



Editorial

Asystolic syncope – To pace or not to pace, that is the question



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ARTICLE INFO

Article history:

Received 18 April 2019

Accepted 26 April 2019

Available online 30 April 2019

Treatment of syncope due to asystole is not uniform and depends on clinical setting. In patients with structural heart disease cardiac pacing is generally indicated and the recurrence rate is low. However, when cardiac disease is not obvious and asystole is of reflex origin, pacing is indicated only in a minority of patients after other treatment modalities have failed [1]. Pacing efficacy is lower in reflex syncope. Syncope recurrence is observed especially in patients with hypotension susceptibility, usually documented as hypotension during tilt test. In addition, patients with reflex syncope, frequently young and otherwise healthy individuals, are often reluctant to embark on cardiac pacing.

In patients with normal heart adenosine-dependent mechanism of asystole may also play a role (adenosine sensitive syncope). Patients with normal heart, normal ECG and no prodromes frequently exhibit low plasma adenosine level. In this situation adenosine receptors are up-regulated and hypersensitive. Sudden increase in plasma adenosine leads to their activation and bradycardic response. Typical mechanism of asystole is AV block; sinus arrest is less common because of less dense presentation of A1 adenosine receptors in SA node compared to AV node. Efficacy of pacing in adenosine sensitive syncope is high [2]. But is the pacemaker insertion always necessary?

Brignole and co-authors in this issue of the journal proposed different therapeutic approach in group of patients with syncope, normal heart and asystole documented by ILR [3]. Study population was characterized by no (or only very short) prodromes and low plasma adenosine. Oral theophylline therapy decreased the number of syncopal episodes and the incidence of asystolic events (paroxysmal third degree AV block and/or sinus arrest). Benefit of the long-term theophylline therapy can be explained by non-selective blockade of adenosine A1 and A2 receptors and normalization of their sensitivity.

Although the number of patients included into study was low (16 patients), results are interesting and challenging. Syncope due to paroxysmal AV block is often caused by infrahisal conduction disorders, has traumatic consequences and even sudden cardiac death due to bradycardia-induced ventricular tachycardia was reported [4]. The majority of cardiologist is considering pacemaker implantation in paroxysmal AV block, regardless of etiology.

Patients with adenosine induced AV block represent a specific type of paroxysmal AV block (so called idiopathic AV block). This type is different from reflex AV block as well as from AV block due to intrinsic conduction disturbances. There are differences in ECG manifestation, clinical characteristics and purinergic profile [5]. Genetic differences were also suggested but results are not uniform [6,7]. Adenosine dependent mechanism of asystole can be demonstrated by exogenous adenosine administration. Patients with asystole lasting more than 6 s or AV block lasting more than 10 s could benefit from cardiac pacing, although evidence for this approach is relatively weak (IIb class of ESC recommendation) [1].

How to identify patients with asystolic syncope who could benefit from long-term oral theophylline therapy? Should we use clinical characteristics, plasma adenosine level or exaggerated response to exogenous adenosine injection?

Selection based on clinical characteristics represents the easiest approach in the routine clinical practice. However, the recognition of prodromal symptoms is not always accurate. Due to retrograde amnesia, decline in cognitive function or emotional distress symptoms preceding syncope could be missed. Patients with no prodromes and normal heart compared to patients with prodromes and normal heart have significantly higher incidence of asystole (66% vs 47%) and paroxysmal AV block (47% vs 21%) but tachycardia or no rhythm changes could be also present at the time of syncope [8]. Reflex syncope could also manifest with no prodromes.

The majority of patients with no prodrome, normal heart and normal ECG have low plasma adenosine level and can be considered as a distinct clinical and biological entity [2]. Prediction of theophylline efficacy by low plasma adenosine thus seems to be elegant and promising. However, low adenosine level failed to predict asystole during ILR monitoring in the previous study, adenosine plasma levels were low both in patients with and without asystole. Some patients with low adenosine levels did not experience asystolic episode during ECG monitoring [8]. Also in the present study 3 from 16 patients with asystolic syncope did not exhibit low plasma adenosine levels [3].

Positivity of adenosine test can be considered as another marker of adenosine-dependent syncope. Positivity of adenosine test was

DOI of original article: <https://doi.org/10.1016/j.ijcard.2019.03.043>.E-mail address: peter.mitro@upjs.sk.

suggested as a predictor of pacing effectivity [9], but mechanism of syncope in patients with positive adenosine test is not exclusively asystolic [10]. On the other hand, in selected group of patients without structural heart disease and absent prodromes the diagnostic accuracy of the test could be different [2]. Question if results of adenosine test could predict effectivity of theophylline therapy remains to be answered. In the present study majority of patients with positive adenosine test (4 out of 6) have asystolic syncope during follow up and responded well to theophylline therapy [3].

In summary, the combination of all three methods should be considered in identification of theophylline therapy candidates. The crucial moment remains the documentation of asystole during syncope (namely AV block, theophylline efficacy in sinus arrest is significantly lower). This underlines the importance of ILR implantation also in patients with absent structural heart disease.

Theophylline therapy could be considered especially in two situations. First, in young patients (under 40 years of age) in which no indication to pacemaker therapy according to current guidelines exists. Second, it could be used in patients hesitating with decision to implant a permanent pacemaker. Pacemaker therapy remains as a back-up modality, if pharmacological approach fails. Considering the results of the present study it seems that theophylline reduces syncopal burden, but is not able completely prevent syncope recurrences in all patients [3]. One possible explanation is an overlap between adenosine sensitive and reflex syncope. These two entities cannot be always clearly differentiated in an individual patient. Data comparing effectivity of theophylline and pacing therapy in adenosine sensitive syncope are not available at present time.

The present study should be considered as a pilot study, which indicates the need for further studies with larger number of patients.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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