LILIA ROMANCIUC[1], NINEL REVENCO[1,2] , PETRU MARTALOG[1]

VENTRICULAR PREMATURE CONTRACTIONS AND PROGNOSIS IN CHILDREN

[1]State University of Medicine and Pharmacy „Nicolae Testemitanu",
Pediatrics Department, [1, 2]Institute of Mother and Child

SUMMARY

VENTRICULAR PREMATURE CONTRACTIONS AND PROGNOSIS IN CHILDREN

Key words: Premature ventricular contractions, severity of symptoms, children.

Premature ventricular contractions are early depolarizations of the myocardium originating in the ventricle. PVCs are common with an estimated prevalence of 40% to 75% in the general population on 24 to 48 h Holter monitoring. Frequent premature contractions are rare in healthy children and young adults. Traditionally, they have been thought to be relatively benign in the absence of structural heart disease but they represent increased risk of sudden death in structural heart disease. In the treatment of PVCs, it is important to consider underlying heart disease, the frequency of the PVCs and the frequency and severity of symptoms.

REZUMAT

EXTRASISTOLE VENTRICULARE ȘI PROGNOSTICUL LA COPII

Cuvinte cheie: extrasistole ventriculare, severitatea semnelor clinice, copii

Extrasistolele ventriculare reprezintă depolarizarea precoce a miocardului cu origine în ventricule. Prevalența extrasistolelor ventriculare în populația generală, conform datelor monitorizării Holter ECG timp de 24 și 48 ore, constituie de la 40% la 75%. Extrasistolele ventriculare sunt rare la copiii și adolescenții sănătoși. Tradițional, se consideră că sunt relativ benigne în absența maladiilor cardiace structurale, dar reprezintă un risc crescut de moarte subită în prezența maladiilor structurale cardiace. Tratamentul extrasistolelor ventriculare trebuie să considere prezența maladiei cardiace, frecvența extrasistoliilor și severitatea semnelor clinice.

Introduction

Premature ventricular contractions (PVCs) are commonly in apparently healthy individuals with a reported incidence of approximately 1% on standard electrocardiograms (ECG) and 40% to 75% on routine 24-hour to 48-hour Holter monitoring ECG. In an early database of 122 043 clinically healthy males age 16 to 50 years, PVCs were recorded in 0.78% on a 48-second tracing of a 12-lead ECG [1]. Kostis et al studied the characteristics of PVCs on a 24-hour ambulatory ECG monitoring in healthy males and females, in whom any preexisting heart disease had been previously excluded by ECG, echocardiogram, stress test, left and right heart catheterization, and coronary angiogram [1]. They found that as many as 40% of the subjects had ≥1 PVC during the 24-hour monitoring period, only 5% of the subjects had >5 PVCs in any given hour, and 4% had >100 PVCs per 24 hours.

PVCs are frequent in neonates, infants, and children. When these are rare and isolated, they rarely need further evaluation, when premature ventricular contractions becomes more frequent, more than 10% of beats in a 24-hour Holter ECG period, its should be followed up. The prevalence of PVCs in healthy children varies with age, 20% of the neonates have uncomplicated ventricular ectopy consisting of uniform PVCs or couplets. This decreases to 10% of toddlers and school-age children and increases to 20%–30% of then normal adolescents. In normal adolescent boys, although some ventricular ectopy is common, less than 5% will have more than 50 beats per 24 hours and less than 2% will have multiform PVCs, couplets, or non sustained VT on 24-hour monitoring [2]. The origin of the PVCs and the response to exercise should be analyzed. Some reports suggest that the suppression of PVCs with exercise indicates a more benign condition, but suppression with exercise is so common that it is difficult to use this criterion diagnostically. There is evidence that PVCs that originate from the left ventricle are more likely to regress over time [3].

PVCs that originate from the right ventricular outflow tract are typically benign. Thus, when PVC burden exceeds age-based normal ranges, it is important to evaluate patients for possible underlying pathology.

