Reversible Atrioventricular Block Associated With Closure of Atrial Septal Defects Using the Amplatzer Device

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OBJECTIVES We sought to determine the incidence, nature, and predisposing factors of atrioventricular block (AVB) associated with closure of atrial septal defects (ASDs) using the Amplatzer septal occluder (ASO).

BACKGROUND In our institution, 162 patients underwent ASD closure using ASO between December 1997 and December 2001. This includes small children with large defects.

METHODS Electrocardiographic tracings during ASO implantation and at follow-up visits were reviewed. Anatomic characteristics and device size were assessed as potential risk factors for AVB.

RESULTS Ten patients (6.2%) presented with new-onset (n = 9) or aggravation of preexisting (n = 1) AVB. Atrioventricular block occurred during the procedure (n = 3) or was first noted one day to one week later (n = 7). Patients had first-degree (n = 4), second-degree Wenckebach (n = 4), or third-degree (n = 2) AVB, with no symptoms or hemodynamic compromise. First-degree AVB persisted in two patients at 12 and 33 months of follow-up, whereas most recovered normal AV conduction within one (n = 7) or six months (n = 1). A larger shunt (Qp/Qs ratio 2.8 ± 0.9 vs. 2.1 ± 0.8, p < 0.01) and device size (24 ± 5 vs. 19 ± 6 mm, p < 0.01) were the only determinant factors for AVB. A device size ≥19 mm was used in 90% (9 of 10) of patients who developed AVB, as compared with 49% of those without AVB (p < 0.02).

CONCLUSIONS Closure of ASDs using the large ASO can be associated with the development of AV block and mandate a closer follow-up. In our series, however, all AVBs resolved or improved spontaneously, with no recurrence at mid-term follow-up. (J Am Coll Cardiol 2004;43:1677–82) © 2004 by the American College of Cardiology Foundation

Percutaneous closure of ostium secundum atrial septal defects (ASDs) has been widely accepted and is becoming one of the standard treatments of this malformation (1–6). Among these devices, the Amplatzer septal occluder (ASO; AGA Medical Corp., Golden Valley, Minnesota) seems to provide the highest level of effectiveness and safety (1,7–10). However, some complications have been reported with the use of the ASO, such as arrhythmia, embolization, thrombus formation, pericardial effusion, and transient ischemic attack (4–6,10). Because of the close proximity between the discs of the device and the atrioventricular (AV) node (11), atrioventricular block (AVB) is a likely complication. However, limited data are available concerning AVB associated with ASD closure using the ASO (4–6,10,12). Therefore, the aim of this study was to determine the incidence, evolution, and predisposing factors of AVB associated with ASD closure using the ASO in a single-institution experience.

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Manuscript received July 30, 2003; revised manuscript received October 1, 2003, accepted December 9, 2003.

METHODS

From December 1, 1997, to December 31, 2001, 162 patients with ASDs underwent ASD closure using the ASO at Sainte-Justine Hospital, Montreal. Before August 2000, some patients were referred for surgical closure without any attempt to close the defect via catheterization (n = 16) or after a failed attempt (n = 2). Since August 2000, all patients with an isolated secundum ASD underwent successful ASD closure using the ASO, regardless of the defect anatomy (size, number of defects, or rim characteristics) or the patient's size and age. Among these patients, multiple ASDs were closed using a single device in 40 patients and using two devices in one patient with distant defects.

All patients had an electrocardiogram (ECG) before and during closure and at one day, one week, one month, three months, and yearly after the procedure, according to our protocol. Patients with second- or third-degree AVB were further evaluated on a daily or weekly basis until 1:1 conduction was restored. All ECG tracings, including rhythm strips during the procedure, 12-lead ECGs during visits, and 24-h ambulatory ECGs before closure and at follow-up visits were reviewed.

In this study, patients with new-onset AVB or aggrav-
tion of a pre-existing AV conduction disturbance were identified and defined as patients with AVB. A PR interval exceeding the upper normal limits for a given age and heart rate was defined as first-degree AVB (13).

To determine the predisposing factors of AVB, we compared the following variables between patients with and without AVB: demographic data, ECG findings before ASD closure (heart rate and PR interval), size of primary ASD, number of multiple ASDs, procedure time, device size, device size indexed to body height (device/height), and pulmonary to systemic flow ratio (Qp/Qs).

