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FIRST EXPERIENCE OF HIS BUNDLE PACING IN PEDIATRIC PATIENTS

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Aim. To present our clinic's experience of His bundle pacing in pediatric patients.

Methods. Six patients underwent endocardial pacemaker implantation with a ventricular lead in the Hisian position. A standard diagnostic examination was carried out, including routine general clinical and laboratory examinations, an ECG with an assessment of QRS width, Holter monitoring, echocardiography (Echo) with an assessment of the sizes, volumes of the heart chambers, left ventricle (LV) contractile function and Speckle-tracking Echo with an assessment of LV global longitudinal strain (LV GLS). To assess dynamic control ECG, Holter monitoring, Echo and Speckle-tracking Echo were performed.

Results. Selective His bundle pacing (isolated capture of the His-Purkinje system) was achieved in only one patient; non-selective His bundle pacing was performed in the remaining 5 patients. With His bundle selective and non-selective pacing, a significant normalization of the LV electromechanical dyssynchrony index (GLS) was noted from -17 [-15; -19] to -21.4 [-21;-22] ($p = 0.013$). The most significant normalization of LV longitudinal strain was recorded in a patient with previous epicardial stimulation of the right ventricle (RV).

Conclusion. Physiological His bundle pacing favours ventricular synchronization, providing the most physiological myocardium pacing, both during primary pacemaker implantation and in patients with previous long-term RV pacing, accompanied by ventricular dyssynchrony.

Key words: cardiac pacing; His bundle pacing; ventricular dyssynchrony; complete atrioventricular block; children

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The only treatment for symptomatic bradycardia in children with complete atrioventricular block (AVB) is pacemaker implantation [1]. The choice of the optimal pacemaker system for a child requires a clear understanding of the main characteristics of modern devices and indications for continuous stimulation, advantages and disadvantages of epicardial and endocardial electrodes, intensive phisical development of the child and possible complications [2, 3]. Stimulation electrodes can be placed transvenously or epicardially. Given the high risk of venous occlusion, in children with a body weight of less than 25 kg, it is safest to place the electrodes for cardiac pacing epicardially at the apex of the left ventricle (LV) [4, 5]. In children weighing more than 25 kg, endocardial stimulation is used, in which the common place of electrode localization is the apex of the right ventricle (RV) [4]. However, the onset of propagation of the stimulated electrical impulse from the apical region promotes paradoxical septal motion, causing electrical and mechanical asynchronous ventricular contraction, leading to the development of pacing-induced dyssynchronous cardiomyopathy (PIC) [6-8]. Research indicates that stimulating the His-Purkinje system via endocardial access can prevent the development of both interventricular and intraventricular dyssynchrony. This approach promotes phisiological ventricular depolarization, thereby maintaining synchronous ventricular contraction kinetics [9].

Stimulation of the His bundle can be achieved either through direct activation of the His bundle itself, referred to as selective His bundle pacing, or by stimulating both the His bundle and the surrounding ventricular myocardium, known as non-selective His bundle pacing [10]. Published criteria exist to differentiate between the two types of His bundle stimulation. Selective His bundle pacing is characterized by the capture of the His bundle at low thresholds, without stimulating the ventricular myocardium. This occurs because the His bundle is in direct contact solely with the membranous portion of the interventricular septum (IVS), rather than with the surrounding myocardial tissue. In contrast, non-selective His bundle pacing typically requires higher power, resulting in a higher stimulation threshold. This approach involves ventricular capture because the electrode is positioned closer to the myocardium, thereby stimulating both the His bundle and the adjacent myocardial tissue. Both methods of His bundle stimulation result in a narrower QRS complex compared to conventional ventricular myocardial stimulation [9, 11-13].

Given that a high percentage of ventricular stimulation is usually required in the pediatric population [5], as well as the known complications of chronic RV stimulation [6, 7], phisiologic His bundle stimulation has become of interest in this age group. In this article, we present our experience with His bundle stimulation in children in our clinic.

