Cardioneuroablation as a treatment for reflex neurocardiogenic syncope – case report

Petra Novak,[1] Bor Antolič,[2] Dan Wichterle,[3] Matjaž Šinkovec[2]

[1] General hospital Murska Sobota, Murska Sobota, Slovenia

[2] Department of Cardiology, Division of Internal Medicine, University Medical Centre Ljubljana, Ljubljana, Slovenia

[3] Department of Cardiology, Institute for Clinical and Experimental Medicine (IKEM), Prague, Czech Republic

Correspondence:
Petra Novak,
e: petran1023@gmail.com

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Abstract

Reflex neurocardiogenic syncope is one of the most common causes of transient loss of consciousness. Pathophysiological mechanism consists of an excessive response of parasympathetic nervous system, which leads to a drop in blood pressure and/or heart rate. Reflex neurocardiogenic syncope is usually not associated with any organic disease, it has a good prognosis and mortality is not increased. The goal of treatment is to improve the patient's quality of life. For patients with frequent episodes of reflex neurocardiogenic syncope with predominant cardioinhibitory component, who are unresponsive to non-pharmacological and pharmacological methods of treatment, and in whom pacemaker implantation is not indicated, there is now a new treatment possibility – cardioneuroablation. In this percutaneous electrophysiological procedure epicardial parasympathetic ganglia are ablated with radiofrequency energy. The result is a partial parasympathetic denervation of the heart, which leads to reduction of parasympathetic influence on the heart and hence resolution of symptoms.

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1 Introduction

Reflex neurocardiogenic syncope is one of the most common forms of transient loss of consciousness and is present in all age groups (1). It represents 22 % of all syncope in the general population and amounts to 50–66 % of all unexplained syncope (2,3). It is a benign form of syncope, which is usually not associated with an organic disease; the prognosis is good and the mortality is not increased (4,5). The underlying mechanism is complex and not fully explained. Trigger factors, including fear, pain, post-physical activity, and other forms of stressful situations increase the tonus of the sympathetic nervous system and, therefore, the heart rate and cardiac contractility. Reflexive irritation of cardiac C-fibres occurs. These are unmyelinated nerve fibres that run from the heart to the brain stem and transmit proprioceptive information about the tension of the heart muscle fibres. The excitation of these fibres leads to the activation of the vasodepressor area in the medulla oblongata. The result is an excessively increased tone of the parasympathetic nervous system, which is reflected in bradycardia / asys-

tole and a reduced tone of the sympathetic nervous system. This leads to peripheral vasodilation, reduced venous return into the heart, and thus reduced cardiac output. The consequent reduced cardiac output causes cerebral hypoperfusion, and, consequently, a loss of consciousness (1,5,6-9). The described reflex activity of the parasympathetic nervous system is, in this case, non-physiological or excessively expressed, and leads to syncope.

The vagus nerve, the tenth cranial nerve, interfaces with parasympathetic control of the heart. Its preganglionic fibres originate from the medulla oblongata, more precisely, the dorsal nuclei. The fibres run to the heart, where they connect into postganglionic fibres in the epicardial parasympathetic para-cardiac ganglia, containing *postganglionic* cell bodies.

The function of parasympathetic fibres is reducing automatism, excitability, and conductivity (6,10-12). There are three main parasympathetic cardiac ganglia: ganglion A (located between the superior vena cava and the ascending aorta), which contains most postganglionic fibres; ganglion B (lies between the right superior pulmonary vein and the right atrium) with most of the cardiac parasympathetic innervation; and ganglion C (localized in the inferior – posterior interatrial septum), which is key for the innervation of the AV node (8,13).

The function of the sympathetic cardiac nervous system is, simplified, the opposite of the parasympathetic, and increases all cardiac properties: automatism, excitability, conduction, and contractility.

