Atrioventricular conduction time in foetuses assessed by Doppler echocardiography

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Summary

We performed measurement of mechanical atrioventricular conduction time intervals in human foetuses assessed by Doppler echocardiography and provided reference values. We found that atrioventricular conduction time interval had prolonged with gestational age and decreased with increasing foetal heart rate. No correlation between gestational age and heart rate was found. Using normal limits established by this study, mechanical atrioventricular interval >135 ms in the 20^{th} week and/or >145 ms in the 26^{th} week of gestation could be suspected of having $1^{st\circ}$ AV block. We compared reference values with foetuses of mothers with anti-SSA Ro/SSB La autoantibodies, being in risk of isolated congenital heart block development. 1 of 21 foetuses of mothers with positive autoantibodies was affected by prolonged atrioventricular interval according to the established limits, with sinus rhythm after the birth.

Key words: atrioventricular block, prenatal ultrasonography, foetus, Doppler echocardiography

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Introduction

Isolated congenital heart block is a rare but devastating condition with an incidence of 1 in 15000-20000 liveborns (Buyon *et al.* 1995). But it occurs in 2-5% of pregnancies with anti-SSA/Ro and anti-SSB/La positive autoantibodies (Buyon *et al.*1998*).* Complete atrioventricular block is considered to be irreversible, however, maternally administered corticosteroids may limit the progression of the 1st or the 2nd atrioventricular (AV) block as described by anecdotal cases (Copel *et al.* 1995, Saleeb *et al.* 1999, Shinohara *et al.* 1999). AV block may occur as the first sign of the conduction disorder (Askanase *et al.* 2002). However, a gradual development of atrioventricular block has mostly been described (Sonesson *et al.* 2004). Initially, normal heart rate with a prolonged AV conduction time interval may progress to a complete form of AV block. Dexamethasone given during pregnancy may achieve normalization of prolonged atrioventricular conduction time interval and averts the progression to complete heart block, which is irreversible (Friedman *et al.* 2008, Sonesson *et al.* 2004). The prophylactic treatment of all Sjögren´s positive pregnancies is not reasonable due to foetal side effects of corticotherapy (Costedoat-Chalumeau *et al.* 2003). The measurement of Doppler derived mechanical AV conduction time interval could identify affected foetuses within the first-degree AV block stage. Those foetuses might benefit from direct transplacental steroid administration to avoid progression to complete and irreversible AV block.

Some authors observed that the AV conduction time prenatally is independent of gestational age and heart rate (Glickstein *et al.* 2000), some others found a correlation between those variables (Andelfinger *et al.* 2001).

The purpose of this study was to establish reference values for mechanical atrioventricular conduction time intervals by Doppler echocardiography in foetus and to evaluate the correlation with gestational age and heart rate. Subsequently, mechanical AV conduction time

intervals measured in normal foetuses were compared with those measured in pregnancies with positive SSA/SSB antibodies.

Methods

Study cohort

Over a period of 3 years (2007-2009) all foetuses of healthy pregnant women with structurally normal hearts referred to our laboratory because of a family history of congenital heart disease or because of previously suspected heart defect not confirmed by evaluation were included in the study (Group A, N=180). Each foetus was examined just once. The gestational age at evaluation varied from the 18th to the 39th week (median 25). The study protocol was evaluated and approved by the institutional ethical committee. Normal limits of mechanical PQ intervals were established. Finally, mechanical PQ intervals from foetuses of SSA/SSB-positive mothers examined in the period between 2003 and 2009 (Group B, N=21) were compared with normal limits as established in Group A.

Echocardiography technique

All pregnancies underwent transabdominal echocardiography revealing a normal heart structure and function by two-dimensional, colour and pulsed Doppler examination. Studies were performed on Vivid 7 (GE Medical Health Systems) using 2.5-8 MHz convex transducers. A physician experienced in prenatal echocardiography did every examination. The mechanical AV conduction time intervals were obtained from a four-chamber view tilted anteriorly to the outflow tract of the left ventricle. Pulsed Doppler sample volume was adjusted. The sample volume of pulsed Doppler was established in the width enabling to receive simultaneous traces from the mitral valve and left ventricular outflow tract (LVOT). The Doppler pattern of inflow and outflow traces was stored and measured offline. The mechanical AV conduction time interval was assessed as the interval between the onset of the

mitral A-wave and the onset of the LVOT (V-wave). The time interval between A-wave and V-wave is equal to the onset of atrial and ventricular contraction and represents the mechanical AV conduction time interval (Fig. 1).

