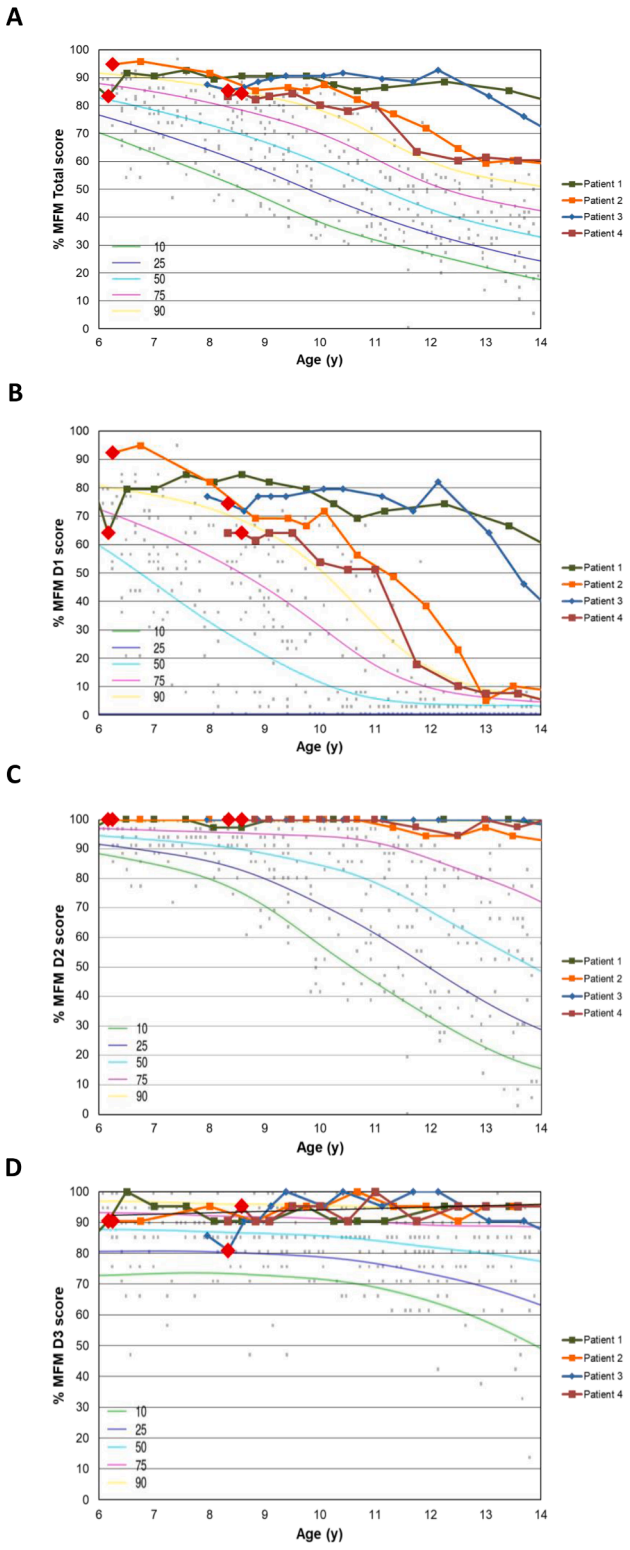

Fig. 1. Monitoring motor skills with the Motor Function Measure (MFM): Example of evolution curves over time for four patients treated with prednisone.

Evolution curves over time of MFM total score (**A**), MFM-D1 subscore (standing position and transfers) (**B**), MFM-D2 subscore (axial and proximal motor skills) (**C**), and MFM-D3 subscore (distal motor skills) (**D**) of the four patients are displayed on MFM percentiles curves of non-treated DMD patients.

Individual percentile curves of MFM scores can be obtained from https://dkfbasel.shinyapps.io/mfmpercentiles/ [66]. Red squares represent age at introduction of corticosteroids for each patient. y = Years.

eye pressure and search for the presence of cataract. Osteodensitometry should be performed. Finally, patients and their family should receive specific education regarding health and dietary rules, especially if risk factors are identified (particularly overweight), as well as regarding the side effects and their monitoring (a written information note should be provided). The general practitioner should be informed.

Choice between available compounds

Two compounds can be used as treatment in the context of DMD: prednisone/prednisolone and deflazacort. These are glucocorticoids and belong to the class of steroidal anti-inflammatory drugs. Prednisolone is a prodrug of prednisone. Deflazacort (a prodrug of prednisolone) is rapidly converted into an active compound, 21-deacetyl-deflazacort. These compounds have been derived from the natural hormone hydrocortisone (i.e., cortisol) in order to retain the glucocorticoid properties (particularly the anti-inflammatory, antiallergic, and immunosuppressive properties) while minimizing the mineralocorticoid properties (antidiuretic, antinatriuretic, and kaliuretic). The synthetic cortisol derivatives are distinguished by their anti-inflammatory properties, their duration of action, and their mineralocorticoid residual action. Prednisone and prednisolone have an intermediate duration of action, a mineralocorticoid effect equivalent to 80% of the cortisol effect, and a fourfold anti-inflammatory potency compared with cortisol. The anti-inflammatory potency of deflazacort is somewhat inferior: 6 mg of deflazacort is equivalent to 5 mg of prednisone or prednisolone (equivalent to 20 mg of hydrocortisone).

Deflazacort has been reported to delay gait loss more effectively than prednisone [16–18]. However, according to the American Academy of Neurology, it is not possible to validate the overall superiority of one compound over the other [3]. A recent controlled trial confirmed the equivalent benefit of both compounds after 3 years on motor skill, respiratory parameters, and parental satisfaction and reported that daily doses are better than alternative doses [19]. Moreover, the weight gain associated with treatment and the final height were both smaller with deflazacort [3,18,20]. Finally, deflazacort appears to be associated with a higher risk of cataract [2]. Since 2021, a nominative temporary authorization of use (*Autorisation Temporaire d'Utilisation*, ATU) can be requested for the delivery of deflazacort in France.

