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Magnetophysiologic and echocardiographic comparison of blocked atrial bigeminy and 2:1 atrioventricular block in the fetus

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Abstract

BACKGROUND—Blocked atrial bigeminy (BAB) and second-degree atrioventricular block with 2:1 conduction block (2:1 AVB) both present as ventricular bradycardia and can be difficult to distinguish by echocardiography. Since the prognosis and clinical management of these rhythms are different, an accurate diagnosis is essential.

OBJECTIVE—To identify magnetic and mechanical heart rate and rhythm parameters that could reliably distinguish BAB from 2:1 AVB.

METHODS—A retrospective fetal magnetocardiography (fMCG) and pulsed Doppler ultrasound study of 10 subjects with BAB and 7 subjects with 2:1 AVB was performed in order to identify parameters that could reliably distinguish BAB from 2:1 AVB.

RESULTS—Distinguishing BAB from 2:1 AVB by using fMCG was relatively straightforward because in BAB the ectopic P wave (P') occurred early, resulting in a bigeminal (short-long) atrial rhythm. The normalized coupling interval of the ectopic beat (PP' of the blocked beat to PP of the conducted beat) was 0.29 ± 0.03 . In contrast, the echocardiographic assessment of inflow-outflow gave a normalized mechanical coupling interval (AA'/AA) near 0.5, which made it difficult to distinguish BAB from 2:1 AVB. Heart rate distinguished most subjects with BAB from those with 2:1 AVB (82 ± 5.7 beats/min vs 69 ± 4.2 beats/min), but was not a completely reliable indicator. In most subjects, BAB alternated with sinus rhythm or other rhythms, resulting in complex heart rate and rhythm patterns.

CONCLUSIONS—Fetal BAB and 2:1 AV block can be difficult to distinguish using echocardiography because in many fetuses with BAB the mechanical rhythm does not accurately reflect the magnetic rhythm. fMCG provides a more reliable means of making a differential diagnosis.

Keywords

Fetal magnetocardiography; Bigeminy; Atrioventricular block; Blocked atrial bigeminy; Fetal cardiac arrhythmia

Introduction

Blocked atrial bigeminy (BAB) and second-degree atrioventricular block with 2:1 conduction block (2:1 AVB) are among the most common forms of bradycardia in the fetus. BAB results from premature atrial contractions (PACs) that are blocked at the atrioventricular (AV) node and reset the sinoatrial node. Although the PACs can come from an automatic focus, it is believed that the vast majority of cases of fetal BAB are due to an accessory connection that gives rise to reentrant PACs. 2:1 AVB results from the block of every other sinus beats and shows a regular atrial rhythm. The prognosis and the clinical management of BAB and 2:1 AVB differ markedly. BAB spontaneously resolves in the vast majority of fetuses without treatment and warrants only diligent rhythm surveillance. On the other hand, 2:1 AVB signifies either ongoing immune-mediated damage from maternal anti-Ro antibodies, a cardiac channelopathy, congenital heart disease, or long QT syndrome. Rarely, it is idiopathic or acquired due to drugs or disease. In utero treatment with fluorinated steroids may halt the progression of immune-mediated second-degree AVB to complete AVB,¹ and lidocaine/magnesium can restore sinus rhythm in fetal long QT syndrome.²

Although the mechanisms of these 2 rhythms are different, distinguishing between them by using fetal echocardiography is not always straightforward. Sonesson³ reported that there was a high degree of resemblance during midgestation, which is the peak time when differentiation of the 2 rhythms would be most critical to the clinician, given the disparate therapies and clinical follow-up.