The same measurements of mechanical PQ interval were performed in the 20th and the 26th week in a group B consisting of SSA/SSB-positive pregnancies.

Statistical analysis

Data were analysed using SPSS 9.0 software. Continuous variables were expressed as mean or median as appropriate given by the data distribution pattern. Unpaired *t*-test or the Mann-Whitney rank sum test was used for comparison of patient groups. To evaluate the relation between the mechanical AV conduction time interval and heart rate and gestational age, linear regression models were used. The 1st and 99th percentile determined normal range.

To increase the diagnostic specificity of first-degree AV block assessed by Doppler derived measurement, 99% confidence interval was used due to described large variability of inflow/outflow Doppler methodology (Friedmann *et al*. 2008).

Results

The heart rate varied from 124 to 152 beats per minute (bpm), mean 140.6 ± 6.6 bpm. The mechanical AV conduction time interval varied from 92 to 150 ms, mean 122.4 ± 11.5 ms. Mechanical AV conduction time interval (Fig. 2) positively correlated with gestational age ($P<0.001$) and negatively with heart rate ($P<0.001$). There was no correlation between heart rate (HR) and gestational age ($P=0.385$). Normal values (Table 1) in the 20th week of gestation ranged from 94 to 135 ms (mean 113 ms) and in the 26th ranged from 102 to 145 ms (mean 123 ms). Mechanical AV conduction time intervals in the 20th week of gestation >135 ms and in the 26th week of gestation >145 ms would be suspicious of the presence of a 1$^{st°}$ atrioventricular block. However, mechanical AV conduction time intervals changed not only with gestational age, but also with a different foetal heart rate (Table 2). Using multiple linear

regression (Fig. 3), we could estimate predicted AV conduction time intervals including both foetal heart rate and week of gestation in the following regression equation: atrioventricular conduction time = 174,976 + (1,315 * WOG) - (0,612 * HR). Using this formula the predicted mechanical atrioventricular conduction time interval for a given gestational age and heart rate may be calculated. An individual value over the 99% confidence interval will identify a patient suffering from 1$^{st°}$atrioventricular block.

AV conduction time intervals of 21 foetuses with positive maternal SSA/SSB antibodies (Group B) were compared to the reference group (Group A). Atrioventricular conduction time intervals did not differ statistically in the 20th or the 26th WOG (P=0.503, respectively 0.614). However, 1 of 21 foetuses was identified as having prolonged AV conduction time (1st AV block) in the 26th WOG (151ms). Foetus was treated with dexamethasone, did not progress to 2nd or the 3$^{rd°}$ atrioventricular block and AV conduction interval was normal after the birth at the case.

Discussion

Our study showed that the mechanical PQ interval is positively correlated with gestational age and negatively correlated with foetal heart rate reflecting the dependence on sympathetic drive. We did not find any correlation between gestational age and heart rate.

Our results are in accordance with some recently published studies by echocardiography (Friedman *et al*. 2008,Wajakowski *et al*. 2009) or by foetal magnetography (Leuthold *et al*. 1999). However, some other papers suggested that PQ interval is independent on gestational age and foetal heart rate (Bolnick *et al*. 2004).

