Author's response to reviews

Title: A Dutch Guideline for the Treatment of Scoliosis in Neuromuscular Disorders

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Version: 3 Date: 9 September 2008

Author's response to reviews: see over
RESPONSE TO THE REVIEWERS’ COMMENTS:
Foremost the authors are grateful to the reviewers for their extensive review of the manuscript and suggestions. The reviewers have made valuable suggestions which have contributed to improvement of the manuscript. We have given our response to the reviewer below each comment.

Reviewer 1: ATHANASIOS TSIRIKOS

Comments:
1. The title of the paper is slightly misleading in the sense that when most authors refer to neuromuscular scoliosis in general, they include disorders affecting the central nervous system, such as cerebral palsy, which by definition is the most common neuromuscular condition causing permanent disability in children and adolescents, as well as myelomeningocele (spina bifida). I can appreciate the resemblance in approach for patients with DMD and SMA where the generalised muscle weakness and the similar pattern of clinical presentation allows for a more direct comparison, as well as easier extracted conclusions which can apply to guidelines compared to, for example, patients with CP where the pathology and pattern of presentation are different. Therefore, I do not find it unreasonable to confine the study to only patients with DMD and SMA and extrapolate these conclusions also to patients with more rare forms of congenital myopathies. However, I would recommend that, in this case, the title of the paper should be changed to represent accurately the groups of patients included in the study and this could be: “A Dutch Guideline for the Treatment of Scoliosis in patients with Duchenne Muscular Dystrophy and Spinal Muscular Atrophy”, or alternatively “A Dutch Guideline for the Treatment of Scoliosis in patients with Myopathic Conditions”.

Response:
We are aware that the term neuromuscular disorders is interpreted diversely. This is the reason that we have defined this term explicitly in the section “Definitions”. In this definition we have excluded patients with disorders of the central nervous center, such as cerebral palsy. Furthermore, the title of the manuscript corresponds to the official Dutch title for the Guideline. This is why we would prefer to keep the title unchanged.

2. On Page 7, 3rd paragraph, under Recommendation, the authors suggest that “the vital capacity is a possible indicator of the progression of scoliosis”. In my view, they should make a comment to clarify that decline in vital capacity is, however, expected to occur as part of the natural history of the condition in patients with DMD and/or SMA and this is not necessarily related to the development of scoliosis. This statement is additionally supported by the fact that surgical stabilisation of the spine and correction of the scoliosis does not influence further decline in respiratory function which is expected to occur as part of the natural process of the disease.

Response:
We agree with you and have added this remark in the discussion of section “Factors affecting the progression of scoliosis in DMD”.

3. On Page 8, 1st paragraph, under Evidence, last sentence, in my view the authors should also add a statement to say that a spinal brace, especially if this is rigid, can potentially restrict chest movements and affect the patient’s respiratory function with detrimental consequences. In my opinion, for the few of these patients where trunk support is required and surgical correction cannot be performed, posture improvement
could be easier and safer achieved by seating adaptations built on the patient’s wheelchair rather than the use of a spinal orthosis. If the authors agree, it might be helpful to include this statement in their recommendations.

Response:
We have included this addition in the text.

4. On Page 9, under Steroid Treatment, I would expect the authors to refer to the associated problem of osteopenia that these patients inherently have but which is also induced by the corticosteroid management. I would suggest that the authors could include their recommendations for bone quality assessment through a bone mineral density scan, as well as their suggestions for treatment of a diagnosed osteopenia and osteoporosis possibly with biphosphonates, especially in view of the need for scoliosis surgery and the importance of reducing the risk of pseudarthrosis.

Response:
The treatment of these patients with corticosteroids, including the risks and management of side effects, has been described in a previously published Dutch Guideline (VSN, Richtlijn 'het gebruik van corticosteroïden bij Duchenne Spierdystrofie', www.vsn.nl/hulpverleners, 2004) and this falls outside the scope of this article. We have, however, inserted osteopenia and osteoporosis explicitly as side effects of the corticosteroid treatment.