Preamature ventricular contractions in children and risk factors

Preamature ventricular contractions in children without structural heart disease are generally benign, especially if they disappear during exercise. Beaufort-Krol et al studied the natural history of PVCs in children with anatomically normal hearts. They classified the PVCs according to the site of origin [4]. They followed a cohort of 51 children with a mean duration of 3.1±3.1 years who were first examined at a mean age of 7.1±4.3 years. Premature ventricular contractions with left bundle branch block pattern were seen in 41% of the children, those with a right bundle branch block pattern were seen in 36%, and the morphology was undetermined in 23%. It was observed that although the mean percentage PVC with left bundle branch block did not change, PVC with a right bundle branch block decreased significantly at the end of follow-up. Another important observation was that

PVCs tended to disappear in younger children more often than in older children, though this was not statistically significant when comparing the age group of 1 to 3 years and those age >16 years (P =0.08). Although the authors did not recommend follow-up in children with PVC right bundle branch block in the absence of heart disease, they still thought those with PVC left bundle branch block, needed to be seen every 2 to 3 years for the development of left ventricular (LV) dysfunction. This is in the wake of recent data showing association between PVCs of right ventricular outflow tract (RVOT) origin and development of LV dysfunction [4]. In contrast, Gaita and colleagues followed 61 patients with PVC left bundle branch block for 15±2 years and found out that there was no increase in the incidence of sudden cardiac death (SCD) or arrhythmogenic right ventricular dysplasia among their subjects.

The PVCs being considered as benign in the absence of structural heart disease, although the majority of the recent studies focus on the role of PVCs in causing cardiomyopathy, other disease associations such as stroke, and SCD are worth mentioning. The prospective Atherosclerosis Risk In Communities (ARIC) study demonstrated that PVCs were present in 6.2% of the subjects at baseline [5]. This was associated with an increased risk of stroke, especially in the subgroups of subjects without traditional risk factors for stroke (eg, diabetes and hypertension). Whereas the latter occurred in 4.9% of all subjects, the cumulative proportion of incident stroke in individuals with PVCs was 7.3%, compared with 4.8% in those without PVCs. Another interesting observation in this study was the demonstration of association between PVCs and embolic stroke, as thrombotic stroke occurred with equal frequency irrespective of the presence of PVCs. The increased incidence of embolic stroke underscores the possible association between PVCs and atrial fibrillation, as previously cited by other studies [6]. In the same ARIC study, Massing et al found that PVCs increased the risk of cardiovascular-event rates independent of the presence of cardiovascular disease at baseline [7]. The presence of PVCs on a 2-minute rhythm strip at baseline was associated with 3× increased risk of mortality (7.8% vs 2.1%; P <0.05) from cardiovascular disese in this study, compared with those without PVCs. The event rate still remained as high as 2× after adjusting for age, sex, and other risk factors using proportional hazards regression. An important implication of this observation is that regardless of whether PVCs inherently increase mortality, their presence certainly incurs a higher cardiovascular risk, which should be at least managed by aggressive modification of traditional risk factors. Cheriyath et al studied the association of atrial premature contractions (APCs) and PVCs and risk of SCD in the ARIC cohort [8]. They found that PVCs were in fact associated with an increased risk of SCD with a hazard ratio of 2.1, whereas APCs did not show any significant association. They also could demonstrate an increased incidence of CAD and fatal CAD in association with PVCs, as already reported by previous investigators. The exact mechanism responsible for SCD in patients with PVCs is still not well understood; however, a large PVC burden, LV dysfunction, short coupling interval with R-on-T phenomena, increased automaticity, as well as sympathetic overdrive are potential substrates for more malignant ventricular arrhythmias [9].

Stress and ventricular arrhythmias

Stress can exert adverse effect on cardiovascular health. Psychosocial stress adversely affects the autonomic homeostasis. This in turn can result in metabolic abnormalities, inflammation and dysfunction of endothelium. Changes in the autonomic homeostasis can be a major trigger for ventricular tachyarrhythmias [10]. Increased sympathetic nervous activity can cause increased proarrhythmic repolarization instability leading to spontaneous ventricular arrhythmias. During stress-induced autonomic nervous system activity, the heart rate rises and the heart rate variability indices like *low frequency power* falls before the onset of ventricular tachycardia . Psychological stress has been shown to induce T wave alternans, which in turn predicts future ventricular tachyarrhythmia events. Fluctuations in T wave amplitude after psychological stress are predictive of subsequent arrhythmic events [11].

The mechanism of arrhythmia in children with structurally normal heart is the same as in an adult patient. Arrhythmias in children with heart disease can be the result of any underlying structural abnormality. It may also be due to surgical interventions [12]. Psychological

stress stimulate sympathetic nervous system and this in turn can become proarrhythmic.

Catecholaminergic ventricular tachycardia is a rare primary ventricular tachyarrhythmia seen in children, which has a poor natural history. This potentially lethal tachyarrhythmia in children with structurally normal heart can be induced by stress or emotions [13].

