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Supplementary appendix

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Supplement to: 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* 2017; published online Jan 23. http://dx.doi.org/10.1016/S1474-4422(18)30025-5.

Appendix – Diagnosis and management of Duchenne muscular dystrophy, an update, part 2: Respiratory, cardiac, bone health, and orthopedic management

Methods

It is important to understand that the guidance in this update is not conventionally evidence-based. As is typical for a rare disease, there is a lack of large-scale and randomized, controlled trials in this field, with the possible exception of studies favoring the use of corticosteroids.[1] Therefore, as we did with the 2010 care considerations,[2,3] the guidance in this document were developed using a method that queries a group of experts on the appropriateness and necessity of specific interventions, using clinical scenarios. This method is intended to "objectify" expert opinion, and to make the care considerations a true reflection of the views and practices of the expert panel based on their interpretation and application of the existing scientific literature. This methodology is designed to produce an essential "tool kit" for DMD care; only interventions that have been deemed both appropriate *and* necessary are recommended. For a detailed discussion of Methodology, see Part 1 of these care considerations.

Search strategy and selection criteria

Articles for the literature review were identified by searching Medline, Embase, Web of Science, and the Cochrane Library databases for peer-reviewed English-language articles published from 2006 through September 2013 for the eight original topics and from 1990 through September 2013 for the three new topics. The literature was searched using the key search terms of "Duchenne" or "muscular dystrophy," or both, paired with one of 626 search terms. The detailed search strategy and terms are included in the appendix. The literature search identified 1,215 articles after duplicates were removed. Reviews, meta-analyses, case series, case reports, animal models, and articles on unrelated diseases or Becker muscular dystrophy only were excluded upon further review. Of the 672 remaining articles, the steering committee reviewed 430 articles that were potentially relevant to the update of the care considerations. The steering committee members then classified each one using the following criteria: (1) consistent with the existing care considerations, (2) conflicts with the existing care considerations, (3) requires an update to the care considerations, or (4) presents promising research. Articles that were identified as required for the update were used to create clinical scenarios in accordance with the RAND method. Subject matter experts, with the assistance of RTI, also continually updated the references during the development of the manuscript. Before publication, an updated literature search was conducted for articles published between October 2013 and July 2017, which identified 880 articles. Committee chairs reviewed 115 articles potentially relevant to care and updated the references and text as necessary.

Surgical Considerations

Important surgical considerations for individuals with DMD are detailed in Figure 6. A cardiologist and pulmonologist should be consulted before all surgical procedures, and anesthesiologists should be aware that individuals with DMD are at risk for cardiac and respiratory decompensation during and after surgery. Respiratory care may include providing non-invasive assisted ventilation and assisted cough after surgery for individuals with significant respiratory muscle weakness.[4] Young men with DMD are at risk for developing rhabdomyolysis when exposed to inhalational anesthetics or when administered succinylcholine. These complications are frequently confused with malignant hyperthermia (MH) but are associated with hyperkalemia, which must be recognized and treated expediently if the individual is to survive.[5] This reaction frequently occurs at the end of the surgical case as the individual is emerging from a previously uneventful anesthetic, unlike MH, which frequently manifests on induction of anesthesia. An exception is nitrous oxide, which appears to be a safe inhalational anesthetic if used with proper monitoring, support and precautions. Intravenous anesthetic agents including ketamine, propofol, benzodiazepines, and rocuronium can be considered safe agents if used with proper monitoring, respiratory support, and precautions.[6] Total intravenous anesthesia is strongly advised. Significant blood loss is a major concern when providing anesthesia for spinal fusion surgery in individuals with DMD. Patients with DMD may be at increased risk for blood loss during surgery as a result of abnormalities of hemostasis associated with the dystrophin deficiency,[7,8] and patients treated with beta-blockers may be unable to respond to blood loss with compensatory tachycardia. Therefore, consideration should be given to withholding beta-blockers perioperatively, at least on the day of surgery. Surgical and anesthesia protocols should be enacted to address these risks, with specific interventions directed by the pre-operative clinical team.

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