Dosage, adjustments, and discontinuation

The recommended therapeutic target dose for prednisone/prednisolone is 0.75 mg/kg/day (maximal dose: 30–40 mg/day) and 0.9 mg/kg/day for deflazacort (no reported maximal dose). These compounds should preferably be introduced at the therapeutic target dose, but a gradual introduction can be discussed in the case of behavioral problems. Parents are instructed to give the treatment in the morning during breakfast, to avoid the afternoons, and not to discontinue treatment abruptly. Finally, parents are also instructed not to give nonsteroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen and aspirin) without medical advice.

No long-term benefit can be expected if the treatment duration is less than 12 months. Therefore, treatment should be continued based on the evaluation of its effectiveness and clinical tolerance.

Regarding dosage adjustment, there is no published evidence supporting a systematic reduction in the corticosteroid treatment after 12 months at the optimal dose. No study has reported any advantage of alternating corticosteroid doses in terms of efficacy or safety [21–23]. The dose (in mg/kg/day) should therefore be maintained over time and adapted to the weight if tolerated (without exceeding the maximal dose). Occurrence of side effects, or a poor treatment tolerance balanced with the benefits, can prompt dosage adjustments, which can entail not increasing the dose according to the patient weight gain, alternating administration every other day (or other intermittent therapy), or gradually decreasing the dose. The minimal dose reported as effective is

0.33 mg/kg/day for prednisone/prednisolone, but it is not determined for deflazacort [5]. The adaptation of corticosteroid treatment dosage after loss of walking has not been documented; however, treatment remains relevant due to effects on upper limb and respiratory functions.

The indications for the discontinuation of corticosteroid treatment are essentially related to the presence of major side effects. Discontinuation should involve a gradual decrease in dose and hydrocortisone replacement therapy until recovery of endogenous corticosteroid synthesis [24], according to local protocols, and should take into consideration endocrinological recommendations to prevent acute adrenal insufficiency.

Part 2: side effect monitoring

Corticosteroid treatment side effects are frequent (weight gain, growth retardation, behavioral problems, osteoporotic fractures, cataracts, delayed puberty, cushingoid appearance, etc.) but generally moderate. Medical management must consider the induced immunosuppression. Each side effect entails a specific course of action in terms of screening, follow-up, prevention, impact on the prescription of corticosteroids, and prescription of adjuvant treatments.

In the absence of available international guidelines on these subjects, proposed guidelines were produced regarding these concerns.(Table 2)

Osteopenia

Osteoporosis is a common complication of long-term corticosteroid treatment, a risk that is increased by hypomobility and reduced weight-bearing activities after loss of ambulation in DMD patients. Osteoporosis-induced bone fragility can lead to long bone fractures, sometimes asymptomatic vertebral fractures, and bone pain. The prevention of osteoporosis and the screening of these complications are therefore essential for the management of patients with DMD under corticosteroid treatment.

The following guidelines regarding the diagnosis, monitoring, and prevention strategy for osteoporosis are based on two key publications on the topic [25,26] and on the French recommendations relative to the management of children at risk of bone fragility [27].

Guideline

Osteoporosis screening should be performed as soon as corticosteroid treatment is initiated, and should comprise the following: (a) a thoracolumbar spine side profile X-ray performed every 2 years. The frequency of this examination can be increased in the case of back pain or a decrease of −0.5 SD in bone mineral density (BMD) Z score over a period >12 months; (b) a dual-energy X-ray absorptiometry (DEXA) scan performed every year for the determination of the BMD of the lumbar spine, distal femur, hip, and whole body. The total BMD score can be converted into age- and sex-specific Z-scores. Since BMD can be underestimated in patients with DMD, it is useful to use the apparent BMD.

The prevention and control of osteoporosis risk factors should cover the following: (a) promoting mobility; (b) ensuring a satisfactory nutritional state, i.e., avoiding both undernutrition and overweight; (c) controlling calcium intake annually and introducing a calcium supplementation (diet or medical supplementation) only in the case of insufficient daily nutritional intake in order to avoid hypercalciuria [28]; and (d) controlling the vitamin D intake annually by determining the 25-OH vitamin D_3 levels late during winter (if possible). The target 25-OH vitamin D_3 concentration is 30 ng/mL (75 nmol/L); if necessary, vitamin D supplementation can be performed for initial concentrations of 20–30 ng/mL, supplementation of 1000 IU/day for 1 year should be considered; for initial concentrations of <20 ng/mL, supplementation of 2000 IU/day for 1 year should be considered; and for initial concentrations of <10 ng/mL, supplementation of 4000 IU/day for 1 year should be considered. In the case of supplementation, 25-OH vitamin D_3 levels should be determined 3 months after supplementation initiation.

Table 2
Key points for the evaluation of tolerance and management of side effects of long-term corticosteroid therapy in patients with DMD.