METHODS

Patient characteristics

Between June 2020 and October 2022, six patients underwent endocardial cardiac pacing with ventricular electrode implantation in the His bundle position. All surgeries were performed by a single surgeon with 20 years of experience in pacemaker implantation in adults and children. The clinical data of the patients are summarized in Table 1. The mean age of the children was 12.5 years [11.25;14.5]; mean weight 49 kg [41.8;64.5]; all patients were girls. Two patients underwent a change from epicardial to endocardial stimulation; in one case the change of system was due to exhaustion of the pacemaker battery, in the other due to dysfunction of the epicardial electrodes. In the remaining four cases, primary endocardial stimulation was performed. In three patients the reason for pacemaker implantation was congenital complete AVB, in one of them in combination with congenital heart disease (CHD) - atrial septal defect. In two patients, complete AVB was a complication of cardiac surgical correction of CHD - Fallot's tetrad in one case and an interventricular septum defect in the other. Another patient, after a history of infection, suffered from frequent presyncopal states accompanied by long pauses of rhythm up to 6.5 sec registered during daily Holter monitoring of electrocardiogram (HM ECG), the cause of which turned out to be transient AVB of 2-3 degree with Wenhkebach's periodicity of 6:1.

Indications for cardiac pacing were determined based on current recommendations, considering the child's weight at the time of pacemaker implantation or reimplantation, prognosis of function, and integrity of primary epicardial electrodes [1].

Table 1.

Clinical and instrumental characteristics of patients

	№ пациента					
	1	2	3	4	5	6
Age*, years	11	12	13	17	15	8
Weight*, kg	71	47	40	69	51	27
Principal diagnosis	conAVB 3, CHD	secAVB 3, CHD	conAVB 3	conAVB 3	secAVB 1-3, CHD	acAVB 1-3
Primary stimulation	RVES DDD, 10 лyears	-	-	RVES DDD, 7 years	-	-
Reason for changing the pacemaker	Electrode fractures	-	-	Electrode ruptures	-	-
Pacemaker device	Adapta ADDR01	Enitra 6 DR	Enitra 6 DR	Estella DR-T P1D50	Adapta ADDR01	Sorin SR 1CV1125
Mode of operation	DDD	DDD	DDD	DDD	AAI-DDD	VVI
Atrial threshold, V	0.25	0.5	0.6	0.6	0.375	-
Ventricular threshold, V	0.5	0.7	1.1	0.5	0.375	1.25
QRS complex width**, ms	100/100	100/80	80/100	100/90	140/140	80/100
LV EDV**, %.	111/114	127/97.6	125/90.1	131/125	145/122	81.3/102
LVEF in B-mode**, %	65/62	65/66	71/66	63/70	71/61	63/63
GLS LV**, %	-18/-21	-15/-23	-19/-22	-15/-21.2	-16/-17	-19/-21.6
IVS thickness, mm	9	8	7	9.2	7.9	6
POP, months	6	12	3	n/a	24	3
LVEF***, %	63	67	67	n/a	61	66
QRS complex width***, ms	100	80	100	n/a	100	80
LV GLS***, %	-21	-23	-22	n/a	-17	-22
STVE***, V	1.0	1.9	1.0	n/a	0.625	2.5

Note: * - at the time of implantation; conAVB, secAVB and acAVB - congenital, secondary and acquired atrioventricular block, respectively; CHD - corrected congenital heart disease; RVES - right ventricular epicardial stimulation; ** - before/after; LV EDV - left ventricular end-diastolic volume; LVEF - LV ejection fraction; LV GLS - left ventricular global longitudinal strain; POP - prospective observation period; STVE - stimulation threshold of ventricular electrode; *** - during POP; n/a - no data.

On admission to the hospital all patients underwent standard diagnostic examination including routine general clinical and laboratory examinations, ECG with QRS width estimation, HM ECG, echocardiography (Echo) with estimation of the size, volumes of heart chambers and LV contractile function and Speckle-tracking echocardiography with estimation of global longitudinal LV deformation (GLS LV). ECG, HM ECG, Echo and Speckle-tracking Echo were performed at dynamic follow-up.