Recently, fetal magnetocardiography (fMCG), a noninvasive electrophysiological technique, has been shown to be highly effective for detecting fetal arrhythmias.⁴⁻⁷ Like fetal electrocardiography, fMCG directly records rhythm but it also exhibits a much higher signal-to-noise ratio, allowing fetuses as early as 20 weeks' gestation to be evaluated with a high success rate. While a number of studies of fetal AVB have been published recently^{8,9} there is a paucity of studies of fetal BAB. In this study, we used fMCG to evaluate the characteristics of BAB and 2:1 AVB for the purpose of improving the accuracy of differential diagnosis.¹⁰

Methods

fMCG

We searched our fMCG database for subjects referred with fetal bradycardia by echocardiogram or auscultation. We found 10 fetuses with BAB and 7 with 2:1 AVB, which were studied between 2002 and 2012. Three of the fetuses with BAB were thought to have 2:1 AVB at the time of referral. The gestational ages ranged from 21 to 29.3 weeks for the subjects with BAB (Table 1) and from 25 to 37.2 weeks for the subjects with 2:1 AVB (Table 2). Of the 7 cases of 2:1 AVB, 6 were associated with maternal SSA/SSB antibodies and 1 was associated with structural disease. The institutional review board approved the experimental protocol, and informed consent was obtained from each participant.

A 37-channel axial gradiometer (Magnes, 4D Neuroimaging, Inc, San Diego, CA) or a 21-channel (Tristan Technologies, San Diego, CA) vector gradiometer was used to record the

fMCG. Several 10-minute recordings were taken from each subject in a magnetically shielded room.

The fMCG was recorded in a 0.1–200 Hz passband and was sampled at 520 Hz. A digital filter was applied to further band limit the signals to 1.0–80 Hz. Spatial filtering was used to remove maternal interference from the fMCG recordings.¹¹ The fetal heart rate (FHR) was computed from the RR intervals, and the fMCG averaged waveforms were computed by averaging 20–50 consecutive beats.

The interval between the conducted and the blocked P waves (PP') was measured in each subject. In BAB, P' is due to a PAC. In 2:1 AVB, P' is due to a blocked sinus beat (Figure 1). The baseline FHR was measured during quiescence when the FHR tracing was relatively flat. The QT intervals were measured from the onset of the QRS complex to the end of the T wave. The corrected QT intervals Bazett's formula (QT_c) are reported in Table 1. The presence of conducted PACs and rhythms other than BAB and sinus rhythm were also noted.

Echo/Doppler

After 2007, echo/Doppler recordings were made during the fMCG session and were available from 6 of the 10 subjects with BAB and from 2 of the 7 subjects with 2:1 AVB. A SonoSite M-Turbo (Bothwell, WA) ultrasound scanner equipped with a 60-mm broadband (2–5 MHz) phased array transducer was used to perform the in-lab echo/Doppler recordings. This device is powered by a battery and produces relatively low magnetic interference, which allows us to perform ultrasound and fMCG recording simultaneously. We recorded atrial contractions by positioning the gate between the mitral valve and the aortic valve for the inflow-outflow measurement. The interval between the onset of atrial systole for the sinus beat and the ectopic beat (AA') was measured, and the AA'/AA ratio was computed. The referral echo/Doppler studies were available in 3 of the 10 subjects with BAB and in 7 of the 7 subjects with 2:1 AVB, and they were assessed in the same fashion as the in-lab echo/Doppler studies.

Statistical analysis

All statistical analyses were performed by using GraphPad Prism Version 5 for Macintosh (GraphPad Software, Inc, San Diego, CA). For each parameter the mean and standard deviation from the mean were computed. Linear regression was used to assess the relationship between each parameter and the percent time in BAB; $P < .05$ was considered significant.

Results

Characterization of BAB and second-degree AVB using fMCG

The electrophysiological characteristics of the subjects with BAB and those with 2:1 AVB are shown in Tables 1 and 2, respectively. The main result is that PP' intervals were much shorter for the subjects with BAB (209 ± 23 ms) than for the subjects with 2:1 AVB (419 ± 50.5 ms). Similarly, the PP'/PP ratios were much smaller for the BAB subjects (0.29 ± 0.03) than for the 2:1 AVB subjects (0.49 ± 0.01). Using linear regression, the percent time in BAB showed a significant negative correlation with the PP' interval ($n = 10$; $P = .027$, $R^2 = -.48$; Figure 2).