Risk of osteopenia	• *Vitamin D supplementation: adapted to blood levels* • *Calcium supplementation: adapted to dietary intake* • *Systematic* search for *the presence of vertebral settlements on spine X-ray in profile and clinical fracture* • *Symptomatic osteoporosis on bone densitometry (including for painful grade 1 vertebral compression) requires treatment with* bisphosphonates
Risk of obesity	• *Aim to keep BMI within normal limits, especially during adolescence, to maintain longer autonomy of transfers and prevent metabolic syndrome* • *Increasing BMI may require a decrease in dosage*
Risk of delay in height growth	• *Management is dependent on the patient's tolerance: seek specialist advice if the height growth curve differs by more than 2 SD to discuss treatment with GH in* the *case of GH deficiency*
Risk of delayed puberty	• *After 3–5 years on corticosteroids, puberty is often delayed* • *If puberty has not started by 14 years, an endocrinological consultation should be proposed to discuss testosterone treatment initiation, taking into consideration the clinical situation and according to the wishes and concerns of the boy*
Risk of cataract	• *It occurs after 4–6 years of treatment* • *Surgical treatment is* an *exception (more frequent for deflazacort)* • *An annual ophthalmological examination is performed for early detection of cataract and measurement of intraocular pressure* • *A closer examination every 6 months is performed if cataract is detected* • *The corticosteroids are continued at the same dosage unless aggravation and/or contradictory ophthalmological opinions*
Risk of hypertension	• *DMD patients on corticosteroids develop hypertension in 22%–47% of cases; the interpretation of the measured values is* made *according to the standards established for height or age considering aggravating factors for cardiac pathology* • *Blood pressure is measured at each consultation and, if necessary, by a 24-h Holter blood pressure recording* • *In* the *case of confirmed hypertension, proposal to reinforce low-sodium diet and, if necessary, begin early or adjust treatment with a conversion enzyme inhibitor and/or beta-blocker at the maximum tolerated doses; then, if necessary, reduction of the corticosteroid therapy*
Risk of increased behavioral disturbance	• *A search for symptoms of neurodevelopmental disorders and behavioral disturbances should be performed* • *Questionnaires and assessments can be proposed* • *If necessary, corticosteroids can be started at lower doses and the dosage can be adjusted to the side effects, depending on the impact on family life and schooling. Adjuvant treatments may also be prescribed*
Infectious risk (from immunosuppressive effect)	• *Varicella serology and vaccination if necessary, before initiating the treatment* • *Live attenuated vaccines should be updated before starting corticosteroids and prohibited afterwards. An evaluation of the risk of latent infections should be performed*
Digestive and metabolic risks	• *Symptoms of GERD are treated with a proton pump inhibitor* • *Monitoring of diabetes (especially in* the *case of obesity) and of hypokalemia (no systematic supplementation)*

DMD: Duchenne muscular dystrophy; BMI: body mass index; GH: growth hormone; GERD: gastroesophageal reflux disease.

For fractures and bisphosphonate treatment, the Genant semi-quantitative method allows for the classification of vertebral fractures according to the decrease in size (ratio): grade 0 corresponds to no fracture, grade 1 corresponds to moderate fractures (>20%–25%), and grade 3 corresponds to severe fractures (>40%) [29].

Treatments such as bisphosphonates have been shown to be associated with a decrease in morbidity and mortality. Although the frequency of fractures is high in the context of DMD, no study has evaluated the value of administrating bisphosphonates as a preventive treatment (before the occurrence of the first fracture). The current approach consists of a secondary prevention strategy following the diagnosis of fractures, including vertebral fractures, which have limited potential for spontaneous healing. Bisphosphonate treatment is indicated for pediatric patients presenting with risk factors for bone fragility with at least one clinically significant fracture (i.e., long bone or vertebral fracture).

Treatment is recommended for grade 1 vertebral fractures if they are associated with symptoms (back pain); otherwise, it is recommended to perform radiography 6 months later in order to assess the radiological progression of the vertebral fracture.

Birnkrant et al. have published an algorithm for the monitoring, diagnosis, and treatment of osteoporosis in DMD patients [26].

Growth

Some of the most frequent complications affecting DMD patients under long-term corticosteroid treatment are growth and pubertal abnormalities.

Long-term corticosteroid treatment induces a delay in height and pubertal growth related to the suppression of growth hormone (GH) production and/or to the resistance to GH or IGF-1 and has direct effects on bone.

Bianchi et al. reported that the height growth rate was significantly slowed down after 12–18 months of deflazacort use, and that the height was reduced by at least 20–25 cm on average compared with the age-matched general population at the age of 13–15 years [30]. This difference in height is less important for patients under prednisone treatment.

Both treatments alter growth parameters; however, patients under deflazacort treatment have been reported to experience a reduced growth in height, weight, and body mass index (BMI) compared with patients under prednisone/prednisolone over the first 48 weeks of treatment [17].

Guideline

Height should be measured every 6 months. Specialist advice should be sought if the height curve differs by more than 2 SD and/or height < −2 SD. GH treatment should be administered in the case of GH deficiency (insufficient data regarding the indication of GH treatment in cases of absence of proven deficit). Physicians should be aware of the rare cases in which there is an ectopic posterior pituitary associated with DMD but for which the growth delay often occurs earlier, even before the initiation of corticosteroid treatment. In France, current practices involve a switch to an alternate prescription (every other day) in order to reduce the growth delay. Stimpson et al. [31] demonstrated that deflazacort daily and prednisolone daily subgroups showed more stunting compared with the corresponding intermittent regimen subgroups. Reduction in dose is not recommended because of the impact on motor function, but it should be adapted to each situation, particularly according to the difficulty for children to accept the delay in height growth.

Weight

DMD patients are naturally at risk of overweight/obesity due to the progressive motor function decline. This risk is increased by chronic corticosteroid treatments, as they tend to increase appetite, to have direct effects on blood sugar levels, and to stimulate the lipolysis and accumulation of fat in unusual tissues, leading to facio-troncular obesity. In addition, peripheral insulin resistance may follow weight gain [3].

Maintaining a BMI within the normal range is an important goal, especially during adolescence, in order to maintain transfer independence for longer and to prevent the occurrence of metabolic syndrome.

