Headaches in children after transcatheter device closure of atrial septal defects: a single centre experience

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Abstract

Background

Transcatheter device closure (TDC) is the most common treatment for isolated atrial septal defects (ASD) in children. In the adult population, the incidence of new-onset migraine headache after TDC is well-recognized, and is estimated at 15%. New-onset headache has not been well-described in an exclusively pediatric population. We reviewed our center’s experience to estimate the rate of headache complaints among pediatric patients undergoing TDC.

Methods

We performed a single-center retrospective review of all children undergoing TDC between January 1, 2018 and December 31, 2021. Among included patients, we comprehensively reviewed the electronic medical record (EMR), to identify patients reporting headache.

Results

165 consecutive patients underwent TDC during the study period. Of these, 134 met inclusion criteria. 20 (14.9%) patients had headache documented in the EMR. Of those, 7 (7/134, 5%) had persistent headaches (lasting greater than four weeks) or required further investigations. Two patients had headaches that were investigated with a brain MRI, which demonstrated normal or non-specific findings. One patient with a prior history of migraine required admission to hospital for migraine exacerbation. Another required emergency room management for status migrainosus. In addition to symptomatic pain management, 3 patients had a change in their anti-platelet regimen changed to clopidogrel. All patients with persistent headache were female (p < 0.1).

Conclusions

Our study demonstrated persistent headaches in 5% of children who underwent TDC. It is important for practitioners to discuss this association prior to TDC. Determination of the true incidence will require focused prospective data collection.

Introduction

Transcatheter device closure (TDC) of atrial septal defects (ASD) has become an established alternative to surgery [1, 2], and is now considered first-line therapy of isolated pediatric ASDs meeting indications for closure [1]. TDC offers a minimally-invasive approach with a high procedural success-rate [1], shorter hospital stay [3], and freedom from exposure to cardiopulmonary bypass. Procedural complications are rare, with reporting of late complications focused on major device-related events such as device embolization or erosion. The potential for device-related thrombus is routinely managed by prescribing ASA at a dose of 3-5mg/kg daily for 6 months post-procedurally, during which time patients are also recommended to observe endocarditis prophylaxis measures [4].

Among adults undergoing TDC, new-onset migraine headache is now recognized as a relatively common procedure-associated occurrence, with an estimated incidence as high as 15% [5]. Although some younger patients have been included in large, previously-reported cohorts, the rate of new onset headaches in children, specifically, has been the subject of very little direct scrutiny [6]. A large retrospective study in Poland[7] characterized the incidence of transient
headache episodes after TDC, but did not detail whether those headaches resolved or required further investigation and management. As a result of the recognized incidence among adults, and the proposed platelet-activation-mediated mechanism, recommendations for practice change toward dual-antiplatelet therapy post TDC has been advocated \[8\]. A better understanding of the rate of new headache among children may have implications for pre-procedural counseling and post-procedural management in this population. Leveraging an institutional practice of routine post-procedural telephone follow up, we conducted a single-center exploratory study to estimate the rate of headache complaints early after TDC among pediatric patients.

**Methods**

**Patients:**

We performed a single center retrospective review of all children undergoing TDC between January 1, 2018 and December 31, 2021 as derived from a comprehensive institutional database. We excluded patients under four years of age and those with developmental delay, anticipating some difficulty in obtaining a clear history of headache in these populations. We also excluded patients who had additional cardiac interventions performed at the same catheterization. Having identified our study cohort, we reviewed all available documentation in the EMR, including routine post-procedural follow-up calls and cardiology follow-up appointments, to determine the incidence of patient-reported headache. Patient and procedural variables, such as age, prior history of headache, procedural imaging modality, device-size, and any identified procedural complications, were collected.