Atrioventricular block occurs mainly in SSA/SSB-positive pregnancies as the result of maternal antibodies transfer (Brucato *et al.* 2001). However, the concurrent risk factors triggering the immune-mediated inflammation of the atrioventricular nodal and myocardial

tissue have not been identified, yet. Complete heart block is not reversible by trans-placental treatment and carries a significant risk of death (Jaeggi *et al.* 2004, Schmidt *et al.* 1991). The majority of children born alive with complete AV block require pacemaker before reaching adulthood (Fesslova *et al.* 2009). The administration of corticosteroids to all autoantibody positive pregnancies is not justified because of a potential risk for the mother and the foetus (Costedoat-Chalumeau *et al.* 2003, Saleeb *et al.* 1999). CAVB is a progressive disease (Sonesson *et al.* 2004) and early detection of this process should be the key in the identification of affected foetuses and subsequent prevention of severe forms of the conduction lesion. It has been documented that treatment with fluorinated corticoids may the second degree AV block (Saleeb *et al.* 1999). Preventive treatment of foetuses having developed $1^{st\circ}$ AV block would even be a better option. Thus the essence of PQ measurement lies in the early detection of foetuses affected with $1^{st\circ}$ AV block.

Our study suggested reference values for foetuses at various gestational ages. Using normal limits established by this study PQ interval >135 ms in the 20^{th} week and/or >145 ms in the 26^{th} week of gestation can be described as $1^{st\circ}$ AV block. One of the 21 foetuses (9.5%) from autoimunne-positive pregnancies was identified to have pathologically prolonged AV conduction. The foetus was treated with dexamethasone and did not progress to higher degree of AV block. Thus identification of foetuses with prolonged AV conduction and subsequent treatment may be reasonable and could be of a great importance if applied electively. A different frequency of the first-degree AV block in foetuses was described (Rosenthal *et al.* 2002, Sonesson *et al.* 2004).

Two Doppler-based methods for foetal assessment of mechanical PQ intervals were described. We used the recording of Doppler signal from the modified 5-chamber view. The other possible method lies on simultaneous acquisition of the superior vena cava and aorta velocities. We considered the second method as more difficult and less practical because of

problems with the quality of Doppler signal from the vena cava superior. The question is whether measurement of mechanical PQ interval would be routinely possible in the gynecologist's practice. However, at least foetuses from known maternal antibody positive pregnancies referred to specialized centres could benefit from this Doppler based measurements and benefit from early detected conduction disease based on the described normal limits.

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Conflicts of interests: none declared

LEGENDS

Fig. 1: Mechanical PQ intervals measured from modified four-chamber view. The simultaneous flow through the mitral valve (E- and A-waves) and the aortic valve (V-wave).

Fig. 2: Left - Linear regression of mechanical PQ interval and gestational age (GA). Right – linear regression of mechanical PQ interval and foetal heart rate (HR). Median and 1/99% confidence intervals are shown.

Fig. 3: Prediction of mechanical PQ intervals by multiple linear regression . Median and 1/99% confidence intervals are shown. An individual value over the 99% confidence interval would identify a patient suffering from 1st° atrioventricular block.

Table 1: Mechanical PQ intervals (in milliseconds) according to gestational age (in weeks) with 1/99% confidence intervals, WOG- week of gestation

Table 2: Mechanical PQ intervals (in milliseconds) according to foetal heart rate (beats per minute) with 1/99% confidence intervals, WOG- week of gestation

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TABLE 1

WOG	1%	99%
16	90	131
17	90	132
18	91	133
19	92	134
20	94	135
21	95	137
22	97	138
23	98	140
24	101	142
25	101	143
26	102	145
27	103	146
28	105	147
29	106	148
30	108	149
31	109	151
32	110	152
33	112	154
34	113	155
35	115	156
36	116	158
37	117	159
38	120	161

TABLE 2

HR	1%.	99%
100	127	183
101	126	182
102	126	181
103	125	180
104	124	180
105	123	179
106	123	178
107	122	177
108	121	176
109	120	175
110	120	174
111	119	174
112	118	173
113	117	172
114	116	171
115	115	171
116	115	170
117	114	169
118	113	168
119	112	168
120	111	167
121	111	166
122	110	165
123	109	165
124	108	164
125	107	163
126	106	162
127	106	162
128	105	161
129	104	160
130	103	159
131	102	159
132	101	158
133	101	157
134	100	156
135	99	155
136	98	154
137	97	153
138	97	152
139	96	152
140	95	151