Guidelines

Weight should be measured every 6 months. The administration of long-term corticosteroid treatment requires a nutritional adaptation: boys who have not lost their ambulation ability require 80% of the calorie intake of a healthy child, and non-walking boys require about 70% of the calorie intake of a healthy age-matched child. Consultation with a dietician should be considered at least once a year. In the case of excessive weight gain (curve lane deviation), not adapting the dosage to weight could first be considered followed by a dose reduction if necessary. Blood glucose, insulin, and HBA1C should be monitored, especially during adolescence and in the presence of other signs of metabolic syndrome.

Puberty

The onset of puberty in boys is manifested by an increase in the testicular volume and occurs at the bone age of 13 years (corresponding to the appearance of the thumb sesamoid). Delayed puberty is defined as the absence of pubertal development after 14 years of age or by the absence of complete development 4 years after its onset. In DMD patients treated for more than 3–5 years with corticosteroids, puberty is often delayed (whereas untreated DMD patients undergo normal puberty).

There is no comparative study available regarding the effects of deflazacort vs. prednisone/prednisolone on puberty.

Guidelines

The Tanner stage should be evaluated at each consultation from the age of 9 years, and early referral to an endocrinologist should be considered if there is doubt regarding the occurrence of pubertal development.

If puberty has not started by the age of 14, a testosterone supplementation should be discussed. Such supplementation has beneficial effects on bone mass but side effects are also possible, such as acne, oily skin, mood changes, increase in BMI, increase in libido, and a possible reduction in final height due to advancement of bone age and epiphyseal fusion. Hence, the decision to initiate testosterone supplementation should be made while taking into consideration the clinical situation as well as the patient's wishes and concerns.

Cataract

The study by Rice et al. [32] including 596 male pediatric patients with DMD, the vast majority of whom (514/596) were under deflazacort or prednisolone treatment, found a significantly elevated risk of cataract (22.4%) for patients under corticosteroid treatment [32,33]. This risk was twice as high with deflazacort compared with prednisolone. Cataract occurs on average after 4–6 years of treatment and requires surgical treatment only in very few cases.

Guidelines

An annual ophthalmologic examination should be performed for the early detection of cataract and for the measurement of intraocular pressure. In the case of cataract, a close follow-up (every 6 months) should be established, especially for patients treated with deflazacort, which is associated with a higher risk of cataract surgery.

The corticosteroid treatment should be continued at the same dose, except in cases of aggravation or contradictory ophthalmological advice. The reduction or discontinuation of the treatment should be discussed while taking into account the risk–benefit ratio of corticosteroids.

Arterial hypertension

Arterial hypertension (HTN) is a classic complication of long-term corticosteroid treatment, but the published data concerning this complication in the specific context of DMD are divided and sometimes contradictory. The exact frequency of occurrence of HTN in DMD patients treated with corticosteroids is thus poorly known and probably underestimated due to the absence of specific investigation or due to the sole consideration of isolated blood pressure measurements.

Several cohort studies or meta-analyses investigating the use of corticosteroids in the context of DMD do not mention the evaluation of HTN [22]. Other studies do not show an increased risk of HTN related to corticosteroid therapy in DMD [34–37]. This complication was, nevertheless, found to be associated with corticosteroid therapy in the context of DMD in 22% of cases in the study by Ricotti et al. [38] and in 47% of cases in the study by Braat et al. [39], in which blood pressure was measured continuously. The discrepancies observed between these different studies are probably related to the use of different angiotensin-converting-enzyme inhibitors (ACE inhibitors) and other treatments with an antihypertensive effect, in addition to different blood pressure measurement protocols.

The most reliable way to record blood pressure is to perform 24-h ambulatory recordings (Holter blood pressure) or, alternatively, by taking measurements at home. The interpretation of the measured values should take into account the standards established for height or age [40,41]. Using these prolonged daytime and overnight measurements, abnormalities in the blood pressure profile have been demonstrated in two thirds of DMD patients treated with corticosteroids, including children in the 6- to 11-year age range [39,42].

No statistically significant difference in the occurrence of HTN has been found depending on the type of corticosteroid used (prednisone or deflazacort) [3]. The occurrence of HTN is significantly greater in the case of continuous corticosteroid therapy (22%) than in the case of intermittent corticosteroid therapy (5%) [38], but this difference has not been found in all studies [23].

It should, nevertheless, be emphasized that the link between HTN and corticosteroid treatment is not unequivocal in this context. Some authors have indeed reported that HTN can also be observed in DMD children and adolescents who are not under corticosteroid treatment, which is possibly related to fibrous changes in the arterial wall and to abnormalities of the vascular endothelium. Consistently, greater arterial wall stiffness has been observed in this context [43]. During the late stages of DMD, impaired renal function may also contribute to the occurrence of HTN [44]. Conversely, some DMD patients, especially non-ambulatory patients, have an abnormally low blood pressure that is often well tolerated on a daily basis but that may require special vigilance in the setting of general anesthesia [45]. This low blood pressure may also constitute a limit to the dose increase of cardiac treatments, mainly for patients with significant systolic dysfunction [43,46].

The presence of HTN, whether or not related to corticosteroid therapy, could be an aggravating factor for the cardiac pathology in the context of DMD and constitutes a therapeutic target in itself [47]. The use of ACE inhibitors or beta-blockers to prevent cardiomyopathy in DMD patients is associated with better blood pressure control, which significantly contributes to their clinical benefit in terms of decreased mortality [48].

Guidelines

The regular measurement of blood pressure should be performed at each consultation during the entire follow-up [1], even more so in the case of corticosteroid treatment.

If there are abnormal values or doubts, a 24-h Holter blood pressure recording can confirm the existence of HTN. In the case of confirmed HTN, a more stringent low-sodium diet (that does not impact the nutritional balance) may be proposed first, possibly followed by an adjustment or early initiation of a treatment containing the conversion enzyme inhibitor and/or beta-blocker, at the maximum tolerated doses. A decrease in the corticosteroid treatment dose may be discussed as a last resort.

