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Review Article

Iatrogenic neurological injury in children with trisomy 21

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ABSTRACT

Purpose: Children with trisomy 21 are at a greater risk for craniocervical junction instability than the general population. These children frequently require administration of anesthesia due to surgical (including otolaryngological) interventions and are at risk for neurological injury. We reviewed the current literature describing iatrogenic neurological injury in children with trisomy 21 undergoing anesthesia in order to facilitate the development of safety recommendations.

Methods: A systematic review of the literature was performed using Medline, Embase, Scopus, and Google Scholar, following the PRISMA statement. All cases of perioperative neurological injury in children with trisomy 21, aged 18 and under were identified. Clinical and radiographic data were extracted for each report. The data were synthesized to develop recommendations regarding perioperative management.

Results: Of 348 articles screened, 16 cases of iatrogenic neurological injury (in children ages 0.7–18 years) were identified. Three injuries occurred during otolaryngological surgeries, nine during sedation for intubation for non-otolaryngological surgery, one during sedation for neuroimaging, one while restraining a child, and two were due to intraoperative head and neck positioning while anesthetized. Preoperative screening was reported in four cases. A diagnosis of atlantoaxial instability (AAI) or atlantooccipital instability (AOI) was made immediately following symptom presentation in three cases but was often delayed by a median (IQR) of 30(11.5–912.5) days. No cases resolved spontaneously, with 2 patients progressing to brain death and 12 requiring surgical stabilization. Of the latter, seven showed improvement, whereas one died 5 months later. No intraoperative precautions during the index procedure were reported in any of the 16 cases.

Conclusion: Iatrogenic neurological injury in children with trisomy 21 are rare but severe and likely under reported. Although the role of preoperative screening remains controversial, all children with trisomy 21 undergoing surgery should be considered at risk for neurological injury due to confirmed or undiagnosed AAI or AOI and should be transferred and positioned with appropriate caution. Children with instability should be referred for neurosurgical attention for preoperative stabilization to mitigate perioperative risk. It is imperative to consider the possibility of neurological injury secondary to medical procedures, as it is clear that neck manipulation of any sort places these children at risk.

1. Introduction

Trisomy 21 occurs in approximately 1/700 live births and is associated with a multitude of anatomical and physiological abnormalities [1,2]. As a result, these children often require surgical interventions necessitating the administration of general anesthetic or procedural sedation [3]. Health issues such as obstructive sleep apnea, otitis media, and subglottic stenosis are not uncommon making these patients frequent visitors to the Otolaryngologist's operating theatre [4–6]. Moreover, varying levels of maturity and cognitive impairment may necessitate a general anesthetic for simple procedures that would otherwise be performed while awake.

Upper cervical spine instability is a significant concern in children with trisomy 21 due to bony anomalies and ligamentous laxity associated with this condition [7]. Craniocervical spine instability can occur at both the atlantoaxial joint (C1-C2) as well as the occiput-C1 junction [8]. AAI has been reported to occur in 10–20% of patients with trisomy 21 [9–12], with 5 mm typically used as the upper limit for a normal

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atlantoaxial distance [13]. AOI is said to occur anywhere from 6 to 63% of patients with Trisomy 21, [14,15] but the true incidence of AOI remains unknown [8]. Various methods exist to determine AOI, but a standard method has yet to be determined [7].

The frequent need for multiple anesthetics, combined with vulnerable anatomy predisposes children with trisomy 21 to iatrogenic neurological injury [16]. Under sedation, the patient's head may be positioned in a way that may threaten or compromise the neural elements in the context of confirmed or undiagnosed AAI and AOI. Although iatrogenic neurological injury is rare, it is likely underreported in the literature. Despite being commonly listed amongst the perioperative considerations for children with trisomy 21 in the anesthetic and otolaryngological literature, little consensus exists regarding perioperative care for this at-risk population [4].

Here we perform a systematic review of neurological injury in children with Trisomy 21. We identify 16 cases of iatrogenic neurological injury in children with trisomy 21 who have craniocervical instability. We hope to advance our understanding of neurological decline in these patients, with the goal of compiling a list of safety recommendations that may ensure the safest possible perioperative experience for these patients.

2. Methods

A systematic review of the literature was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [17]. Four electronic databases (Medline, Embase, Scopus, and Google Scholar) were queried from inception until March 13, 2018. All case reports and case series outlining neurological injury in children with trisomy 21 were identified through a comprehensive search strategy. Search terms included: “Down's syndrome”; “trisomy 21”; “atlantoaxial joint instability”; “atlantooccipital joint instability”; “craniocervical joint instability”; “intraoperative complications”; “postoperative complications”. The references of all screened articles were reviewed for additional studies. When appropriate, truncation was used with the text words to account for variations in word endings. No date or language limits were applied.

Following removal of duplicates, 348 abstracts were screened by two authors (R.E.H., N.E.W.) for full text review (Fig. 1). Reports were included if they described intraoperative or postoperative neurological complications in children with Trisomy 21. Exclusion criteria included cervical injury unrelated to surgery, as well as cases > 18 years of age. Each of the remaining articles was then reviewed by three authors (R.E.H., N.E.W., G.M.I.) for relevance.