The clinical presentation of reflex neurocardiogenic syncope includes the presence of warning signs, most commonly nausea, pallor, feeling of dizziness, foggy vision, palpitation, headache or paraesthesia. The loss of consciousness is followed by the loss of postural tonus. It lasts up to a few minutes; the patient is often sweaty and pale. Recovery of consciousness is, as a rule, rapid and complete, with no postictal phase (6,10-12). Disease management should aim to exclude structural heart disease, heart arrhythmias, drug effects, and other non-cardiac causes. Head-up tilt-table test plays an important role and is interpreted as positive when the table tilt causes patients the same warning symptoms and signs and loss of consciousness as in its spontaneous form (1,9). An electrocardiogram (ECG) recorded during an event (Holter ECG or implantable recorder) is helpful in the diagnosis (3).

The treatment of reflex neurocardiogenic syncope is meant to provide patients an improvement in the quality of life. However, the treatment is not necessary as far as symptoms and signs are not associated with a significant decline in the quality of life.

Cardioneuroablation (CNA) is a more recent method of treatment of the cardioinhibitory form of reflex neurocardiogenic syncope, where the parasympathetic denervation of specific areas of the heart (denervation of sinus and / or AV node) is achieved by percutaneous interventional electrophysiology with radiofrequency (RF) ablation.

The method is still relatively unknown worldwide and is only performed in a few centres. Each of these centres, which published multi-year tracking results for their patients, reported the effectiveness of preventing neurocardiogenic syncope with few complications (13,15-18). In addition to known complications of invasive interventional electrophysiology (local complications at the site of insertion of the vascular guide systems, thromboembolic complications and perforation with pericardial

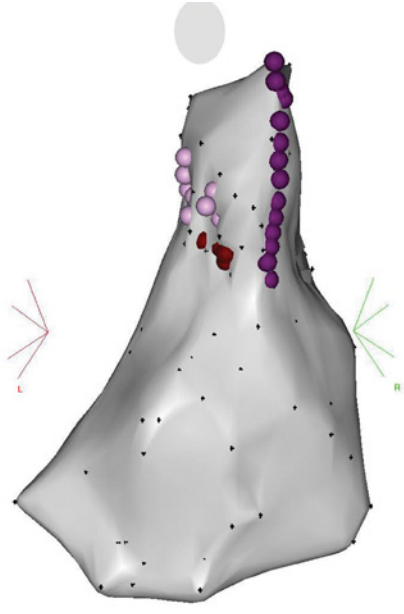

Figure 1: View of the three-dimensional map of the right atrium (posterior view). Dark purple dots indicate the pathway of the phrenic nerve, and light pink dots indicate unsuccessful ablations. Dark red color indicates successful ablations with an increase in sinus rhythm.

effusion / tamponade), a specific complication in this procedure is symptomatic sinus tachycardia. Sinus tachycardia is expected to some extent, and in most cases it is satisfactorily managed by beta-adrenoceptor antagonists or ivabradine. Approximately 3–6 months after the procedure we expect the sinus tachycardia to subside. The procedure may be unsuccessful due to partial or incomplete denervation of the aforementioned areas of the heart, which makes the impact of the parasympathetic nervous system still strong, thus not resolving the patients' clinical picture. Low procedure effectiveness may also occur in cases where the mechanism of reflex cardiovascular syncope is combined with the components of situational syncope or mixed-type syncope. One of the characteristics of CNA is also a common failure in eliminating prodromal symptoms. They belong to the vasodepressor component of syncope, and, therefore, remain after the procedure and are still present in many patients (13,14).

CNA is intended for those patients who have frequent episodes of cardioinhibitory reflex neurocardiogenic syncope for whom non-pharmacological and pharmacological treatments are ineffective, and a permanent pacemaker implant is not suitable because of their young age (13,14).

CNA is also used to treat other bradycardia heart rhythm disorders resulting from an increased parasympathetic activity that are not the result of structural damage of the heart. Such conditions are a functional disorder of the sinus node, a functional transient AV block, and a carotid sinus hypersensitivity syndrome (13,20,21).

2 Case report

A 22-year-old with no clear risk factors for cardiovascular disease was treated due to frequent syncope with warning signs. We performed a head-up tilt table test, which resulted in a drop in blood pressure and a 10-second asystole. Non-invasive cardiac diagnostics, including echocardiogram, was normal.