The baseline FHR in subjects with BAB was 82 ± 5.7 beats/min and ranged from 71 to 91 beats/min. The baseline FHR in subjects with 2:1 AVB was 69 ± 4.2 beats/min and ranged from 62 to 74 beats/min. Although the baseline FHR of the 2 groups showed little overlap,

the range of the instantaneous FHR often overlapped due to accelerations and rhythm changes. There was no correlation between the FHR during BAB and the percent time in BAB.

Additional rhythms accompanying BAB and AVB

In subjects with BAB, the FHR and rhythm tracings were often complex owing to the alternation of BAB with other rhythms (Figures 3 and 4), including atrial trigeminy ($n = 3$), conducted PACs ($n = 4$), supraventricular tachycardia (SVT; $n = 1$), Wolff-Parkinson-White syndrome ($n = 1$), and blocked atrial couplets (BACs; $n = 2$), as well as sinus rhythm. Atrial trigeminy caused the instantaneous FHR to oscillate between a normal and a low FHR; conducted PACs caused the instantaneous FHR to oscillate between a normal and a high FHR. BACs resulted in a lower FHR compared to that of BAB. Subject 3 was in BAB less than 1% of the time; however, the predominant rhythms were blocked atrial trigeminy and BACs with a virtual absence of sinus rhythm. The second beat of the couplet was occasionally conducted.

The 4 subjects with conducted PACs had above average values of PP' . In 3 of these subjects, PP' was significantly longer for the conducted PACs (257, 242, and 300 ms, respectively) than for the blocked PACs (224, 219, and 227 ms). In the fourth subject with a PP' interval of 225 ms for blocked PACs, the conducted PACs were too infrequent to permit signal averaging. These data permit an estimate of the refractory period of the AV node, which should be greater than PP' for blocked beats and shorter than PP' for conducted beats. Taking the mean of the PP' values for the blocked and conducted beats yields an estimate of 244.8 ms.

The subjects with AVB did not show other rhythms, except that 1 AVB subject showed Wenckebach patterns owing to variable AV conduction, accompanied by premature ventricular contractions (Figure 3G). QTc was mildly prolonged in both subjects with BAB (493 ± 35.6 ms) and subjects with AVB (488 ± 39.6 ms). This is compatible with our previous finding that QTc shows a stronger dependence on heart rate in the fetus than in the adult [9], resulting in mild QTc prolongation at low heart rates.

Characterization of BAB using Doppler techniques

Using inflow-outflow, the mean AA' interval in BAB was 384 ± 18.3 ms and in 2:1 AVB was 443 ± 26.8 ms (Tables 1 and 2). This result is similar to those obtained by others, but it is much longer than the PP' interval in subjects with BAB obtained in this study by fMCG. This is exemplified in Figure 5, where inflow-outflow echo/Doppler yields AA' of 400 ms and fMCG yields PP' of 204 ms.

Discussion

This study demonstrates that BAB and 2:1 AVB can be reliably distinguished by using fMCG, whereas this study and others show that making a differential diagnosis using ultrasound can be difficult. The main differences between the electrophysiological characteristics of BAB and 2:1 AVB demonstrated here are as follows: (1) BAB is characterized by a PP'/PP ratio (0.29 ± 0.043) much less than 0.5, whereas 2:1 AVB is characterized by a PP'/PP ratio nearly equal to 0.5, (2) BAB shows a baseline FHR significantly greater than that of 2:1 AVB (83 ± 4.5 beats/min vs 69 ± 4 beats/min); however, FHR cannot always be used to differentiate the rhythms, and (3) BAB can exhibit a diverse FHR and rhythm patterns, most of which are associated with the presence of an accessory connection, whereas 2:1 AVB typically shows only varying degrees of conduction of sinus beats.