Behavioral disorders

The side effects of corticosteroids include behavioral changes. The side effect profile of prednisone frequently reports euphoria, insomnia, excitement, etc., as well as risks of decompensation in cases of treatment discontinuation. The impact of treatment on behavior is not always confirmed in DMD but the studies do not all use the same scales to evaluate behavior [6]. Behavioral problems have been reported in 3%–6% of DMD patients under long-term corticosteroid treatment [2], without any difference between compounds (prednisone vs. deflazacort) or between the dosage regimens [23]. More hyperactivity and insomnia cases have been reported in DMD patients under daily vs. intermittent regimens, but there was no difference in terms of symptoms of aggressiveness and emotional lability [38]. Another study found no link between emotional, behavioral, and neurodevelopmental profiles and steroid treatment or age [49]. Using the PARS III questionnaire adapted for DMD cases, there was no difference between corticosteroid-treated and untreated patients in any of the six subdomains (peer relationships, dependence, hostility, withdrawal, productivity, anxiety/depression) [50]. In our experience, disabling behavioral problems are rarely (<5%) the cause of treatment discontinuation. Accordingly, the rate of treatment discontinuation related to behavioral problems was 2% in a study published by Darmahkasih et al. [51] and 0% in a study published by Escolar et al. [23].

Before introducing corticosteroids, the neurodevelopmental profile of the DMD patient should be taken into account, as associated disorders are common in the natural history of the disease: intellectual disability (17%–27% [52], 36% in France [53]), learning disorders (26%) in which the verbal domain is more affected than the non-verbal domain and which include the specific disorder of written language [52], impairment of working memory [54] or executive functions with inhibition and planning deficit, attention-deficit/hyperactivity (32%), autism spectrum disorders (15%), anxiety disorders (27%) [1,49], motor or vocal tics (2.4%), emotional and behavioral regulation disorders (38%), obsessive–compulsive disorders (25%), and depressive symptoms (15.9%) [51]. These disorders are not degenerative and can be influenced by life events, treatments, and rehabilitation, but some symptoms may be exacerbated by corticosteroids.

Sleep may be impaired early in DMD children as part of their associated anxiety or autistic disorders, and difficulties in falling asleep may be increased by treatments (corticosteroids, methylphenidate).

Guidelines

We recommend evaluating the patient's neurodevelopmental, behavioral, and emotional profile, preferably before the initiation of

corticosteroid treatment, using assessments and questionnaires adapted to the suspected disorders, and possibly seek for a complementary opinion from a psychologist or child psychiatrist (WISC recommended from the age of 6 years).

The presence of externalized behavioral disorders, anxiety disorders, or autistic spectrum disorders does not constitute a contraindication to corticosteroid treatment but should encourage caution: The introduction of corticosteroids should be performed progressively and the family should evaluate the benefit–risk ratio (including the impact on schooling and family life) at each therapeutic stage and return to previous stages if necessary. In all cases, a screening for behavioral problems after the initiation of treatment should be carried out, by at least interviewing the parents.

In the case of attention-deficit disorder with or without hyperactivity, there is no contraindication to methylphenidate under cardiological supervision [55]. The indication should be assessed according to the usual criteria of impact on several areas of life (questionnaires and attentional assessment before and after treatment). Other psychotropic drugs may also be prescribed if necessary.

Difficulties in falling asleep justify, in addition to reviewing the rules of sleep hygiene, a modulation of the schedule for treatment administration (in the morning only). Melatonin is a classic adjuvant treatment. The combination of nocturnal agitation, hyperhidrosis, and daytime sleepiness should prompt the investigation for sleep apnea syndrome.

Vaccination and immunodepression

According to the National Protocols for Diagnosis and Care (*Protocoles Nationaux de Diagnostic et de Soins*, PNDS) [56], all DMD patients should receive a pneumococcal vaccine and an annual influenza vaccine. The vaccination schedule recommended by the French National Authority for Health (*Haute Autorité de Santé*, HAS) should also be followed, considering the immunosuppressive effect of long-term corticosteroid treatment.

Corticosteroid-induced immunosuppression is considered only beyond 2 mg/kg/day in children (or 20 mg/day in children over 10 kg after 15 days) for prednisone or beyond 10 mg/day in adults [57].

Guidelines

The use of live attenuated vaccines is more likely to cause complications and is not recommended under corticosteroid treatment. It is therefore advisable to propose, at least 2 weeks before the initiation of corticosteroid therapy, an update of the measles, mumps, and rubella (MMR) vaccination, yellow fever vaccine if necessary (in the case of stays in endemic areas), and varicella vaccination if the serology is negative.

For patients not immunized against varicella and not vaccinated, the administration of specific immunoglobulins should be discussed in the event of contagion, or the administration of aciclovir in the event of varicella symptoms under corticosteroids.

Progressive signs of infection may be masked by the corticosteroid treatment: Families should be warned to seek medical attention more readily if infectious symptoms occur. Given the risk of reactivation of latent infections, an interview should be held investigating trips to an anguillulosis-endemic area, primary infections, or contacts with a person with tuberculosis before the initiation of corticosteroids.

Gastrointestinal and metabolic complications

Children with DMD often suffer from overweight after the loss of walking, whereas adult patients tend to be malnourished [2,9,58–60]. The risks associated with corticosteroid therapy include obesity, glucose intolerance, and type 2 diabetes [61,62], the worsening of the gastroesophageal reflux disease as well as risk of gastritis and ulcer [9,63,64], and less severely swallowing problems and constipation [65].

