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Original research article

Diagnostic value of electrocardiographic (resting and 24-h Holter) monitoring in comparison with NT-proBNP in the differential diagnosis of patients with cardiogenic and neurogenic syncope

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ARTICLE INFO

Article history:
Received 3 April 2015
Received in revised form
26 August 2015
Accepted 3 September 2015
Available online 12 October 2015

Keywords:
24-h Holter
Electrocardiography
NT-proBNP
Syncope

ABSTRACT

Background: Syncope is a cause of 1–6% of hospitalizations. Both European and American syncope guidelines recommend a 12-lead ECG as part of the evaluation of all patients with unexplained loss of consciousness.

Objectives: The aim of this study was the assessment of the significance of ECG, Holter ECG and the concentration of NT-proBNP that would be useful in the differentiation of patients with cardiac and reflex syncope.

Methods: We investigated 100 patients (56 men), aged 18–77 years with reflex or cardiac syncope over the last 3 years. The following factors were investigated: age, sex, systolic and diastolic blood pressure, the presence of cardiovascular disease. Moreover, we assessed basic resting ECG parameters and 24-h Holter ECG parameters, and NT-proBNP concentration in the differential diagnosis of syncope.

Results: Patients with reflex syncope were younger compared to patients with cardiac syncope (44.4 ± 16.5 vs. 60.8 ± 12.6; $p < 0.001$). A pathologic resting 12-lead ECG was present more frequently in the group with a cardiogenic type of syncope – 12 (24%) vs. 8 (16%). 24-h Holter ECG monitoring showed no statistically significant difference between minimal, mean and maximal heart rates in the analyzed groups. However, statistically significant differences were observed in the occurrence of ventricular and supraventricular arrhythmias between the investigated groups. Patients with cardiac syncope had significantly higher concentrations of NT-proBNP compared to patients with reflex syncope (448.7 ± 212.2 vs. 68.2 ± 64.1; $p < 0.0001$).

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http://dx.doi.org/10.1016/j.crvasa.2015.09.001

Conclusions: Elevated NT-proBNP concentration is present in patients with a cardiogenic mechanism of syncope, despite the fact that a resting ECG is inconclusive.

Introduction

Syncope is a transient loss of consciousness caused by transient global cerebral hypoperfusion and is characterized by rapid onset, short duration, and spontaneous complete recovery [1].

Syncope is common in the general population and constitutes a significant clinical problem. It is the cause of 1–6% of hospital admissions, numerous outpatient consultations and 1–1.5% of emergency medical interventions [2]. In syncope patients who are referred to the emergency room minor injuries are found in 29.1% and severe injuries in 4.7% of cases [1].

In general, syncope is divided into reflex (neurally mediated) syncope, syncope due to orthostatic hypotension and cardiac (cardiovascular) syncope [1]. The most common cause of syncope is a reflex syncope, which is benign in nature. Vasovagal syncope is the most predominant type of reflex syncope and it constitutes up to 40% of all syncopes of unclear origin [1]. It is defined as a sudden loss of consciousness caused by a reflex overreaction of the autonomic nervous system [1].

Cardiac syncope is the second most prevalent type of syncope, mainly caused by arrhythmias: (supraventricular and ventricular) tachycardias, and bradyarrhythmias, as a consequence of sinus node dysfunction, atrio-ventricular (AV) node disease or a dysfunction of implanted cardiac devices. All these conditions lead to hemodynamic instability, which can cause a fatal decrease in the cardiac output and cerebral blood flow [1].

The etiological diagnosis and the assessment of syncope are challenging for the physician due to the unpredictability of the symptoms, an unknown recurrence rate and the short- and long-term risks associated with variable causes of syncope. The prognosis varies markedly with both underlying comorbidities and the etiological causality of the syncopal event. The initial investigations (history, physical examination, ECG and orthostatic blood pressure measurements) can provide the diagnosis in up to 50% of cases [3].

Syncope is a risk factor for sudden cardiac death (SCD) in many conditions associated with structural heart disease as well as inherited heart disease. Both European and American syncope guidelines recommend a 12-lead ECG as part of the evaluation of all patients with unexplained loss of consciousness. However, clinical research suggests that an ECG is performed as part of the evaluation in only 60–95% of patients with syncope [4].

Contemporary diagnostics of syncope based on the European Society of Cardiology (ESC) guidelines [1] does not include the routine biochemical determinations. In recent years there have been a few reports that have shown the usefulness of B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) in the diagnosis of syncope [5–8]. Still, there are no conclusive data to determine the value of NT-proBNP that could guide differentiation of patients with cardiac and reflex syncope.

The aim of this study was the assessment of the significance of ECG, Holter ECG and the concentration of NT-proBNP that would be useful in the differentiation of patients with cardiac and reflex syncope.

Methods

It was a prospective cohort study. One hundred consecutive patients were enrolled, 50 with reflex and 50 with cardiac syncope, including 56 women and 44 men, aged 18–77 years (mean age 52.6 ± 16.7 years) admitted to the Emergency Room, Medical School of Jagiellonian University, John Paul II Hospital, Cracow from January 2009 to December 2011 due to syncope.

According to the ESC guidelines [1], in order to determine the cause of the loss of consciousness all the patients were interviewed and clinical examination, including blood pressure as well as anthropometric measurements was performed. Additional diagnostic steps were taken, comprising a 12-lead resting ECG, 24-h ECG monitoring, echocardiography, and laboratory tests. The concentration of NT-proBNP was assessed in 100 patients enrolled in the study.

At admission to the Cardiology Department blood samples were collected into tubes containing an anticoagulant (edetate). Then the material was centrifuged in a centrifuge at the speed of 3000/min for 10 min. The obtained plasma samples were frozen at −30 °C for no longer than 7 days.

After determining the etiology of syncope and patient enrollment, NT-proBNP concentration was assessed using electrochemiluminescence immunoassay in previously prepared plasma. The analysis was performed using Cobas 6000 analyzer and two polyclonal antibodies that recognize epitopes within the chain of NT-proBNP. The total assay duration was 18 min. Roche reagent was used in the study. The immediate precision of the assay applied in the study was based on the producer's information and its value ranged from 1.7% to 3.1%.

All patients underwent a tilt test (maximum of 24 h after the last syncope) according to the Westminster protocol published by Fitzpatrick et al. [9]. Forty-one patients had carotid sinus massage, 19 subjects carotid ultrasound, while coronary angiography was performed in 15 patients. Before admission to the Coronary Disease Department the structural neurological causes of the loss of consciousness and orthostatic hypotension were excluded in all patients.

The ECG was analyzed for the presence of disturbances of chronotropic competence in the sinus node, conduction in the AV node (first, second and third degree AV block), left bundle