In each clinical case, patients underwent detailed analysis of the electrocardiogram by recording in 12 leads at a recording speed of 50 mm/s according to a generally accepted protocol. HM ECG was performed using the Schiller 300 ECG daily monitoring system according to the generally accepted methodology. Echo in M- and B-mode and Doppler ultrasound were performed to assess intracardiac hemodynamics. Affinity 70 ultrasound systems (Philips, USA) were used. Standard methods and positions were used to measure the main sizes and volumes of heart chambers, indicators of intracardiac hemodynamics. The indices were determined automatically, according to the study protocol. LV end-diastolic diameter and intraventricular septum (IVS) thickness were measured by parasternal long-axis echo in M-mode. Left ventricular ejection fraction (LVEF) was calculated using Simpson's biplane method. LV systolic function was considered low if LVEF was below 55%. In addition to standard measurements of chamber volumes, the deviation of LV end-diastolic volume from individually predicted anthropometric norms, expressed as a percentage, was assessed. This approach is associated with age and anthropometric heterogeneity of patients, and is also necessary for dynamic evaluation of echo parameters due to the increase in heart size with changes in age and anthropometric data. These indices were determined automatically, in the software application «Child Heart» [14].

To assess LV wall deformation, all patients underwent Echo using Speckle-tracking Echo and measurement of LV GLS according to the recommendations of the European Society of Cardiology (ESC), European Association of Cardiovascular Imaging Techniques (EACVI) and American Society of Echocardiography (ASE) [15]. Reduction of global LV deformation in the longitudinal direction detected by Speckle-tracking Echo has a higher sensitivity with respect to LV dysfunction than PV and allows to detect «subclinical» myocardial contractility abnormalities that cannot be detected by standard Echo protocol [16].

Implant procedure

The intervention was performed under mixed anesthesia, which included local infiltrative and intravenous anesthesia on spontaneous respiration (a combination of propofol and fentanyl was used). For successful implantation of the system, it is important to have the heart's own rhythm, which allows mapping and recording of conduction system signals, since it is difficult to detect conduction system signals against the background of ventricular stimulation. Therefore, in patients on ventricular pacing the pacemaker was switched to VVI mode at 30 imp/min until a replacement rhythm appeared. The first step was a Seldinger puncture of the right femoral vein with placement of a 7 French intraducer, through which a Marinr electrophisiologic electrode (Medtronic plc, Dublin, Ireland) was passed to record the conduction system and as an x-ray guide. The second step was to make a 3-4 cm incision in the left subclavian region, the outer third of the incision should cross the deltoid-chest sulcus. Further, v.cephalica sinistra was isolated, a ventricular electrode was passed into the lumen of the vein by venesection, and if the lumen of the vein was sufficient, an atrial electrode was also passed into it. If the lumen diameter was insufficient for the atrial electrode, the v.subclavia sinistra was punctured according to Seldinger and the electrode was inserted into the right heart.

The atrial electrode was positioned in the upper portions of the right atrium using a preformed J-stiletto and fixed. The radiographic anatomic target for the ventricular electrode was the distal tip of the electrophisiology catheter, where the highest amplitude His signal was recorded. Due to the unavailability of specialized delivery systems at the time of implantation, the stylet approach was used for electrode positioning. For this purpose, a stiletto curvature in the direction of the RV and an additional septal bend for perpendicular positioning of the electrode relative to the IVS were formed by hand. In the monopolar configuration, the signal from the implanted electrode was recorded for detection of the His bundle and estimation of the lesion current when the electrode was screwed in. A ventricular electrode loop was formed in the right atrial cavity to compensate for future growth. The electrodes were fixed in the wound, connected to the body of the pacemaker, which was placed in a bed in the subcutaneous tissue. The wound was sutured with absorbable thread and intradermal sutures. Removal of the previously implanted stimulator housing was performed immediately after endocardial implantation. The criteria of successful selective His bundle stimulation on ECG were the presence of an isoline after the applied stimulus and complete correspondence of the morphology of the stimulated QRS complex to the native one. The criterion of successful non-selective His bundle stimulation was a narrow QRS complex repeating all directions of native vectors; activation started immediately after the electrical stimulus and imitated pre-excitation as in Wolf-Parkinson-White syndrome.