Guidelines

The BMI should be determined at each follow-up visit, referring to the curves specific to DMD children. Also, the assessment of glucose metabolism is recommended for overweight patients whose obesity is resistant to dietary control: assessment of insulin and HbA1C levels and an oral glucose tolerance test. In the case of difficult-to-control obesity or overweight, a change of steroid medication is to be considered.

Symptoms of gastroesophageal reflux disease should be systematically investigated; the initiation of treatment with a proton pump inhibitor is recommended. Occult blood in stool should also be investigated in the case of anemia. Symptomatic treatment of constipation should be proposed. Finally, laboratory monitoring of hypokalemia should be performed and potassium supplementation proposed if necessary.

Conclusion

At a time when pediatricians are restricting the use of corticosteroids in most chronic diseases, their benefit for children with DMD, i.e., the gain of years of mobility, justifies their use. Furthermore, while waiting for a treatment with fewer side effects on bone mineralization and growth in particular, therapy for DMD should aim to finely manage corticosteroids and their side effects by maintaining tolerable optimal doses.

Declaration of competing interest

None.

Acknowledgments

We would like to thank the organ specialists who reviewed and validated certain sections: Dr. Ariane Zaloszyc (CHU Strasbourg, nephrologist), Prof. Karim Wahbi (Hôpital Cochin, Paris, cardiologist), Prof. Thomas Edouard (CHU Toulouse, endocrinologist), Dr. Marie-Noelle DUFOURG (Hôpital Armand-Trousseau, Paris, endocrinologist), and Dr. Diem-Trang Nguyen (Hôpital Armand-Trousseau, Paris, ophthalmologist).

The authors acknowledge Hélène Boyer and Verena Landel from DRS (Direction de la Recherche en Santé) of Hospices Civils de Lyon for help in manuscript preparation.

References

[1] Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol 2018;17:251–67.
[2] McDonald CM, Sajeev G, Yao Z, et al. Deflazacort vs prednisone treatment for Duchenne muscular dystrophy: a meta-analysis of disease progression rates in recent multicenter clinical trials. Muscle Nerve 2020;61:26–35.
[3] Gloss D, Moxley RT, Ashwal S, et al. Practice guideline update summary: Corticosteroid treatment of Duchenne muscular dystrophy: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology 2016;86:465–72.
[4] Matthews E, Brassington R, Kuntzer T, et al. Corticosteroids for the treatment of Duchenne muscular dystrophy. Cochrane Database Syst Rev 2016;2016:CD003725.
[5] Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol 2010;9:77–93.
[6] Manzur AY, Kuntzer T, Pike M, et al. Glucocorticoid corticosteroids for Duchenne muscular dystrophy. Cochrane Database Syst Rev 2008:CD003725.