In addition, to evaluate the relationship between device disc and AV node, we measured the distance between the right atrial disc and the tricuspid annulus in a standard echographic apical four-chamber view immediately after tricuspid valve closure. Results were compared between the six patients who received a device ≥19 mm and developed AVB and a randomly selected group of 23 patients who received a device ≥19 mm but did not develop AVB.

Protocol of ASD closure. The full description of the ASO and the protocol of device closure were reported previously (2,3). In short, all procedures were done under general anesthesia with continuous transesophageal echocardiographic monitoring. A complete hemodynamic study and the protocol of device closure were reported previously (2,3). Written, informed consent was obtained from all patients and/or their guardians.

Statistical analysis. Data are expressed as the mean value ± SD or median value (range) for continuous and categorical data, respectively. The unpaired t test was used to compare continuous data (demographic, ECG parameters before procedure, ASD size, number of ASDs, device size, device/height, ratio, fluoroscopic time, and procedure time), and the Mann-Whitney U test was used in case of non-normal distribution. Data distribution was evaluated using the Kolmogorov-Smirnov normality test. The Fisher exact test was used for comparison of categorical data (frequencies of multiple ASDs, device size ≥19 mm, and indexed size ≥0.18 mm/cm). A value of p < 0.05 was considered significant. All calculations were performed using the statistical package Stat View version 5.0 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Among the 162 patients, 10 (6.1%) developed new-onset AVB (n = 9) or aggravation of pre-existing first-degree AVB (n = 1). Among those, 6 (3.6%) developed second- or third-degree AVB (Table 1).

In three patients (Patients 1 to 3), second- or third-degree AVB was noted during the procedure. Normal AV conduction resumed spontaneously before the catheters were withdrawn in two cases and one month after the procedure in the third case, after resuming 1:1 conduction with first-degree AVB during the procedure (Figs. 1 and 2). In the remaining seven patients (Patients 4 to 10), AVB was first noted between one day and one week after the procedure. The AVB was characterized as first-, second-, or third-degree in four, two, and one patient, respectively. In these patients, normal AV conduction was restored within one month (n = 4) and six months (n = 1). Two patients persisted in first-degree AVB at 12- and 33-month follow-up visits. In both cases, however, the PR interval had improved compared with its immediate postprocedural value (Table 2).

The minimum heart rate in the six patients with second-

### Table 1. Biometric and Atrial Septal Defect Characteristics of Patients With Atrioventricular Conduction Disturbance

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yrs)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>Number of ASDs</th>
<th>Primary ASD Size by TEE (mm)</th>
<th>ASD Balloon Size (mm)</th>
<th>Device Size (mm)</th>
<th>Device/Height Ratio</th>
<th>Qp/Qs Ratio</th>
<th>Associated Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.1</td>
<td>28.5</td>
<td>138.0</td>
<td>4</td>
<td>4</td>
<td>11.0</td>
<td>18</td>
<td>0.13</td>
<td>0.9</td>
<td>Ebstein’s anomaly</td>
</tr>
<tr>
<td>2</td>
<td>3.1</td>
<td>15.2</td>
<td>96.7</td>
<td>1</td>
<td>17.8</td>
<td>27.0</td>
<td>26</td>
<td>0.27</td>
<td>3.2</td>
<td>S/p neuroblastoma</td>
</tr>
<tr>
<td>3</td>
<td>4.3</td>
<td>14.8</td>
<td>109.8</td>
<td>1</td>
<td>14.0</td>
<td>21.0</td>
<td>20</td>
<td>0.18</td>
<td>2.7</td>
<td>Trisomy 21</td>
</tr>
<tr>
<td>4</td>
<td>6.9</td>
<td>26.3</td>
<td>106.5</td>
<td>Fenestrated</td>
<td>10.8</td>
<td>20.8</td>
<td>20</td>
<td>0.19</td>
<td>2.7</td>
<td>Pulmonary stenosis</td>
</tr>
<tr>
<td>5</td>
<td>15.0</td>
<td>62.5</td>
<td>163.0</td>
<td>1</td>
<td>16.0</td>
<td>28.6</td>
<td>34</td>
<td>0.21</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>6.8</td>
<td>19.1</td>
<td>122.0</td>
<td>1</td>
<td>16.0</td>
<td>23.5</td>
<td>24</td>
<td>0.20</td>
<td>3.2</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>2.6</td>
<td>12.4</td>
<td>92.5</td>
<td>1</td>
<td>16.5</td>
<td>23.0</td>
<td>22</td>
<td>0.24</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>7.3</td>
<td>15.9</td>
<td>120.3</td>
<td>1</td>
<td>20.5</td>
<td>29.3</td>
<td>30</td>
<td>0.25</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>4.9</td>
<td>16.2</td>
<td>106.0</td>
<td>3</td>
<td>5.2</td>
<td>15.0</td>
<td>19</td>
<td>0.18</td>
<td>2.8</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>5.3</td>
<td>17.4</td>
<td>109.1</td>
<td>1</td>
<td>24.0</td>
<td>24.9</td>
<td>28</td>
<td>0.26</td>
<td>2.8</td>
<td></td>
</tr>
</tbody>
</table>