Statistical analysis

Statistical processing of the obtained data was performed using STATISTICA 10 program. Qualitative data are presented as absolute and relative values. Quantitative data were analyzed for conformity to the normal distribution law using the Shapiro-Wilk and Kolmogorov-Smirnov criteria. With normal distribution, results were presented as mean and standard error of the mean (M±Sd). Quantitative data not conforming to the normal distribution law are presented as median and interquartile range (Me [Q25;75]). The Wilcoxon test was used to compare quantitative data in two dependent samples in the case of a distribution other than normal. In the case of normal distribution - paired Student's T-criterion. The critical level of significance for testing statistical hypotheses was 0.05 (p - achieved level of significance).

RESULTS

Table 1 presents the clinical characteristics of the examined children. All patients successfully underwent a His bundle stimulation procedure. The mean operative time was 94 min (60 to 135 min). The mean time of radioscopy was 9 min 43 s (range 5 min to 18 min 27 s). Five patients underwent permanent cardiac pacing system in DDDR mode. One patient with transient AVB grade 3 who did not require continuous ventricular stimulation was placed on a single-chamber VVI system with a baseline HR of 50 min as a safety net for significant pauses in rhythm, with a low percentage of ventricular stimulation during the day. Selective stimulation of the His bundle (isolated seizure of the His-Purkinje system) was achieved in only one patient; the remaining 5 patients had nonselective His stimulation. There were no intraoperative complications except for the sixth clinical case: an incomplete blockade of the right bundle branch of the His bundle, which was transient in nature, occurred in an 8-year-old girl at the time of electrode implantation. In the third clinical case, a 13-year-old child presented with atrial electrode dislocation in the early postoperative period. The patient was re-admitted to the operating room to correct the electrode localization.

Initially, in two patients (clinical cases 3 and 6) with structurally normal hearts undergoing primary pacemaker implantation, the QRS complex duration was within normal limits and was 80 ms. In three patients, a slight widening of the QRS complex up to 100 ms was registered, associated with intraventricular conduction disturbance in the form of right bundle branch blockade after cardiac surgical correction of CHD and in one patient with congenital AVB on the background of primary epicardial RV stimulation. After implantation of pacemaker in the His bundle position, in one patient (with surgical correction of IVS defect complicated by progressive AVB), a narrowing of QRS duration from 100 ms to 80 ms was noted (2 clinical cases). In the sixth case, in the early postoperative period the patient had incomplete right bundle branch block with QRS complex extension up to 100 ms; by the time of discharge in 7 days, normalization of ventricular conduction with restoration of the initial QRS complex duration was recorded. In the remaining patients QRS duration on the background of stimulation did not change.

In all patients before implantation or change of pacemaker system LVEF (B-mode) was within the normal range and ranged from 63% to 71%. After the His stimulation LV EF remained in the previous normal values. Initially, LV end-diastolic volume in three patients was higher than normal values - in one patient on the background of prolonged stimulation of RV, and in two patients after surgical correction of CHD. Normalization of LV volume was observed in all three patients against the background of the His bundle stimulation. In addition, all patients underwent an extended Echo study before and after performing His bundle stimulation, including Speckle Tracking Echo in 2-D Strain mode with measurement of longitudinal LV deformation to assess LV dyssynchrony. Prior to the His bundle stimulation, all patients had a decrease in LV longitudinal strain Me - 17% [-15; -19]. Low rates of LV longitudinal deformation were noted in the first, second, fourth, and fifth clinical cases, two patients with a previously implanted epicardial stimulation system, and patients after surgical correction of the IS defect and tetrad of Fallot with secondary complete AVB. Statistically significant normalization of LV longitudinal deformation from -17 [-15; -19] to -21,4 [-21; -22] (p=0,013) was registered in all patients on the background of the His bundle stimulation (Fig. 1).

Stimulation parameters were measured intraoperatively and 1-2 days after surgery. The stimulation threshold for the atrial electrode ranged from 05, to 0.7 V. For the ventricular electrode, 0.6-1.4 V. The follow-up period was 6 months [3; 12] (range 3 to 24 months). In the postoperative period, HM ECG, echocardiogram, chest X-ray, and pacemaker function control were performed. During prospective observation, three patients had an increase in the stimulation threshold at the ventricular electrode - two patients with secondary postoperative AVB and one patient with AVB diagnosed after an infection, while the values of the stimulation threshold remained within normal limits. QRS complex duration, and hemodynamic parameters did not change during follow-up.

