

Anaesthesia recommendations for Distal arthrogryposis type 1

Disease name: Distal arthrogryposis type 1 (A and B)

ICD 10: Q74.3

Synonyms: Distal arthrogryposis multiplex congenita type I, distal arthrogryposis type 1A, distal arthrogryposis type 1B

Disease summary: Distal arthrogryposis type 1A (DA1A; MIM 108120) and 1B (DA1B; MIM 614335) – congenital non-progressive myopathies – manifest contractures of the hands and ankle-foot complex strongly resembling those observed in Freeman-Burian and Sheldon-Hall syndromes (FBS and SHS) but lack additional craniofacial findings. Limb malformations accepted in the diagnostic criteria that were common to FBS and the distal arthrogryposes include two or more of the following: talipes equinovarus, metatarsus varus, vertical talus, talipes equinovagum, calcaneovalgus, camptodactyly, ulnar deviation of wrists and fingers, overlapping fingers or toes, and hypoplastic or absent interphalangeal creases. DA1A and DA1B demonstrate an autosomal dominant inheritance pattern. There is no apparent gender, ethnic, or geographical preference, and environmental and parental factors are not implicated in pathogenesis.

DA1A and DA1B were considered phenotypically identical (hence, DA1), differing only in genotype, and both demonstrated an autosomal dominant inheritance pattern [1]. There was no apparent gender, ethnic, or geographical preference, and environmental and parental factors were not implicated in pathogenesis [1]. DA1A was caused by allelic variations of the tropomyosin 2 (TMP2; MIM 190990) gene, located at 9p13.3[6-7], and DA1B was caused by allelic variations of the slow type myosin-binding protein C (MYBPC1; MIM 160794) gene, located at 12q23.2 [8]. DA1 was considered to belong to the group of phenotypically similar entities termed distal arthrogryposes [9, 10]. Arthrogryposis multiplex congenita was a distinct entity from the distal arthrogryposes [9]. Other differential diagnoses included distal arthrogryposis types 3, 7, and 8; Schwartz-Jampel syndrome; and non-syndromic distal extremity contractures. DA1 was primarily distinguished from all other condition by a lack of additional findings but contractures more treatment-resistant than in non-syndromic presentations.

Although literature on DA1 was negligible [11-12], general principles relevant to care of patients with DA1 was deduced from the better-documented experience with FBS. This recommendation, developed through literature review and clinical experience, aimed to address the deficiency in available clinical guidance by providing essential outcomes-directed advice for evaluation and management of anaesthetic care for patients with DA1. The protocol for and results of the systematic review and meta-analysis underpinning this recommendation were described elsewhere [11-12]. AGREE II and GRADE Guidelines [13-14] were followed in the recommendation development process.

Medicine is in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong



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Typical surgery

Though not as severe as with FBS or SHS, patients with DA1 still frequently undergo many orthopaedic surgeries, as attempts at operative deformity correction may have suboptimal results and require subsequent revision. Due to the wide variability of DA1 presentation and the paucity of research, there is a great diversity of operative approaches employed primarily for ankle-foot complex contracture correction and hand contracture correction. Less frequently, involvement of more proximal joints (e. g., dislocation or dysplasia of shoulders and hips, contracture of elbows) is the focus of operative interventions.

Type of anaesthesia

Although lacking craniofacial malformations and limited neck mobility that universally complicates airway management in other distal arthrogryposes and FBS, this is not meant to imply general anaesthesia may not be the default choice for DA1. While the anaesthetic approach is ultimately dictated by patient safety, the patient's understanding and affect regarding surgery, and technical feasibility, there may be reasons to avoid pre-medication, sedation, and general anaesthesia for appropriately selected patients with DA1 [15]. Though mild spinal deformities are seen in DA1, this typically does not preclude epidural or spinal anaesthesia, which may still have fewer syndromic-associated challenges and complications and a more favourable safety profile over sedation and general anaesthesia. Whenever possible, consider and explore local, regional, spinal, and epidural anaesthesia with patients during the pre-anaesthetic consultation. Age is not necessarily a contraindication to any particular anaesthesia modality [16]. Many adults are poor candidates for local or regional anaesthesia, and many children handle the experience very well [16]. Proper psychological preparation for patients undergoing surgery exclusively under local or regional anaesthesia does not differ substantively from any other pre-operative consent and preparation process [16].