ASD = atrial septal defect; Qp/Qs = pulmonary to systemic flow ratio; TEE = transesophageal echocardiography; S/p = status post.
or third-degree AVB ranged from 39 to 80 beats/min (with an effective junctional escape rhythm for the two patients in third-degree AVB) on 24-h ambulatory ECG monitoring obtained one to seven days after the procedure. No patient presented with symptoms or hemodynamic compromise that required removal of the device or pacemaker implantation.

Seven other patients presented with first-degree AVB before ASD closure. Atrioventricular conduction remained unchanged after the procedure and therefore was not included in the AVB group, as defined earlier. No patient was documented to have sinus node dysfunction or second- or third-degree AVB before the procedure. Five of the seven patients remained in first-degree AVB and two were in normal AV conduction at final follow-up of 10 to 51 months. Interestingly, four of these five patients who remained in first-degree AVB had an underlying disease, including Steinert myopathy or Holt-Oram syndrome.

There was no significant difference in age, weight, height, ECG findings before the procedure, size of primary ASD, frequency of multiple ASDs, fluoroscopic time, and procedure time between patients with and without AVB (Table 3). However, the device size (25 ± 5 vs. 19 ± 6 mm), device/height ratio (0.21 ± 0.05 vs. 0.17 ± 0.05 mm/cm), and Qp/Qs (2.8 ± 1.0 vs. 2.1 ± 0.8) were significantly higher in patients with AVB than in those without AVB (Table 3). Among the 10 patients who developed AVB, 9 (90%), including all 7 who did so after the procedure, received a device ≥19 mm. In comparison, 49% of those without AVB received a device ≥19 mm (p < 0.02). Similarly, 9 of 10 patients with AVB and all seven patients who did so after the procedure had a device/height ratio ≥0.18 mm/cm, compared with 44% of patients without AVB (p < 0.01).

Transthoracic echocardiographic follow-up showed complete ASD closure or a trivial residual shunt in 87% of patients immediately after and in 93% at one and three months after ASO implantation. In this respect, there was no difference between patients with or without AVB. In patients in whom a device ≥19 mm was implanted, there was no significant difference in distance between the right atrial disc and the tricuspid valve among patients with versus those without AVB (6.6 ± 2.0 vs. 6.3 ± 2.5 mm, p = NS)

**DISCUSSION**

Our retrospective study of a large consecutive series in a single institution indicates that ASD closure using the ASO can be associated with AVB, which can occur during the procedure or immediately after and mandates close ECG follow-up. Because hemodynamic compromise was not observed in any of our patients, and spontaneous resolution...
Table 2.
Electrocardiographic Findings of Patients Who Developed Atrioventricular Conduction Disturbance

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yrs)</th>
<th>Main ASD size (mm)</th>
<th>Qp/Qs ratio*</th>
<th>Device size (mm)</th>
<th>Device/height ratio (mm/cm)</th>
<th>PR interval (ms)</th>
<th>Heart rate (beats/min)</th>
<th>Procedure time (min)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.6 ± 3.7</td>
<td>14.6 ± 5.6</td>
<td>2.8 ± 0.9†</td>
<td>24 ± 5†</td>
<td>0.21 ± 0.04†</td>
<td>90</td>
<td>87</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>6.3 ± 7.2</td>
<td>14.8 ± 4.1</td>
<td>2.2 ± 0.8</td>
<td>21 ± 3</td>
<td>0.17 ± 0.05</td>
<td>91</td>
<td>109</td>
<td>60</td>
</tr>
</tbody>
</table>

*Minimum heart rate on 24-h ambulatory electrocardiographic monitoring; †Sinus rhythm but first-degree atrioventricular block.

or improvement was observed in all, we advocate close observation rather than systematic removal of the device.