DISCUSSION

A few clinical studies have demonstrated the adverse effects of prolonged RV stimulation, which can cause electrical and mechanical interventricular and intraventricular dyssynchrony, leading to LV remodeling and the development of PIC. It is known that septal stimulation provides more synchronous contraction and narrow QRS complex with preserved LV function; therefore, the choice of pacing site should be oriented to narrowing of the stimulated QRS complex, improvement of LV synchrony and preservation of LV systolic function. Stimulation of the His-Purkinje conduction system directly causes physiological ventricular depolarization, excluding the development of interventricular and intraventricular dyssynchrony, providing synchronous kinetics [17]. Consequently, patients who are indicated for endocardial stimulation and those with prolonged epicardial stimulation of the RV who are at risk of developing PIC may be considered candidates for the His stimulation.

Continuous stimulation of the His bundle was first described in 2000. P.Deshmukh et al [18]. The authors described stimulation of the bundle of His in 18 adult patients with chronic atrial fibrillation and dilated cardiomyopathy. Successful stimulation of the His bundle was achieved in most patients, and improvement in LV function was seen in nine of those who maintained adequate His bundle stimulation [10]. Results from other studies of adult patients have also demonstrated improved ventricular function, and better quality of life compared to RV stimulation [11]. In pediatric patients, phisiologic His bundle stimulation can be technically challenging because of the small size of the heart and the peculiarities of the conduction system, especially in children with CHD.

In the available literature, experience with pediatric His bundle stimulation is limited to single observations or clinical case series [19]. Thus, E. Jimenez et al. presented a successful experience of His bundle stimulation in eight patients aged 8 to 18 years (mean age was 11.5 years) and weighing 21.5 to 81.6 kg (mean weight 40 kg) with and without structural heart disease who underwent selective and nonselective Hisial stimulation without perioperative complications. Improvement of LV contractile function in a patient with baseline PIC has been demonstrated. Selective stimulation of the His bundle was achieved in all patients without cardiac defects and in one patient with a small muscle defect of the IVS. The authors also indicated that there were no complications related to electrode dislocation or increased stimulation threshold during 5 months of follow-up (range 2-6 months) [20]. All our patients underwent successful endocardial implantation of the pacemaker system in the His bundle position; however, selective stimulation was achieved only in one patient with congenital AVB grade 3 with prior primary epicardial stimulation. In the remaining patients it was not possible to place the electrode in the position for selective stimulation of the His bundle. In three cases, this was probably due to the presence of a patch in the region of the IS in patients with corrected CHD. In the remaining two cases, these were patients with low weight, a sufficiently thin part of the IVS in whom the electrode could not be placed without muscle entrapment.

The problems of His bundle stimulation that concern most arrhythmologists are intraoperative difficulties of electrode positioning, long-term electrode stability, high stimulation threshold and consequently decreased battery life [21-25]. In our pediatric cohort, in the early postoperative period, His bundle stimulation showed a low threshold; however, during prospective follow-up, an increase in stimulation threshold at the ventricular electrode was recorded in three patients, which is consistent with the mentioned publications.

G.Dandamudi et al. [12] presented a multicenter (in 6 centers) retrospective series of 17 young adults with congenital AVB (mean age 27.4±11.3 years) who underwent stimulation of the His bundle. Patients were followed up for 385±279 days. Of 8 patients with previously implanted pacemaker systems, three had LV dysfunction presumably related to RV stimulation, and 5 had problems with RV electrodes. The authors note that none of the patients with de novo implantation had LV dysfunction. In patients who had previously undergone RV stimulation, there was a significant reduction in QRS complex duration during the His bundle stimulation compared with the relatively wide QRS complexes associated with RV stimulation. Three patients with LV dysfunction on the background of chronic cardiac stimulation of RV demonstrated significant improvement of LV EF and functional status. It is important to note that there were 2 electrode revisions associated with increased stimulation threshold in this observational cohort. One case occurred on day 14 and the second developed 722 days after surgery [26].