Non-pharmacological measures were only partially effective in preventing loss of consciousness. Due to syncope recurrence we offered the patient the option of CNA treatment - parasympathetic denervation of the sinus node. Prior to the procedure we performed an atropine test, during which the cardiac output was adequately increased (more than a 50 % increase of the baseline level). At the beginning of the procedure a three-dimensional anatomical map of the right atrium was created using the 3D-mapping system CARTO ™ (Biosense Webster) (Figure 1). The procedure continued with

endocardial radiofrequency ablation on the posterior side of the right ventricle at the junction of the superior vena cava to the right ventricle, where the epicardial parasympathetic ganglion is expected to innervate the sinus node. Ablations were performed in places where fractional electrograms were found indicating the presence of epicardial ganglia (22). We ablated with a cooled ablation catheter (Navistar Thermocool (Biosense Webster), 25–30W, up to 30 seconds with a temperature limit of 43 ° C) at the narrow ablation site. The aim of the ablation was to reduce or eliminate local potential and increase the frequency of the sinus rhythm, which is an indicator of parasympathetic denervation. We concluded the procedure after no additional increase in heart rate was achieved with extra ablation.

Parasympathetic sinus nerve denervation was confirmed by a repeat atropine test, after which there was no additional increase in heart rate.

At the 10-month follow-up, the patient still described presyncopal episodes with warning signs, namely, dizziness and feeling of nausea, which, however, did not lead to loss of consciousness. During the head-up tilt table control test there was a drop in blood pressure, but the heart rate did not decrease.

3 Discussion

The method of cardioneuroablation is based on radio frequency ablation of parasympathetic cardiac ganglia. Such method achieves parasympathetic denervation of specific areas of the heart. In this way we mitigate or eliminate the symptoms and signs of conditions that are the result of the excessive impact of the parasympathetic nervous system on the heart. The ablation of nerve cell bodies in parasympathetic ganglia causes an irreversible impairment, which indicates a long-term success of this intervention (14,23).

In a patient where the intervention was aimed at preventing an asystolic pause that led to episodes of loss of consciousness due to neurocardiogenic syncope, we thus achieved a successful parasympathetic denervation of the sinus node. Despite resolving the main problem, presyncope persisted within the clinical picture due to a remaining vasodepressor component of the reflex neurocardiogenic syncope.

Pachon and colleagues published the longest tracking of CNA patients. They monitored 43 patients in the mean period of 45.1 ± 22 months. They found a significant improvement in their clinical picture. In 93.1 % of patients no syncope was found. Asystole was not monitored during follow-up either spontaneously or with a head-up tilt table test (14).

It is important to emphasize that the above study, as well as that of Zhao and colleagues (24), and Tolga and colleagues (25), all identified the persistence of warning signs after the procedure in certain patients. Parasympathetic denervation eliminates the cardioinhibitory component of the neurocardiogenic syncope, while the vasodepressor component is, in principle, unchanged.

Monitoring patients after CNA with Holter ECG showed a minor increase in the minimal and mean heart rate, while the maximal heart rate was the same as before the intervention. Heart rate variability was significantly reduced after the procedure (14,15). The stress test after the procedure did not reveal any major differences in the basal heart rate measurement and the maximal heart rate; chronotropic incompetence has also not been established (13,15,25).

Only one sinus bradycardia was observed in 55 subjects when testing with

a head-up tilt table, while no asystolic pauses occurred. They found good long-term success of CNA, making pacemaker implantation not necessary (14).

New guidelines by American cardiology associations refer to CNA as a promising method for the treatment of syncope, but for the time being, it has not been sufficiently substantiated by research (19). The procedure is not yet standardized, which makes it difficult to compare the results between published research. Controlled randomized trials with a large number of participating patients are needed to clearly identify the role of CNA in the treatment of cardioinhibitory syncope.

The patient agrees with the publication of the article.

4 Conclusion

CNA is a promising new treatment for reflex neurocardiogenic syncope with predominant cardioinhibitory component according to published data. Although this method of treatment does not eliminate the vasodepressor component of cardioinhibitory syncope, we expect an effectively decreased vagal reflex, fewer warning symptoms and signs, and less syncopal episodes. Randomized multicentre research is needed in order to clearly identify the role of CNA in the treatment of cardioinhibitory syncope.

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