**Procedure:**

TDC was performed under general inhalational anesthetic in all cases, after standard NPO preparations. Femoral venous access was obtained and full heparinization following a dose of 100u/kg was documented by ACT measurement. Varying amounts of baseline hemodynamic data were acquired prior to balloon sizing of the defect. An appropriately-sized device (Amplatzer Septal Occluder, Abbott) was selected and implanted using standard technique. Either transesophageal (TEE) or intracardiac echocardiography (ICE) was used in combination with limited uroscopy to assist with implantation and confirmation of appropriate positioning. Patients were discharged with a recommendation for a six-month course of aspirin (3–5 mg/kg) daily and were instructed to observe antibiotic prophylaxis over that same time.

**Post-procedure:**

At our center, TDC patients discharged on the day of procedure returned the following day for echocardiography and a brief encounter to review procedural results with family. Patients remaining in-house had their echocardiogram performed prior to discharge. In addition, all patients having catheterization at our center received a follow up phone call from dedicated nursing staff 3–4 days after catheterization to reassess the patient’s overall well-being, and to screen for access site issues. These calls were conducted for TDC patients regardless of bedded status post-procedurally, and any issues or concerns were documented in the electronic medical record (EMR). Though there was no standardized questionnaire for the phone follow up, the staff primarily responsible for this service typically inquired about headache when contacting TDC patients. All patients were prescribed ASA alone as initial thrombus prophylaxis.

Patients were characterized as having had a headache if there was documentation of the patient or family reporting either ‘headache’ or ‘migraine’ during the follow up phone call or any early post-procedural ambulatory visit. A ‘persistent headache’ was defined as a headache which continued greater than four weeks after the intervention, or
one that triggered additional investigations such as neurology consultation or neuroimaging. Qualitative variables were expressed as percentages and quantitative variables were reported as medians with ranges or means with standard deviations. Comparisons between categorical variables were performed with a chi-square test. Comparisons between continuous variables were made with student's t-tests. The data were analyzed using R statistical software version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria).

The study was approved by the institutional Research Ethics Board with waiver of informed consent.

**Results**

165 consecutive patients with ASD underwent TDC during the study period. Of these, 134 met our inclusion criteria. 18 were excluded due to documentation of significant developmental delay, 8 were excluded for age criteria, and 8 underwent additional interventions. The demographic data are summarized in Table 1. Study patients had a median age of 7 years (range 4 to 17, mean 9 ± 4.3 years). The records of 20/134 (15%) patients included a documented patient complaint of headache. Of these, 7/134 (5%) met our criteria for persistent headache, and these cases are summarized in Table 2. Two patients had headaches that were investigated with a brain MRI, which demonstrated normal or non-specific findings. One patient with a prior history of migraine required admission to hospital for migraine exacerbation. Another required emergency room management for status migrainosus the week following his procedure. Three patients with persistent headache were switched from aspirin to clopidogrel, two of whom had de novo headaches, and one who had a prior history of migraine. Of note, all patients with persistent headaches were female (p < 0.1).

Most cases (80%) were performed with TEE rather than ICE, and none of the patients imaged by ICE reported headache (p < 0.05). Procedural complications were rare: one patient who developed headaches had transient atrioventricular block during the procedure. There were no other catheterization-related complications in patients who developed headaches.

**Discussion**

In this limited, single center review, we describe the incidence of self-reported headache in a population of pediatric patients after TDC for isolated ASD and report a minimal estimate of 15%. While most were transient, some headaches were persistent and prompted additional evaluation and management. Of these more problematic headaches, none appeared to be related to procedural complications.

ASDs are a common congenital heart disease, accounting for 8–10% of all congenital defects [9], and are often asymptomatic. Often isolated ASD is incidentally diagnosed in evaluation of a benign murmur or non-specific complaint of chest pain or palpitations [9]. Many are small and do not warrant intervention. Larger defects can be associated with significant left to right shunt, increased pulmonary blood flow, and can cause pulmonary vascular changes over time. In the setting of a moderate or large ASD, echocardiographic evidence of hemodynamic burden suggested by right ventricular dilation, constitutes a standard indication for interventional closure in children [2, 10].