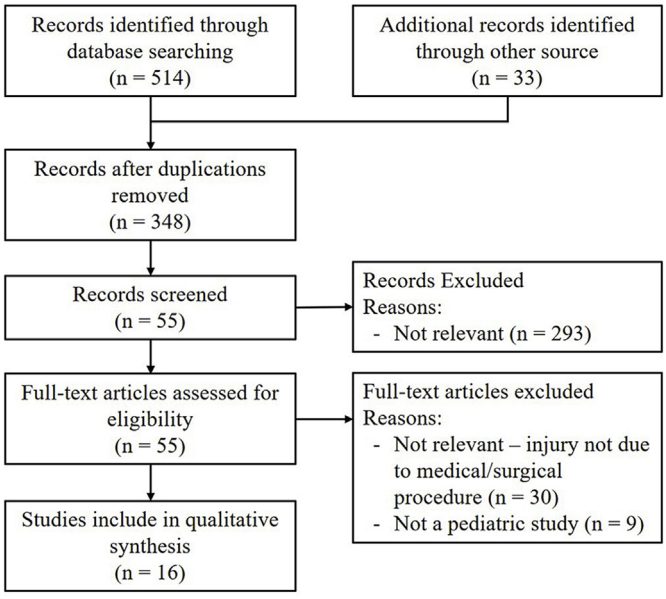

Fig. 1. Flow diagram of literature search based on recommendations of Preferred Reporting Items for Systemic Reviews and Meta-Analysis (PRISMA) [17].

Data extraction was performed independently by three authors (R.E.H., N.E.W., G.M.I.). Clinical and radiographic characteristics of individual cases were collected. The former included surgical indication, preoperative screening methods, safety measures utilized and outcome. The latter included radiographic measurements of the craniocervical junction at all time points collected. In cases of incomplete data reporting, additional information was requested by contacting the corresponding authors directly. Since all reports were observational, unmatched case series and reports, risk of bias and quality of evidence were considered “high-risk of bias” and “low to very low quality of evidence” based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool [18].

The low numbers of participants identified precluded statistical inference. Extracted data were synthesized and analysed qualitatively. The primary endpoint of interest was patient outcomes. Secondary endpoints included procedure type, pre-operative operative screening techniques, patient positioning and time to diagnosis of iatrogenic neurological injury and intervention. Articles that suggested safety recommendations were further examined by all four authors (R.E.H., N.E.W., G.M.I., E.J.P.) for putative preoperative, intraoperative, and postoperative safety measures.

3. Results

Following full-text review, 16 cases of iatrogenic neurological injury in children with trisomy 21 patients were identified (Table 1). The median (IQR) age at diagnosis of AAI was 6 (3–9) years. Preoperative screening was performed in 25% of cases (4/16). This consisted of physical exam (cases 1 and 2) and cervical-spine radiograph (cases 3 and 5). Preoperative screening in cases 1–3 was performed immediately prior to each procedure, and in all three cases there was no evidence of preoperative AAI or AOI. In case 5, the screening had been performed one year prior to surgery, and although instability was identified, no course of treatment was recommended. None of the cases reported performance of intraoperative preventative measures.

Three cases occurred during otolaryngological surgeries (cases 3, 5, and 11), nine during sedation for intubation (cases 1, 2, 4, 6, 8–10, 15 and 16), one during sedation for neuroimaging (case 7), one while restraining a child in clinic (case 14), and two were due to intraoperative head and neck positioning while anesthetized (cases 12 and 13). The three otolaryngological surgeries included myringotomy and tube placement, typanomastoidectomy, and one unspecified procedure. Of the remaining procedures, five were cardiac related (cases 1, 2, 6, 12 and 13). Only one procedure was non-surgical (case 14). In this case, the installation of eye drops required the patient to be physically restrained, resulting in a hyperextension of the neck. The exact nature of each injury is summarized in Table 2. Anteroposterior subluxation was reported in six (37.5%) cases (cases 2, 4, 7, 9, 10 and 14), rotatory subluxation in five cases (cases 1, 3, 5, 8 and 11), and vertical subluxation in one (case 4). Case 6 did not report the type of subluxation, and the remaining four cases did not specify the type of subluxation (cases 12, 13, 15, and 16). A median (IQR) atlantodental distance of 10.3 (7.8–11.6) mm was found postoperatively. Nine cases did not provide a postoperative atlantodental distance (cases 1, 2, 4, 11–16).

Symptoms were first noted immediately in six cases (cases 2, 6, 8–10 and 14). A diagnosis of neurological injury was made immediately following symptom presentation in three cases (cases 5, 7, and 14), and the remainder were diagnosed with a median (IQR) delay of 30 (11.5–912.5) days. Progressively worsening symptoms were experienced by 50% (8/16) of patients (cases 1, 2, 4, 9–13), whereas 31.3% (5/18) did not experience progression (cases 5–8 and 14). The description of symptomatology was unclear for the remaining 18.8% (3/