5. On Page 12, 1st paragraph, under Recommendation, I would suggest that the authors could include their recommendations on the postoperative management of these patients in regard to their associated respiratory compromise. For example, in my practice, this would include often elective endotracheal ventilation for 24-72 hours depending on the severity of preoperative respiratory dysfunction, frequent use of non-invasive ventilation following extubation and cough assist machines in patients with an ineffective cough, intensive respiratory physical therapy, as well as early mobilisation of the patients on a reclining wheelchair with the aim to reduce the risk of pulmonary infection. I believe that this is the only part of the paper where such recommendations could be presented since guidelines on respiratory management are not included further down in the text.

Response:
We have included these remarks in the discussion of the section "Post-operative care".

6. On Page 12, 3rd paragraph 3, under Discussion, I would welcome the authors’ guidelines on whether severe ventricular insufficiency in patients who are already on cardiac medication would be considered in their suggestions as a contraindication for scoliosis surgery. Do the authors have a specific cut-off for cardiac impairment beyond which surgery would be contraindicated? Unfortunately, the current literature does not provide answer in this question and I think that it would be interesting to present the working group’s views.

Response:
Indeed, on this point literature does not give any indications. In our practice, patients are examined according to protocol by a cardiologist. We have up to now never experienced that patients were rejected for surgery on grounds of cardiac impairment. Based on this we are not able to indicate any cut-off for surgery.

7. On Page 13, 2nd paragraph, under Recommendation, do the authors have any suggestions on the need for nutritional supplementation perioperatively in patients with DMD and SMA who are usually malnourished which would decrease primarily the risk for infection? In addition, in patients with severe associated hip deformity and a scoliosis with pelvic tilt, which pathology would they recommend to correct first: the scoliosis
including correcting the pelvic obliquity and fusing to the sacrum or the hip displacement? It would again be very interesting to present the working group’s consensus.

**Response:**
In our experience we have found that the combination of hip displacement and scoliosis with pelvic tilt occurs more often in patients with cerebral palsy then in SMA and or DMD patients. In these cases we correct the scoliosis first and then address the hip displacement.

8. On Page 13, 3rd paragraph, under Evidence, I would expect the authors to mention also the need for hypotensive anaesthesia in order to reduce blood loss intraoperatively, as well as to discuss the use of blood preservation techniques and present their experience and recommendation. In general, the collective experience of such a multidisciplinary group of clinicians and investigators would be of exceptional value to the audience who are treating patients with such conditions. Therefore, wherever possible I would encourage the authors to include their group opinion, especially in regard to aspects of management where the literature does not provide valid information.

**Response:**
We have included these additions in the text (Anesthetic considerations: Evidence).

9. On Page 14, 1st paragraph, under Evidence, I would be interested to read the authors’ experience on initial anterior release and fusion as a supplementary procedure to increase flexibility of the curve, for example in patients with fixed severe lumbar scoliosis and rigid pelvic obliquity, and before a posterior instrumented arthrodesis is performed. Do the authors have clear indications and recommendations for anterior surgery in this group of patients?

**Response:**
It was already mentioned that we do not advise to use an anterior approach in these DMD and SMA patients, since their pulmonary function is already compromised.

10. On the same paragraph, I think that the authors should mention that fusion to L5 in this group of patients who have limited arm function, which allows mobility of the lumbosacral junction can be performed in patients with minimal pelvic obliquity and, in addition to the advantages already mentioned in the text, this could preserve at least to some extent the ability for independent postoperative feedings.

**Response:**
We believe that whether or not we include L5-S1 in the fusion length does not affect the arm function significantly. As stated, it does influence the sitting balance.

11. On the same section of the text, 2nd paragraph, where the authors discuss application of growing rods for these deformities, I would suggest that they mention the significant risks associated with the repeat lengthenings that are usually performed every 6 months (serial anaesthetics, instrumentation problems, wound infections) for such a medically compromised group of patients.

**Response:**
We agree. We have inserted this remark in the text (Spinal fixation and fusion: discussion/conclusion).

12. On Page 15, 1st paragraph, under Recommendation, I would welcome the authors’ comment on whether they feel there is any role for the use of BMPs, especially in revision cases with a documented non-union.

**Response:**
We do not use BMPs in these patients.
13. On Page 16, last paragraph, how soon after scoliosis surgery and how often thereafter would the authors recommend monitoring of the patients’ cardiorespiratory function?