The most reliable parameter for distinguishing BAB from 2:1 AVB is the PP'/PP ratio which are thought to be associated. The fMCG data showed that the PP'/PP ratio was much shorter for the BAB subjects (0.29 ± 0.03) than for the 2:1 AVB subjects (0.49 ± 0.01). In contrast, the AA'/AA ratio measured by pulsed Doppler was approximately 0.5 for both groups of subjects. The discrepancy between the PP' intervals measured by fMCG and the AA' intervals measured by pulsed Doppler implies that the mechanical rhythm does not accurately reflect the electric/magnetic rhythm in BAB. This may result because the short PP' in BAB means that the PAC occurs during aortic outflow and thus would be difficult to detect when assessing inflow-outflow; however, using venous Doppler as well as inflow-outflow, Eliasson et al¹² still measured AA' intervals (0.323 ± 0.073 seconds) that were much longer than the PP' intervals (209 ± 23 ms) measured here by fMCG. Their AA' intervals were even longer than the PP' intervals measured here for conducted PACs. This discrepancy between the magnetic and mechanical intervals could be due to intra-atrial conduction delay of the blocked PAC; however, this seems unlikely for several reasons: broadening of the blocked PACs was not observed, the discrepancy is too large to be accounted for by conduction delay alone, and with 1 exception, all subjects with BAB showed no evidence of underlying conduction disease. A more likely explanation is that the electromechanical activation time of the atrium is much longer for an ectopic beat than for a normal beat. This may result because the electromechanical activation time prolongs in response to an abrupt increase in rate and/or prolongs for retrograde conduction.

We found a significant negative correlation between PP' and the percent time in BAB. This result was expected since PACs with shorter coupling intervals are less likely to conduct. However, Eliasson et al¹² found that the AA'/AA ratio was longer for subjects with sustained vs nonsustained BAB, where sustained BAB was defined to be BAB occurring at least 50% of the time. We note that over a wide range of PP' the relationship between PP' and percent time in BAB is likely to be nonlinear with a negative curvature, as suggested by the data in Figure 2.

The PP'/PP ratio in 2:1 AVB is not necessarily 0.5 owing to the phenomenon of ventriculophasic sinus arrhythmia (VSA). VSA causes the PP intervals that embrace systole to be shorter than those that do not, resulting in $PP'/PP < 0.5$, which can further confound discrimination of BAB and 2:1 AVB. The arrhythmia is attributed to an increase in sinus rate due to increased blood flow to the sinoatrial node during systole; however, paradoxical VSA has also been reported prenatally and in adulthood,^{13,14} in which the PP intervals that embrace systole are longer than those that do not. This is attributed to a slowing of sinus rate due to the rise in arterial blood pressure during systole. In our subjects with 2:1 AVB, PP'/PP was close to 0.5, implying that the positive and negative chronotropic influences offset. Also, VSA is most commonly seen in complete heart block,^{15,16} suggesting that it is typically weaker in 2:1 AVB.

The FHR could not be used to reliably distinguish BAB from 2:1 AVB. Although a mean baseline FHR was significantly higher for BAB than for 2:1 AVB, 1 subject with BAB showed a lower FHR than several of the subjects with 2:1 AVB. During accelerations the FHR of subjects with 2:1 AVB often becomes similar to that of subjects with BAB, and during decelerations the FHR of subjects with BAB often becomes similar to that of subjects with 2:1 AVB. In addition, the presence of other rhythms, such as BACs, which resulted in an FHR of approximately 59 beats/min, confounds the inference of rhythm based on the FHR alone. Eliasson et al¹² also concluded that the FHR could not be used to reliably distinguish BAB from 2:1 AVB.

Several of the subjects with BAB showed other rhythms in addition to BAB and sinus rhythm. Most of these rhythms — Wolff-Parkinson-White syndrome, SVT, conducted PACs,

and blocked atrial trigeminy—were likely associated with the presence of an accessory connection. We also observed 2 subjects with BACs, which was unexpected and, to our knowledge, has not been documented previously in the fetus. Using echo/Doppler recordings, this rhythm would manifest as an abrupt drop in heart rate with triple A waves on inferior vena cava Doppler scan. In subjects with blocked and conducted PACs, the measurement of PP' enabled the estimation of the refractory period of the fetal AV node. To our knowledge, this has not been performed previously. SVT was the most serious rhythm we observed. It was present in only 1 subject (10%), but this corroborates that fetuses with PACs are at risk of developing SVT.^{9,12} Martucci et al¹⁷ reported a case study in which the subject was referred with BAB that developed SVT after birth. The subjects with AVB showed fewer other rhythms. One, however, showed complex FHR patterns owing to premature ventricular contractions that resembled the FHR patterns of the subjects with BAB who had conducted PACs. Knowledge of the other rhythms that may accompany BAB and 2:1 AVB can help the clinician make an accurate diagnosis.