Adults with ASDs represent a more heterogeneous group and more commonly have medical comorbidities. Hemodynamically significant ASDs in adults can present with symptoms such as dyspnea and exercise intolerance [11, 12]. Adults are more likely than children to suffer the secondary morbidities of ASDs, specifically pulmonary vascular disease and atrial arrhythmias [11, 12]. The class I indications for closure of isolated secundum ASDs in adults include functional impairment from excess pulmonary blow flow and right-sided volume loading [11]. Less
frequently, ASDs are closed due to risk of paradoxical embolus [11, 12]. The chronicity of the atrial level shunt in adults may contribute to differences in both benefits and complications of ASD closure.

Migraine headaches following TDC in adults are well described [8, 13, 14]. Kato et al. sent structured questionnaires to 247 patients who underwent TDC that allowed for diagnosis of migraine headache in 23 of 207 patients who met inclusion criteria [6]. A randomized study was performed to investigate the efficacy of dual anti-platelet (aspirin and clopidogrel) therapy in reducing total migraine headache days following device closure. The CANOA trial showed that patients in the dual anti-platelet arm had fewer total headache days than patients in the aspirin-only arm [5]. The proposed mechanisms for migraine after TDC in adults are purely theoretical. Suggested mechanisms include silent cerebral micro-embolism, serotonin release from activated platelets on the left atrial disc, the release of vasoactive peptides resulting from atrial septal deformation, and nickel allergy [6, 8, 15, 16].

In our retrospective review, we found that 15% of patients reported headache symptoms that were documented in the EMR early after TDC. Of these, only 5% of patients appear to have had headaches that persisted past the initial recovery and at least 4 weeks post-procedure. The relationship between the observed incidence in our study and the incidence previously reported in adults is difficult to interpret. In a largely adult population, Kato et al. identified headache that persisted in 15 of 207 (7%) patients surveyed at 45 months post-procedure [6]. Of interest, all patients with persistent headaches in our study were female. Kato et al. did not specifically analyze the headache incidence by gender; however, they documented that among patients with de novo migraine headaches after TDC, only 22% were male. A recent retrospective study[17] described an incidence of migraine headaches in 1.5% of patients after TDC, and similarly noted that all were female. The International Classification of Headache Disorders, 3rd edition (ICHD-3) [18] does not specify unique pediatric diagnostic criteria for migraine headache: a common set of criteria are applied for adults and children. Some of these common criteria require specific headache descriptions which may be difficult for younger patients to express. It may therefore be difficult to directly compare the incidence of headache after TDC between adult and pediatric patients.

Our study had some important limitations. We chose to do a small single center review over a relatively short study period in an effort to minimize the variability associated with time- and provider-related changes in follow up practice (i.e. postprocedural phone calls). Even in this study period, questioning about headache after TDC was likely not comprehensively conducted. Therefore, we consider our observed 15% incidence as a minimal estimate. Furthermore, many of the patients who underwent TDC at our institution are referred from cardiologists in the community and returned to these providers for post-procedural care. These patients do not typically have follow-up at our institution beyond the described nursing follow-up call. As we only reviewed our EMR, it is likely that some patients experienced headache reported only to their referring provider was not discoverable in our EMR. This further strengthens our minimal estimate contention.

Conclusions

Our study demonstrated persistent headaches in 5% of children who underwent TDC. We believe this phenomenon is important for practitioners to discuss prior to TDC as it appears to be a relatively common post-procedural occurrence, likely the most common adverse outcome following this now routine procedure. Future studies should focus on prospective data collection in an attempt to elucidate risk factors and possible mechanisms. The use of survey methodology may allow for more comprehensive and specific follow up questioning regarding headache diagnosis. It may also allow for a standardized quantification of functional impairment, such as days of school missed, or perceived morbidity. Additional understanding of risk factors and functional impairment may inform potential changes in postprocedural management.
Declarations

1. All authors have participated in the work and have reviewed and agree with the content of the article.

2. None of the article contents are under consideration for publication in any other journal or have been published in any journal.

3. No portion of the text has been copied from other material in the literature (unless in quotation marks, with citation).

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Disclosures: The authors have no relevant disclosures.