[7] Quinlivan R, Messer B, Murphy P, et al. Adult north star network (ANSN): consensus guideline for the standard of care of adults with duchenne muscular dystrophy. J Neuromuscul Dis 2021;8:899–926.
[8] Barber BJ, Andrews JG, Lu Z, et al. Oral corticosteroids and onset of cardiomyopathy in duchenne muscular dystrophy. J Pediatr 2013;163:1080–4.
[9] Pane M, Fanelli L, Mazzone ES, et al. Benefits of glucocorticoids in non-ambulant boys/men with Duchenne muscular dystrophy: a multicentric longitudinal study using the Performance of Upper Limb test. Neuromuscul Disord 2015;25:749–53.
[10] Szabo SM, Salhany RM, Deighton A, et al. The clinical course of Duchenne muscular dystrophy in the corticosteroid treatment era: a systematic literature review. Orphanet J Rare Dis 2021;16:237.
[11] Koeks Z, Bladen CL, Salgado D, et al. Clinical Outcomes in Duchenne muscular dystrophy: a study of 5345 patients from the TREAT-NMD DMD global database. J Neuromuscul Dis 2017;4:293–306.
[12] Weber FJ, Latshang TD, Blum MR, et al. Prognostic factors, disease course, and treatment efficacy in Duchenne muscular dystrophy: a systematic review and meta-analysis. Muscle Nerve 2022;66:462–70.
[13] Bérard C, Payan C, Hodgkinson I, et al. MFM collaborative study group. A motor function measure for neuromuscular diseases. Construction and validation study. Neuromuscul Disord 2005;15:463–70.
[14] de Lattre C, Payan C, Vuillerot C, et al. Motor function measure: validation of a short form for young children with neuromuscular diseases. Arch Phys Med Rehabil 2013;94:2218–26.
[15] McDonald CM, Henricson EK, Han JJ, et al. The 6-minute walk test as a new outcome measure in Duchenne muscular dystrophy. Muscle Nerve 2010;41:500–10.
[16] Bello L, Gordish-Dressman H, Morgenroth LP, et al. Prednisone/prednisolone and deflazacort regimens in the CINRG Duchenne natural history study. Neurology 2015;85:1048–55.
[17] Shieh PB, Mcintosh J, Jin F, et al. Deflazacort versus prednisone/prednisolone for maintaining motor function and delaying loss of ambulation: A post HOC analysis from the ACT DMD trial. Muscle Nerve 2018;58:639–45.
[18] Marden JR, Freimark J, Yao Z, et al. Real-world outcomes of long-term prednisone and deflazacort use in patients with Duchenne muscular dystrophy: experience at a single, large care center. J Comp Eff Res 2020;9:177–89.
[19] Guglieri M, Bushby K, McDermott MP, et al. Effect of different corticosteroid dosing regimens on clinical outcomes in boys with Duchenne muscular dystrophy: a randomized clinical trial. JAMA 2022;327:1456.
[20] Matthews E, Brassington R, Kuntzer T, et al. Corticosteroids for the treatment of Duchenne muscular dystrophy. Cochrane Database Syst Rev 2016;2016:CD003725.
[21] Li M, Cai Y, Zhong M, et al. A novel treatment regimen for Duchenne muscular dystrophy. NeuroReport 2013;24:924–7.
[22] Straathof CSM, Overweg-Plandsoen WCG, Burg GJ, et al. Prednisone 10 days on/10 days off in patients with Duchenne muscular dystrophy. J Neurol 2009;256:768–73.
[23] Escolar DM, Hache LP, Clemens PR, et al. Randomized, blinded trial of weekend vs daily prednisone in Duchenne muscular dystrophy. Neurology 2011;77:444–52.
[24] Kinnett K, Noritz G. The PJ Nicholoff steroid protocol for Duchenne and Becker muscular dystrophy and adrenal suppression. PLoS Curr 2017;9. ecurrents.md.d18deef7dac96ed135e0dc8739917b6e.
[25] Ward LM, Hadjiyannakis S, McMillan HJ, et al. Bone health and osteoporosis management of the patient with Duchenne muscular dystrophy. Pediatrics 2018;142:S34–42.
[26] Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. Lancet Neurol 2018;17:347–61.
[27] Edouard T, Guillaume-Czitrom S, Bacchetta J, et al. Guidelines for the management of children at risk of secondary bone fragility: Expert opinion of a French working group. Arch Pédiatr 2020;27:393–8.
[28] Meyers LD, Hellwig JP, Otten JJ. Dietary reference intakes: the essential guide to nutrient requirements. Wahington: National Academies Press; 2006.
[29] Genant HK, Wu CY, van Kuijk C, et al. Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res 1993;8:1137–48.
[30] Bianchi ML, Biggar D, Bushby K, et al. Endocrine aspects of Duchenne muscular dystrophy. Neuromuscul Disord 2011;21:298–303.
[31] Stimpson G, Raquq S, Chesshyre M, et al. Growth pattern trajectories in boys with Duchenne muscular dystrophy. Orphanet J Rare Dis 2022;17:20.
[32] Rice ML, Wong B, Horn PS, et al. Cataract development associated with long-term glucocorticoid therapy in Duchenne muscular dystrophy patients. J Am Assoc Pediatr Ophthalmol Strabismus 2018;22:192–6.
[33] Brignol TN, Fort PE, Ventura DF, et al. Cataract development associated with long-term glucocorticoid therapy in Duchenne muscular dystrophy patients. J AAPOS 2018;22:483–4.
[34] Bonifati MD, Ruzza G, Bonometto P, et al. A multicenter, double-blind, randomized trial of deflazacort versus prednisone in Duchenne muscular dystrophy. Muscle Nerve 2000;23:1344–7.
[35] Beenakker EAC, Fock JM, Van Tol MJ, et al. Intermittent prednisone therapy in Duchenne muscular dystrophy: a randomized controlled trial. Arch Neurol 2005;62:128–32.
[36] Markham LW, Spicer RL, Khoury PR, et al. Steroid therapy and cardiac function in Duchenne muscular dystrophy. Pediatr Cardiol 2005;26:768–71.
[37] Hu J, Ye Y, Kong M, et al. Daily prednisone treatment in Duchenne muscular dystrophy in southwest China. Muscle Nerve 2015;52:1001–7.
[38] Ricotti V, Ridout DA, Scott E, et al. Long-term benefits and adverse effects of intermittent versus daily glucocorticoids in boys with Duchenne muscular dystrophy. J Neurol Neurosurg Psychiatry 2013;84:698–705.
[39] Braat E, Hoste L, De Waele L, et al. Renal function in children and adolescents with Duchenne muscular dystrophy. Neuromuscul Disord 2015;25:381–7.
[40] Urbina E, Alpert B, Flynn J, et al. Ambulatory blood pressure monitoring in children and adolescents: recommendations for standard assessment: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the council on cardiovascular disease in the young and the council for high blood pressure research. Hypertension 2008;52:433–51.
[41] Flynn JT, Daniels SR, Hayman LL, et al. Update: ambulatory blood pressure monitoring in children and adolescents: a scientific statement from the American Heart Association. Hypertension 2014;63:1116–35.
[42] Marui FRRH, Bianco HT, Bombig MTN, et al. Behavior of blood pressure variables in children and adolescents with Duchenne muscular dystrophy. Arq Bras Cardiol 2018;110:551–7.
[43] Ryan TD, Parent JJ, Gao Z, et al. Central arterial function measured by non-invasive pulse wave analysis is abnormal in patients with Duchenne muscular dystrophy. Pediatr Cardiol 2017;38:1269–76.
[44] Kutluk MG, Doğan ÇS. Kidney involvement and associated risk factors in children with Duchenne muscular dystrophy. Pediatr Nephrol 2020;35:1953–8.
[45] Finsterer J, Cripe L. Treatment of dystrophin cardiomyopathies. Nat Rev Cardiol 2014;11:168–79.
[46] Masood SA, Kazmouz S, Heydemann P, et al. Under-recognition of low blood pressure readings in patients with Duchenne muscular dystrophy. Pediatr Cardiol 2015;36:1489–94.
[47] van de Velde NM, Roest AAW, van Zwet EW, et al. Increased blood pressure and body mass index as potential modifiable factors in the progression of myocardial dysfunction in Duchenne muscular dystrophy. J Neuromuscul Dis 2019;6:65–73.
[48] Dittrich S, Graf E, Trollmann R, et al. Effect and safety of treatment with ACE-inhibitor Enalapril and β-blocker metoprolol on the onset of left ventricular dysfunction in Duchenne muscular dystrophy - a randomized, double-blind, placebo-controlled trial. Orphanet J Rare Dis 2019;14:105.
[49] Colombo P, Nobile M, Tesei A, et al. Assessing mental health in boys with Duchenne muscular dystrophy: Emotional, behavioural and neurodevelopmental profile in an Italian clinical sample. Eur J Paediatr Neurol 2017;21:639–47.
[50] Hendriksen JGM, Klinkenberg S, Collin P, et al. Diagnosis and treatment of obsessive compulsive behavior in a boy with Duchenne muscular dystrophy and autism spectrum disorder: A case report. Neuromuscul Disord NMD 2016;26:659–61.
[51] Darmahkasih AJ, Rybalsky I, Tian C, et al. Neurodevelopmental, behavioral, and emotional symptoms common in Duchenne muscular dystrophy. Muscle Nerve 2020;61:466–74.
[52] Billard C, Gillet P, Barthez M, et al. Reading ability and processing in Duchenne muscular dystrophy and spinal muscular atrophy. Dev Med Child Neurol 1998;40:12–20.
[53] Humbertclaude V, Hamroun D, Picot MC, et al. [Phenotypic heterogeneity and phenotype-genotype correlations in dystrophinopathies: Contribution of genetic and clinical databases]. Rev Neurol (Paris) 2013;169:583–94.
[54] Tyagi R, Arvind H, Goyal M, et al. Working memory alterations plays an essential role in developing global neuropsychological impairment in Duchenne muscular dystrophy. Front Psychol 2020;11:613242.
[55] Lionarons JM, Hellebrekers DMJ, Klinkenberg S, et al. Methylphenidate use in males with Duchenne muscular dystrophy and a comorbid attention-deficit hyperactivity disorder. Eur J Paediatr Neurol EJPN 2019;23:152–7.
[56] Filière de santé Maladies rares-Maladies neuromusculaires; Société Française de Neuropédiatrie. [Internet] Protocole National de Diagnostic et de Soins (PNDS) Dystrophie musculaire de Duchenne; 2019. https://www.has-sante.fr/jcms/p_3121365/fr/dystrophie-musculaire-de-duchenne.
[57] HCSP. [Internet] Vaccination des personnes immunodéprimées ou aspléniques; 2012. https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=504.
[58] Verhaart IEC, van den Engel-Hoek L, Fiorotto ML, et al. Nutrition in Duchenne muscular dystrophy 16–18 March 2018, Zaandam, the Netherlands. Neuromuscul Disord 2018;28:680–9.
[59] Jeronimo G, Nozoe KT, Polesel DN, et al. Impact of corticotherapy, nutrition, and sleep disorder on quality of life of patients with Duchenne muscular dystrophy. Nutrition 2016;32:391–3.
[60] Davidson ZE, Ryan MM, Kornberg AJ, et al. Strong correlation between the 6-minute walk test and accelerometry functional outcomes in boys with Duchenne muscular dystrophy. J Child Neurol 2015;30:357–63.
[61] Saure C, Caminiti C, Weglinski J, et al. Energy expenditure, body composition, and prevalence of metabolic disorders in patients with Duchenne muscular dystrophy. Diabetes Metab Syndr Clin Res Rev 2018;12:81–5.
[62] Salera S, Menni F, Moggio M, et al. Nutritional challenges in Duchenne muscular dystrophy. Nutrients 2017;9:594.