Limitations include that this study is retrospective and that the number of subjects is small. Subjects were referred from multiple institutions. In addition, not all echocardiograms were performed by the same person. In some cases, the inflow-outflow patterns were not adequate for assessing AA'. The pulsed Doppler data were unavailable in several subjects, especially those studied more than 5 years ago. The in-lab ultrasound scanner does not expand the M-mode tracing when the image is enlarged; therefore, the M-mode tracings were difficult to interpret and were not used. Eliasson et al¹² also reported that it is occasionally difficult to distinguish between BAB and 2:1 AVB using M-mode in mid-gestation. Lastly, fMCG is not readily accessible to clinicians owing to the cost and complexity of the instrumentation; however, a new technology, based on atomic magnetometers,¹⁸ has the potential to rectify this situation.

In summary, fMCG is a direct, accurate noninvasive method for distinguishing between BAB and 2:1 AVB. The fetal period remains the only period where electrophysiologic recordings of conduction and rhythm are not routinely used in the diagnosis of serious arrhythmias.

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Abbreviations

2:1 AVB	2-to-1 atrioventricular block
AA	interval between A waves of consecutive sinus beats
AA'	interval from the A wave of the sinus beat to the A wave of the premature beat
AV	atrioventricular
AVB	atrioventricular block
BAB	blocked atrial bigeminy
BAC	blocked atrial couplet
FHR	fetal heart rate
fMCG	fetal magnetocardiography
PP	interval between P waves of consecutive sinus beats
PP'	interval from the P wave of the sinus beat to the P wave of the premature beat
PAC	premature atrial contraction
QTc	corrected QT interval
SVT	supraventricular tachycardia

VSA ventriculophasic sinus arrhythmia

Figure 1.

PP' intervals were measured from the onset of the first significant positive or negative deflection. **A:** Subject with blocked atrial bigeminy with a PP' interval of 196 ms. **B:** Subject with 2:1 atrioventricular block with PP' interval of 440 ms. PP' = interval from the P wave of the sinus beat to the P wave of the premature beat.

Figure 2.

A negative linear correlation exists between PP' and percent time in blocked atrial bigeminy. $R = -.48$; $P = .027$. PP' = interval from the P wave of the sinus beat to the P wave of the premature beat.

Figure 3.

Representative fetal heart rate tracings. **A:** Typical subject with blocked atrial bigeminy (BAB). **B:** Subject with BAB. **C:** Subject with BAB with occasional atrial trigeminy and conducted premature atrial contractions (PACs). **D:** Subject showing alternating periods of BAB, sinus rhythm, and oscillating heart rates due to conducted PACs. **E:** Subject showing BAB with occasional conducted beats during region 1, supraventricular tachycardia during region 2, normal sinus rhythm during region 3, and BAB during region 4. **F:** Typical subject with 2:1 atrioventricular block (AVB). **G:** Subject with Wenckebach second-degree AVB accompanied by premature ventricular contractions.

Figure 4.

Fetal magnetocardiography tracings of rhythms other than blocked atrial bigeminy: **A:** Typically aberrantly conducted premature atrial contractions (PACs), indicated by asterisks, in subject 4. **B:** Aberrantly conducted PACs in subject 10 with a relatively long PP' interval (300 ms). This unusually long PP' interval and aberrant QRS complex may imply underlying conduction disease. **C:** Blocked atrial trigeminy in subject 9. **D:** Blocked atrial couplets (double arrows) in subject 2. The couplets reduced the fetal heart rate from 85 to 59 beats/min. **E:** Wolff-Parkinson-White syndrome in subject 10. **F:** Supraventricular tachycardia with aberrancy at initiation and near termination in subject 5. PP' = interval from the P wave of the sinus beat to the P wave of the premature beat.