References


### Tables

**Table 1**

Demographics

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 134)</th>
<th>No headache documented (n = 114)</th>
<th>Headache documented (n = 20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>9.0 ± 4.3</td>
<td>8.8 ± 4.2</td>
<td>9.8 ± 4.6</td>
<td>0.36</td>
</tr>
<tr>
<td>Gender male (%)</td>
<td>52 (39)</td>
<td>48 (42)</td>
<td>4 (20)</td>
<td>0.10</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>34.8 ± 26</td>
<td>34.4 ± 25.5</td>
<td>37.2 ± 29.3</td>
<td>0.69</td>
</tr>
<tr>
<td>ASD maximal dimension (mm)</td>
<td>14.6 ± 8.1</td>
<td>14.7 ± 8.6</td>
<td>14.4 ± 5.0</td>
<td>0.84</td>
</tr>
<tr>
<td>Device size (mm)</td>
<td>17.8 ± 5.3</td>
<td>18.1 ± 5</td>
<td>16.5 ± 5</td>
<td>0.20</td>
</tr>
<tr>
<td>Anesthesia time (minutes)</td>
<td>105.7 ± 33.6</td>
<td>105 ± 33.8</td>
<td>109.5 ± 32.6</td>
<td>0.58</td>
</tr>
</tbody>
</table>

**Table 2. Patients with significant headaches**
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Weight (kg)</th>
<th>Maximal ASD Diameter (mm)</th>
<th>Device Size (mm)</th>
<th>Anesthesia Time (minutes)</th>
<th>Procedure Details and Echocardiogram Findings</th>
<th>Headache Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>F</td>
<td>17.9</td>
<td>19.2</td>
<td>22</td>
<td>101</td>
<td>Small intra-device leak and small inferior device leak.</td>
<td>Significant headache for 5 minutes occurring once per month. Last documentation is 7 months after device closure.</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>F</td>
<td>26.5</td>
<td>Not documented</td>
<td>22</td>
<td>194</td>
<td>Transient complete heart block during the procedure that resolved. No residual ASD.</td>
<td>Mother called 2.5 weeks after procedure to say the child had severe headaches with confusion and vomiting. Aspirin was changed to clopidogrel and neurology was consulted. Positive family history for migraine.</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>F</td>
<td>74.4</td>
<td>12</td>
<td>9</td>
<td>103</td>
<td>Tiny residual shunt through the device.</td>
<td>Patient's known migraine headaches were exacerbated, requiring admission for migraine headache 18 days after the procedure. An MRI was done as the patient had hemiplegia and the findings were non-specific. Aspirin was changed to clopidogrel at that time.</td>
</tr>
<tr>
<td>4</td>
<td>17</td>
<td>F</td>
<td>49.1</td>
<td>19</td>
<td>17</td>
<td>79</td>
<td>Small intra-device leak.</td>
<td>New headaches were mentioned during a follow-up visit</td>
</tr>
<tr>
<td>Case</td>
<td>Age</td>
<td>Gender</td>
<td>Device</td>
<td>Diagnosis</td>
<td>Symptoms</td>
<td>Treatment</td>
<td></td>
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<tr>
<td>5</td>
<td>5</td>
<td>F</td>
<td>16.5</td>
<td>Fenestrated</td>
<td>15 95</td>
<td>Small residual shunt</td>
<td>Child developed dizziness and fatigue shortly after device closure which was ultimately investigated with an MRI that was normal. The child later began describing headaches, gradually improving but still documented several years after the procedure.</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>F</td>
<td>114.2</td>
<td>29</td>
<td>30 130</td>
<td>No residual shunt</td>
<td>One week after the catheterization, the patient presented to an emergency room with severe unilateral headaches and vomiting. Aspirin was changed to clopidogrel.</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>F</td>
<td>20.9</td>
<td>10.1</td>
<td>17 70</td>
<td>Small intra-device leak</td>
<td>The child had two events of headache with vomiting immediately after the procedure, and subsequently had monthly occurrences. There is a documented family history of migraine.</td>
<td></td>
</tr>
</tbody>
</table>