[63] Toussaint M, Davidson Z, Bouvoie V, et al. Dysphagia in Duchenne muscular dystrophy: practical recommendations to guide management. Disabil Rehabil 2016;38:2052–62.
[64] Willig TN, Paulus J, Lacau Saint Guily J, et al. Swallowing problems in neuromuscular disorders. Arch Phys Med Rehabil 1994;75:1175–81.
[65] Kraus D, Wong BL, Horn PS, et al. Constipation in Duchenne muscular dystrophy: prevalence, diagnosis, and treatment. J Pediatr 2016;171:183–8.
[66] Hafner P, Schmidt S, Schädelin S, et al. Implementation of motor function measure score percentile curves - predicting motor function loss in Duchenne muscular dystrophy. Eur J Paediatr Neurol 2022;36:78–83.

Stéphanie Fontaine Carbonnel[a,*], Ivana Dabaj[b], Camille de Montferrand[a], Pascal Rippert[c], Vincent Laugel[d], Silvana De Lucia[e], Claudia Ravelli[e], Andreea Seferian[e], Juliette Ropars[f], Claude Cances[g]
[a] *Department of Pediatric Physical Medicine and Rehabilitation, Hôpital Mère Enfant, Hospices Civils de Lyon, 59 Boulevard Pinel, Bron F-69677, CEDEX, France*
[b] *UNIROUEN, Inserm U1245, Department of Neonatology, Pediatric Intensive Care and Neuropediatrics, Normandie University, CHU Rouen F-76000, Rouen, France*
[c] *Service Recherche et Epidémiologie Cliniques, Hospices Civils de Lyon, Pôle Santé Publique, 162 Avenue Lacassagne, Lyon F-69003, France*
[d] *Department of pediatric neurology, Strasbourg University Hospital, 1 avenue Moliere, Strasbourg F-67098, France*
[e] *Assistance Publique Hôpitaux de Paris, Sorbonne Université, Institut de Myologie, AFM-Téléthon, Essais cliniques I-Motion Enfants, Hôpital Armand Trousseau, Paris F-75012, France*
[f] *Service de pédiatrie, CHU Brest, 2 Avenue Foch, Brest F-29609, France*
[g] *Unit of Pediatric Neurology, French Greater South-West Reference Center for Neuromuscular Diseases, Hôpital des Enfants, University Hospital Center Toulouse, 330 Avenue de Grande Bretagne-TSA, Toulouse Cedex F-31059, France*

[*] Corresponding author.
E-mail address: stephanie.fontaine01@chu-lyon.fr (S. Fontaine Carbonnel).