Necessary additional pre-operative testing (beside standard care)

Anaesthetic care for patients with DA1 often presents potential challenges related to extremity contractures that require pre-operative planning. Patients should be evaluated well in advance of proposed procedures, if possible. The anaesthesiologist performing the evaluation should also be the anaesthesiologist assigned for the procedure. A thorough and complete history should include questions about: current medications and allergies, reactive airways disease, gastro-oesophageal reflux disease (GERD), previous acute and chronic respiratory problems, prior anaesthesia and surgeries, seizures, and any symptoms of possible central nervous system dysfunction, especially increased intracranial pressure [16]. Examination includes: vital signs, mental status, airway, spinal, neurological, and cardio-pulmonary assessments [16]. It is important to explain to the patient and family possible risks and ensure questions are answered and concerns fully addressed [15-16]. Findings, concerns, and management plans must be discussed with participating surgeons [16]. The preceding pre-operative consultation and planning process may seem obvious, but unfortunately, this process does not represent a universal standard for the care of potentially high-risk patients undergoing surgery.

Some suggest that malignant hyperthermia (MH) does not have an association [17-18] with most myopathies in which anaesthetically-related hypermetabolic states resembling MH have been reported. Unless there is specific concern, an anaesthetic technique considered MH-

safe is not required for patients with DA1, but this should not preclude the use of such a technique, if desired. An expanded metabolic panel and 12-lead electrocardiogram are appropriately included in pre-operative screening for many patients who carry a potentially higher risk for anaesthesia or sedation and prevent misinterpretation of the pre-existing status as being associated with intra-operative changes. As arterial puncture for blood gases may be infeasible, point-of-care capillary blood testing can be helpful for baseline and subsequent assessment, when available. Alternatively, pulse oxymetry on room air is a valuable non-invasive modality for assessing pulmonary gas exchange, and venous serum bicarbonate is reflective of the state of carbon dioxide exchange. Though muscle biopsy for determination of MH susceptibility can be a worthwhile assessment to make if there is some index of concern, it is not advised, due to the large muscle sample required for the in vitro caffeine-halothane contraction test. Genomic testing for the RYR1 mutation is feasible, but the mutation is not associated with DA1. Notably, DA1 is not associated with any cardiac muscle pathology.

Particular preparation for airway management

Unlike many of the distal arthrogryposes (e.g., SHS and DA3) and phenotypically similar craniofacial syndromes (e.g., FBS), DA1 is limited to limb malformations. Craniofacial malformations exclude a diagnosis of DA1; therefore, no distinctive airway management issues exist in DA1.

Particular preparation for transfusion or administration of blood products

No reports in the literature or known clinical experience indicate any unusual problems or needed precaution for patients with DA1 needing transfusion or administration of any blood components. Moreover, many of the surgeries these patients undergo are not associated with blood loss sufficient to require transfusion. Nonetheless, distal extremity contractures and the consequent poor quality of veins may make establishing peripheral intravenous access challenging in many patients with DA1. Use of a small gauge catheter, 22 or less, is generally required. Need for the use of a small gauge vascular catheter may impair transfusion, intravenous hydration, medication administration, and blood draw efforts. Neck vein access also can be considered, as cervical spine immobility is not a feature of DA1. With increased use of ultrasound assisted peripheral vein cannulation, central line placement has a diminished role in providing vascular access for these patients but still may be necessary in a greater frequency than the general population.

Particular preparation for anticoagulation

While many patients have reduced pre-operative mobility and, therefore, are at a somewhat higher pre-operative thrombogenic risk, no reports in the literature or known clinical experience indicate any disorder of coagulation associated with DA1.

Particular precautions for positioning, transportation and mobilisation

Carefully evaluate patients pre-operatively to assess the extent of contractures. Any range of motion limitations found should be discussed with surgeons to plan the best positioning for

the patient during surgery. If possible, positioning before induction of anaesthesia is recommended but may not be feasible. Patients should always be placed in a comfortable position, with avoidance of unnatural mobilisation under anaesthesia, kept warm, and provided with generous padding to avoid pressure points. Use of padded dressings is recommended for areas at risk for pressure injury (sacrum if supine; breasts and iliac crests if prone). Thin patients and those with extended inpatient confinement are at higher risk for loss of skin integrity. Patients with skin complications should be seen by a plastic surgeon. Active forced air heating systems should be used to maintain patient normothermia during anaesthesia and surgery, as many of these patients may have reduced adipose tissue and be at increased risk of hypothermia.