Atrioventricular block has been reported after ASD closure with most of the devices currently or recently in use (Table 4), such as the Cardio-Seal, ASDOS, Angel-Wings, and ASO (4,5,10,12,14–16). Although none of those studies was looking specifically at the association of AVB with device closure, this occurrence seems to be particularly frequent with the ASO, a finding confirmed in our study. This comparison is difficult to interpret, however, as it is widely accepted that the ASO allows the closure of larger defects than the other devices do. Thus, it might be inappropriate to conclude whether the characteristics of the ASO (material, shape, size of disks for a speciﬁc ASD diameter) alone are responsible for the increased occurrence of AVB with the ASO.

Hill et al. (12) systematically obtained 24-hour ambulatory ECG monitoring in 41 patients before and after ASD closure with the ASO and found second- or third-degree AVB in two patients (4.9%). Given the retrospective nature of our study, 24-h Holter recordings were not obtained according to standard protocol. This may represent a limitation of our study. Nevertheless, the frequency of AVB in our study (6.1%, of which 3.7% was second- or third-degree AVB) is comparable, despite the larger size devices used in our group of patients. Demkow et al. (5) found one patient (2%) with transient AVB of 50 adult patients who had large ASDs closed using the ASO. The lower frequency of AVB in their series might be explained by the larger size of patients, which logically would decrease the device/height ratio, an identified risk factor in our study. Chan et al. (4) reported one patient with transient AVB in a 100-patient series, but the mean size of the device in that study (14.6 mm by our calculation) was much smaller than that in this study (19.3 mm).

Indeed, the size of the device can be a predisposing factor of AVB after ASD closure. In our study, patients with AVB
received significantly larger devices than did patients without AVB, with the device/height ratio being significantly higher. Nine (11%) of 83 patients who received devices ≥19 mm and 9 (12%) of 75 patients with a device/height ratio ≥0.18 developed AVB during or after implantation, compared with one (1.2%) of 79 and one (1.1%) of 87 patients, respectively (p < 0.05 each). Thus, patients meeting those criteria need closer hemodynamic and ECG monitoring of their AV conduction immediately after the procedure. Twelve-lead ECG periodically and 24-h Holter recordings are necessary later on, whereas exercise testing may be required for selected patients. Chessa et al. (10) reported that a patient who showed third-degree AVB with implantation of an 18-mm device had restored normal sinus rhythm after the device was replaced with a 14-mm device. This again strongly suggests that device size may be an independent risk for AV conduction after ASO implantation. This emphasizes the importance of the precise sizing of the ASD to avoid placement of oversized devices.

On the other hand, Du et al. (6) and Hill et al. (12) reported on the same one patient with preexisting sinus node dysfunction who developed complete AVB after ASD closure using a 24-mm ASO and subsequently required pacemaker implantation (Table 4). To our knowledge, this is the only reported case requiring pacemaker implantation after ASO implantation so far. Pacemaker implantation raises the question of device retrieval to alleviate AVB. One may suggest retrieval in case of second- or third-degree block, which occurs during the procedure without spontaneous conversion to 1:1 conduction within 30 min. Implantation of a smaller device may then be attempted. This has not proven necessary in any of our three patients with per-procedural AVB, who all improved rather rapidly. Patients with new-onset AVB that first appears after the procedure has been completed may be observed in the hospital until hemodynamic instability is ruled out or regression of AVB is observed. Subsequent ambulatory follow-up with Holter monitoring may be appropriate in case of proven hemodynamic stability. In our experience, all patients with second- or third-degree AVB presented with an adequate escape rate, suggesting an intact lower AV node function. On the other hand, conversion to 1:1 AV conduction has taken up to two weeks in one of our patients.