Myocardial electrical instability can be triggered by psychological stress. Chronic stress can lead to reduced heart rate variability, increased QT dispersion and reduced baroreceptor sensitivity. Patients with greatest changes in the cardiac neural regulation associated with increased sympathetic activity due to stress have the greatest risk for developing fatal ventricular arrhythmias.

Sudden emotional arousal can even trigger malignant ventricular arrhythmias. It is estimated that about 20 – 40% of sudden cardiac deaths are precipitated by acute emotional stressors. Cardiac autonomic dysfunction triggered by psychological distress can increase the risk of arrhythmias [12]. With the advent of functional neuro imaging, the anatomical substrate and the physiological mechanism by which emotional stress contributes to the arrhythmias and cardiovascular events are now recognized. During emotional stress there is lateralization of cerebral activity. This leads to asymmetrical stimulation of the heart, producing areas of inhomogeneous repolarization, creating electrical instability. This in turn facilitates the development of cardiac arrhythmias.

Conclusions

1. Premature ventricular contractions (PVCs) are commonly in apparently healthy individuals with a reported incidence of approximately 1% on standard electrocardiograms (ECG) and 40% to 75% on routine 24-hour to 48-hour Holter monitoring ECG.
2. PVCs are frequent in neonates, infants, and children, the prevalence in healthy children varies with age, 20% of the neonates have uncomplicated ventricular ectopy.
3. In the treatment of PVCs, it is important to consider underlying heart disease, the frequency of the PVCs and the frequency and severity of symptoms.

Bibliography

1. Jane E.Crosson, David J Callans, David J Brandley Anne Dubin, Michael Epstein, Susan Etheridge,et al.PACES/HRS Expert Consensus Statement on the Evaluation and Management of Ventricular Arrhythmias in the Child with a Structurally Normal Heart. Heart Rhythm. 2014;11(9):55-77.
2. Massin MM, Bourguignont A, Gerard P. Study of cardiac rate and rhythm patterns in ambulatory and hospitalized children. Cardiology. 2005;103:174–179.
3. Beaufort-Krol GC, Dijkstra SS, Bink-Boelkens MT. Natural history of ventricular premature contractions in children with a structurally normal heart: does origin matter? Europace.2008;10: 998–1003.
4. Kanei Y, Friedman M, Ogawa N. Frequent premature ventricular complexes originating from the right ventricular outflow tract are associated with left ventricular dysfunction. Ann Noninvasive Electrocardiol. 2008;13:81–85.
5. Agarwal SK, Heiss G, Rautaharju PM. Premature ventricular complexes and the risk of incident stroke: the Atherosclerosis Risk In Communities (ARIC) Study. Stroke. 2010;41:588–593.
6. Watanabe H, Tanabe N, Makiyama Y. ST-segment abnormalities and premature complexes are predictors of newonset atrial fibrillation: the Niigata Preventive Medicine Study. Am Heart J. 2006;152:731–735.
7. Massing MW, Simpson RJ Jr, Rautaharju PM. Usefulness of ventricular premature complexes to predict coronary heart disease events and mortality (from the Atherosclerosis Risk in Communities Cohort). Am J Cardiol. 2006;98:1609–1612.
8. Cheriyath P, He F, Peters I. Relation of atrial and/or ventricular premature complexes on a two-minute rhythm strip to the risk of sudden cardiac death (the Atherosclerosis Risk in Communities [ARIC] study). Am J Cardiol. 2011;107:151–155.
9. Pacchia CF, Akoum NW, Wasmund S. Atrial bigeminy results in decreased left ventricular function: an insight into the mechanism of PVC-induced cardiomyopathy. Pacing Clin Electrophysiol. 2012;35:1232–1235.
10. Das S. Behavioral cardiology: recognizing and addressing the profound impact of psychosocial stress on cardiovascular health. Curr Atheroscler Rep. 2006;8:111.
11. Lampert R. Anger-Induced T-wave Alternans Predict Future Ventricular Arrhythmias in Patients with Implantable Cardioverter-Defibrillators. J Am Coll Cardiol. 2009;5.
12. Abisse SS. Cardiac repolarization instability during psychological stress in patients with ventricular arrhythmias. J Electrocardiol. 2011;44:678.
13. Brugada J. Pharmacological and non-pharmacological therapy for arrhythmias in the pediatric population: EHRA and AEPC-Arrhythmia Working Group joint consensus statement. Europace. 2013;15:1337.