Response:
The patient has regular check-ups with their physicist and/or specialists according to their individual situation. After recovery from the surgery, the patient resumes the normal regular check-ups with their consultants.

14. On Page 19, 5th paragraph, under Discussion/conclusion, I would suggest that the authors include a statement to say that postoperative bracing could be detrimental to the respiratory recovery, especially at an early stage following surgery when the pulmonary function is significantly reduced.

Response:
We have included this comment in the discussion of section “Postoperative bracing”.

Corrections on writing format:
1. Abstract, 1st paragraph, “...and is perceived as unaesthetic”, what do the authors mean? Please correct.
2. Introduction, 1st paragraph, “Usually contractures...present”, does not read well. This could be changed to: “Usually joint contractures, as well as nutritional disorders are present”.
3. Page 3, line 12, change “live” to “life”.
4. Page 3, line 15, “and revalidation” should be omitted.
5. Page 5, line 21, “tracheostomy” should be corrected.
6. Page 5, line 38, “heart” should be corrected.
7. Page 11, last paragraph, “lung function” should be corrected. This mistake is repeated in the following 2 paragraphs.

We have corrected the typo’s

Reviewer 2: Richard McCall

Comments:
This article is essentially a meta-analysis of the literature concerning treatment of neuromuscular scoliosis, predominantly scoliosis secondary to Duchenne Muscular Dystrophy and Spinal Muscular Atrophy. The article is well reasoned and well balanced, as the authors reached their conclusions by analysis of the literature rather than any independent or bias studies. The standard of writing is also very acceptable. The only real problem with a meta-analysis is that it does not break any new ground. It is essentially a compilation of existing articles and draws conclusions based on the conclusions of previous authors. This article is important because it is a thorough review of the literature concerning medical and surgical treatment of muscular dystrophy and spinal muscular atrophy. However it is very limited in scope and does not really add any new conclusions to the existing body of literature on these two subjects. I feel this article would be of interest to physicians who are heavily involved in treating patients in these two areas or possibly as a review article for residents in training, but as it covers a very limited area and, as a result has only limited interest to the majority of spinal surgeons.

Response:
The article is meant as a review article and indeed summarizes all available evidence in the literature supplemented by expert opinions.

Reviewer 3: Mr. Ashley’s Cole
Comments:
1. They should recognise the Cochrane review: Cheuk et al (2007). Surgery for scoliosis in Duchenne Muscular Dystrophy. The Cochrane Collaboration. I am a co-author on this and it does give a full review. The conclusions are very similar to those in the paper.

Response:
The Cochrane review was published after the guideline was formulated by the work group. However, because we agree that this review should be acknowledged, we have inserted a reference to this work in the introduction.

2. Intra-operative cell salvage should be encouraged in the section on 'anaesthetic considerations' on p13.

Response:
We have placed this remark in the text as suggested.

3. Regarding surgical treatment, I completely agree with the comments on DMD but these cannot be transposed to SMA. Instrumenting to L5 in SMA usually causes a problem with curve progression and pelvic obliquity and these patients should be instrumented T2-pelvis. The SMA patients tend to fall into 2 groups surgically: (1) those who develop a significant scoliosis aged 1-3 who can be well managed with lengthening systems. Interestingly, the lengthenings can be performed on BiPaP, propofol and local anaesthetic in the lateral position which reduces the risks post-operatively of prolonged ventilation in this difficult group; (2) those who develop a curve 4-7. The curve usually remains flexible enough to delay surgery until the age of 7-9. At this age, although a spinal fusion will result in some loss of final sitting height and probably chest volume, the benefits of a single surgical procedure outweigh the risks of multiple lengthening procedures. The use of multiple pedicle screws around the curve apex may reduce the risk of crank-shafting. I am unhappy with the use of the Luque trolley in this group as it is unproven and associated with multiple possible complications - it is also advocated with an anterior release and convex epiphysseodesis.

Response:
We agree with your point of view. We think that your comment is a worthwhile addition and therefore we have included these remarks in our manuscript.

Again, we would like to thank the reviewer for reviewing our manuscript. We hope you will consider the revised manuscript for publication in Scoliosis.

I look forward to hearing from you.

Yours sincerely,

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