The mechanism of AVB secondary to ASO implantation might be partly attributable to continuous pressure or friction of atrial discs on the AV node, inducing transient edema leading to AVB, as suggested by Hill et al. (12). However, in our patients in whom devices ≥19 mm were implanted, there was no significant difference in distance between the right atrial disc and the tricuspid valve among patients with versus those without AVB. Assessment of the real spatial relationship between atrial discs and the AV node using other diagnostic modalities, such as three-dimensional magnetic resonance imaging, may give us more insight on this issue.

Preexisting sinus node dysfunction or AV conduction disturbance should not be ignored, especially in the case of large ASDs requiring large devices. It is well known that ASDs may be associated with subclinical ECG abnormalities, including sinus node dysfunction, conduction delay, and AV block (17–19). In such cases, thorough ECG screening, including 24-h ambulatory ECG monitoring, before closure of larger ASDs, may be valuable. Use of corticosteroids to enhance AV conduction recovery is not supported by experimental data or controlled studies. However, we used them in our patient with postprocedural third-degree AVB. Rapid improvement to second-degree AVB and subsequent full recovery was observed within two weeks. Whether or not this was a spontaneous or corticosteroid-enhanced recovery remains uncertain. Likewise, the indication for and timing of device retrieval are not available in the literature. If selected because of unstable AVB, device retrieval may not necessarily avoid pacemaker implantation.

Conclusions. Closure of ASDs using the large ASO can be associated with transient AVB, which occurs during the first week of ASD closure and mandates close follow-up. Device size ≥19 mm or indexed size ≥0.18 mm/cm seems to be the major predisposing factor. The absence of hemodynamic compromise and spontaneous resolution in all our patients may justify close observation rather than systematic removal of the device. Although the outcome of AV conduction has

Table 4. Reported Atrioventricular Conduction Disturbance Associated With Device Closure of Atrial Septal Defects

<table>
<thead>
<tr>
<th>Device</th>
<th>Number of Patients</th>
<th>Mean Age (yrs)</th>
<th>Stretched ASD Size</th>
<th>Atrioventricular Block</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardio-Seal (13)</td>
<td>50</td>
<td>15.9</td>
<td></td>
<td>Transient first-degree AVB × 1</td>
<td>None</td>
</tr>
<tr>
<td>ASDOS (14)</td>
<td>41</td>
<td>7.8 ± 1.9</td>
<td>14.7 ± 2.6</td>
<td>Transient AVB × 4 (third-degree AVB × 1)</td>
<td>None</td>
</tr>
<tr>
<td>Angel Wings (15)</td>
<td>75</td>
<td>28.3</td>
<td>11.9</td>
<td>Transient third-degree AVB × 3 (4%)</td>
<td>None</td>
</tr>
<tr>
<td>Amplatzer (4)</td>
<td>93</td>
<td>13.3 ± 1.9</td>
<td>14.6 (device)</td>
<td>Transient AVB × 1</td>
<td>None</td>
</tr>
<tr>
<td>Amplatzer (12)*</td>
<td>41</td>
<td>9.2†</td>
<td></td>
<td>Transient second-degree AVB × 1, third-degree AVB × 1</td>
<td>Pacemaker*</td>
</tr>
<tr>
<td>Amplatzer (5)</td>
<td>50</td>
<td>40 ± 15.5</td>
<td>18.5</td>
<td>Transient second-degree AVB × 1</td>
<td>None</td>
</tr>
<tr>
<td>Amplatzer (6)*</td>
<td>423</td>
<td>18.1 ± 19.3</td>
<td>17.8 ± 6.2</td>
<td>Third-degree AVB × 1</td>
<td>Pacemaker*</td>
</tr>
<tr>
<td>Amplatzer‡</td>
<td>162</td>
<td>8.2 ± 7.0</td>
<td>18.4 ± 5.9</td>
<td>Transient second-degree AVB × 4, third-degree AVB × 2</td>
<td>None</td>
</tr>
</tbody>
</table>

*Reported the same patient. †Median value. ‡Our study. Data on mean age and ASD size are presented as the mean value ± SD.

Abbreviations as in Tables 1 and 2.
been favorable in our series, this issue needs to be discussed while obtaining consent from patients with large defects.

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