Figure 5.

A: Inflow-outflow measurement of the AA' interval. **B:** Fetal magnetocardiography measurement of the PP' interval for subject 9. AA' = interval from the A wave of the sinus beat to the A wave of the premature beat; PP' = interval from the P wave of the sinus beat to the P wave of the premature beat.

Table 1

Characterization of Blocked Atrial Bigeminy Subjects Using fMCG

Fetus #	GA (weeks)	FHR (beats/min)	Conducted PACs	PP' during conducted PACs (ms)	PP' (ms)	PP'/PP ratios	QTc during BAB (ms)	Other rhythms	Echo/Doppler		
									AA' (ms)	AA' /AA (ratio)	
1	21	81	No	–	214	0.29	460	–	400	0.42	
2	23.4	85	No	–	199	0.29	502	BAC	–	–	
3	24.2	71	Yes	NM	225	0.27	418	BAT,BAC	–	–	
4	24.3	79	Yes	257	224	0.29	495	–	360	0.45	
5	25	86	Yes	242	219	0.29	519	SVT	400	0.51	
6	26	91	No	–	154	0.23	477	–	374	0.47	
7	27	78	No	–	196	0.25	542	–	400	0.44	
8	28.5	87	No	–	232	0.34	528	BAT	–	–	
9	29	85	No	–	204	0.29	502	BAT	400	0.50	
10	29.3	79	Yes	300	227	0.30	491	WPW	360	0.47	
Average	26 ± 3	82 ± 5.7	–	249 ± 30	209 ± 23	0.29 ± 0.03	493 ± 35.6	–	384 ± 18.3	0.47 ± 0.03	

AA = the interval between two consecutive mechanical atrial contractions; AA' = interval from A-wave of sinus beat to A-wave of premature beat; %BAB = percent time in blocked atrial bigeminy; BAC = blocked atrial couplets; BAT = blocked atrial trigeminy; FHR = fetal heart rate; GA = gestational age; NM = not measurable normal conducted PACs; PACs = premature atrial contractions; PP' = interval from P-wave of sinus beat to P-wave of premature beat; QTc = corrected QT interval; SVT = supraventricular tachycardia; WPW = Wolff Parkinson White syndrome. Fetus #7's ultrasound data was obtained three days before the fMCG session, and fetus #9's ultrasound data was obtained thirteen days after the fMCG session. For subject #10, the 300 ms measurement corresponds to PP' for aberrantly conducted PACs. PP' could not be measured for the normally conducted PACs.

Table 2
Characterization of Second-Degree Atrioventricular Block Subjects Using fMCG

fMCG		Echo/Doppler								
Fetus #	GA (weeks)	FHR (beats/min)	PP' (ms)	PP'/PP ratios	QTc(ms)	SSA/SSB	Other Rhythms	Structural Disease	AA' (ms)	AA' /AA(ms)
10	25	71	423	0.50	493	Yes	-	-	435	0.49
11	27	74	405	0.50	447	Yes	-	-	430	0.47
12	30.4	72	411	0.50	472	Yes	-	-	450	0.56
13	30.5	68	439	0.50	452	Yes	-	-	435	0.47
14	32.2	65	323	0.47	559	No	-	L-TGA	500	0.54
15	34	68	445	0.49	467	Yes	PVCs	-	420	0.52
16	37.2	62	434	0.50	522	Yes	-	-	430	0.43
Average	31 ± 4	69 ± 4.2	419 ± 50.5	0.49 ± 0.01	488 ± 39.6	-	-	-	443 ± 26.8	0.50 ± 0.05

AA = the interval between two consecutive mechanical atrial contractions; AA' = interval from A-wave of sinus beat to A-wave of premature beat; FHR = fetal heart rate; GA = gestational age; L-TGA = L-Transposition of the Great Artery; PP' = interval from P-wave of sinus beat to P-wave of premature beat containing; PVCs = premature ventricular contractions; QTc = corrected QT interval. Fetus #15 had Wenckebach second-degree AVB.