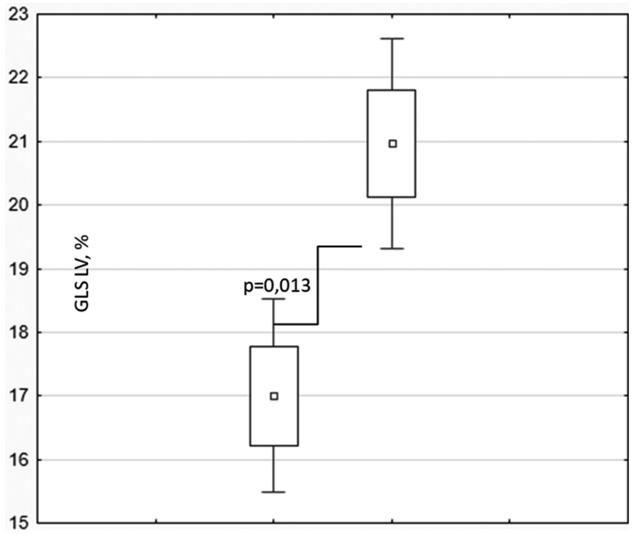

Fig. 1. Left ventricular longitudinal strain (LV GLS) before and after His bundle stimulation.

Another group of authors provided additional evidence that His stimulation is associated with lower LV electromechanical dyssynchrony and shorter QRS complex duration compared to conventional RV stimulation [13]. In our patients before and after the His bundle stimulation, the duration of QRS complexes did not change statistically significantly, which is associated with the baseline normal value of this index in most patients, including the patient with baseline RV stimulation. In only one patient with tetrad of Fallot (5 clinical cases), QRS widening up to 140 ms was associated with the right bundle branch block. Since there were no patients with reduced LVEF in our observation group, we did not observe the dynamics of this index. However, it should be noted that in all our patients on the background of the His bundle selective and nonselective stimulation there was a significant improvement in the indices of LV electromechanical dyssynchrony (Fig. 1). The most significant normalization of LV longitudinal deformation was registered in the patient with previous previous RV epicardial stimulation. The results of our study agree with the data of a group of authors who also demonstrated the advantages of Speckle-tracking Echo with determination of LV GLS as the most sensitive marker of LV contractility impairment compared to standard Echo [27].

Pediatric patients and patients with CHD are particularly vulnerable to LV dysfunction during chronic cardiac stimulation of the RV, so for children the potential benefits of conduction system stimulation are no less significant than for adults. Achieving synchronized ventricular contraction with stimulation of the conduction system provides the most physiologic activation of the myocardium. However, it is necessary to note the difficulties of performing the isolated His bundle stimulation procedure. Nevertheless, experience with the use of His bundle cardiac pacing in adults is increasing and demonstrates high efficacy and safety. It should be noted that a rather limited number of clinics in the world have experience with His bundle cardiac pacing in the pediatric population. Considering that our clinic is one of the few that has a history of using this technique, we consider it advisable to further accumulate experience and improve the technology to ensure the widespread use of physiologic cardiac pacing in the pediatric population. Undoubtedly, it is extremely important to have specialized delivery systems, to standardize the implantation technique and to obtain stable results in terms of implantation success and preservation of electrical parameters.

Limitations of the study

Our study has a limitation due to the lack of results of long-term prospective follow-up, which will be performed in the future. The relatively small number of patients (typical for most pediatric studies) did not allow dividing patients into groups and performing a separate statistical analysis of hemodynamic parameters.

CONCLUSION

Patients who are at risk of developing ventricular dyssynchrony as a result of conventional RV stimulation, as well as patients who are indicated for primary endocardial pacemaker implantation, may be advised to undergo His bundle stimulation, which provides physiologic ventricular activation and prevents the development of pacing-induced cardiomyopathy. The above clinical experience, as well as the data of the literature, allow us to hope for a wide practical implementation of His bundle stimulation in pediatric practice.

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