Interactions of chronic disease and anaesthesia medications

There are no syndrome-specific chronic medications for patients with DA1, and there is no syndrome-specific treatment. Therapeutic interventions focus on improving functional outcomes. There is no cure, though DA1 is believed to be non-progressive.

Anaesthetic procedure

The evidence base does not support an association between MH and DA1 [17-18]. Nonetheless, in some clinical situations it may be desirable to avoid MH-triggering agents, any of which are safely used in patients with DA1, though some are used more extensively. Oral midazolam is routinely used for pre-medication, and intravenous midazolam is often used for mild procedural sedation. If an MH-safe technique is preferred, induction of general anaesthesia is safely achieved with nitrous oxide, which is not a volatile MH-triggering gas. If maintenance of spontaneous respiration is essential, nitrous oxide is used in conjunction with ketamine to achieve and maintain surgical anaesthesia. If vascular access is established before induction, propofol is frequently used for induction and maintenance of surgical anaesthesia. Intravenous infusion of either propofol or dexmedetomidine or both can be used to establish moderate sedation, with preservation of spontaneous ventilation for airway management and surgical anaesthesia. Spontaneous ventilation also can be maintained with nitrous oxide, ketamine, propofol, dexmedetomidine, or low-dose infusion of short-acting opioids, such as remifentanyl.

Lidocaine with or without epinephrine for local anaesthesia or bupivacaine (0.25 – 0.5%) or ropivacaine for local anaesthesia, spinal, or epidural anaesthesia may be used. If performing spinal or epidural anaesthesia, a paediatric size needle and catheter is used, even for adults, as most patients with DA1 are small. When using lidocaine or bupivacaine for anaesthesia without adjuvants, no special precautions are required, except for precautions related to the actual operative intervention itself. Peripheral nerve blocks, either single bolus injection or with catheter placement, may be used for extremity surgery and continued post-operatively for analgesia.

Particular or additional monitoring

Standard modern anaesthesia monitoring modalities (e.g., heart rate, oxygen saturation, blood pressure, end tidal carbon dioxide, respiratory rate and depth, and temperature) are sufficient. Muscle rigidity or relaxation is not a reliable indicator of anaesthesia depth or neuromuscular blockade effectiveness, as syndromically affected muscles, especially those

exhibiting overt contracture, are unaffected by anaesthesia and muscle relaxants. As clip sensors may not fit well, flexible adhesive oxygen saturation sensors are preferred and readily available in all institutions. They are applied circumferentially and fit any digit in the largest or smallest of patients. If a urinary catheter is used for monitoring, during a long surgery, or when epidural anaesthesia-analgesia is used, a paediatric size is typically chosen, even for adults, as most patients with DA1 are small.

Possible complications

As noted previously, evidence suggests DA1 may not have an association with MH [17-18]; however, the following have traditionally been considered potential complications of general anaesthesia or sedation in patients with DA1: hyperpyrexia without the malignant hyperthermia triad, malignant hyperthermia, and neuroleptic malignant syndrome (hypermetabolic syndrome similar to malignant hyperthermia). Other complications of challenging peripheral vascular access and impaired operative access due to ineffectiveness of neuromuscular blockade are much more likely occur. If present, spinal deformities complicate epidural and spinal anaesthesia but rarely preclude it.

Post-operative care

Except as otherwise noted, no reports in the literature or known clinical experience indicate any unique problems or needed precaution for post-operative care in patients with DA1. Some patients, however, are observed in the intensive or intermediate care unit for at least some time, especially after major surgery.

Disease-related acute problems and effect on anaesthesia and recovery

Except as previously discussed, no reports in the literature or known clinical experience indicate any effect of DA1 on sedation, anaesthesia, and post-operative recovery concerning the differential diagnosis of possible acute problems.

Ambulatory anaesthesia

The general principles for the anaesthetic care of patients with DA1 previously described apply with proper balancing of risks and benefits, to all types and settings of anaesthesia, including obstetric, ambulatory, or emergent.

Obstetrical anaesthesia

The general principles for the anaesthetic care of patients with DA1 previously described apply with proper balancing of risks and benefits, to all types and settings of anaesthesia, including obstetric, ambulatory, or emergent.

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