HR	1%	99%
141	94	151
142	93	150
143	92	149
144	91	148
145	90	148
146	90	147
147	89	146
148	88	146
149	87	145
150	87	144
151	86	144
152	85	143
153	84	142
154	84	141
155	83	141
156	82	140
157	82	139
158	81	138
159	81	137
160	80	136
161	79	135
162	78	134
163	78	133
164	77	132
165	76	132
166	75	131
167	75	131
168	74	130
169	74	129
170	73	129
171	72	128
172	72	127
173	71	126
174	70	126
175	70	125
176	69	124
177	69	123
178	68	122
179	67	121
180	66	120

Fig.1

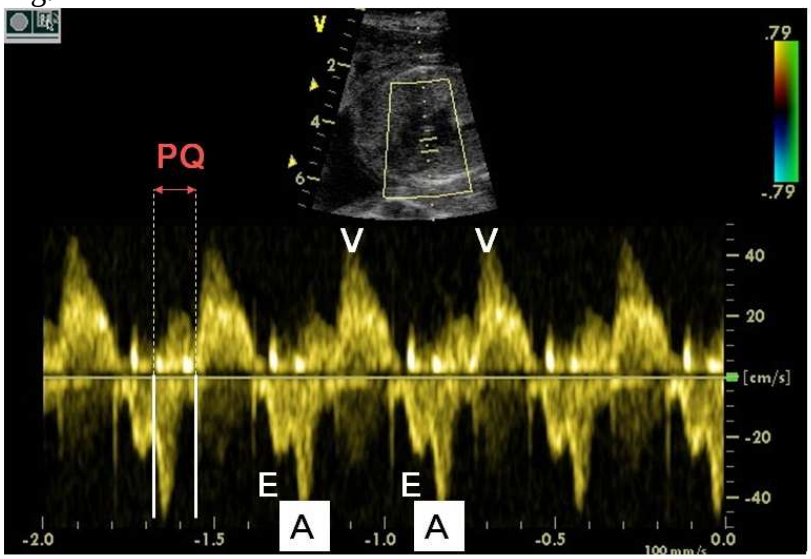

Fig.2

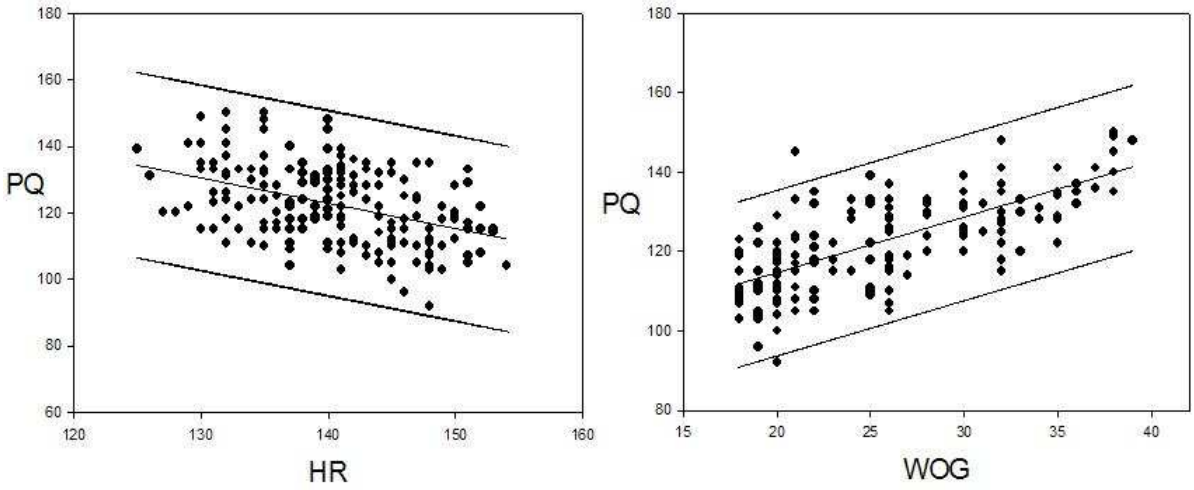

Fig3