SYNCOPE

Psychiatric conditions in patients with recurrent unexplained syncope

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Aims The relationship between syncope and psychiatric disorders is little investigated. This study evaluated the prevalence of psychiatric diseases and prognostic outcome in patients with recurrent unexplained syncope.

Methods and Results After an inconclusive standard diagnostic work-up for syncope, including head-up tilt testing, a psychiatric evaluation was offered to 50 consecutive patients with recurrent syncope. The evaluation was accepted by 26 patients (77% females, 36 ± 16 years) and refused by 24 (63% females, 50 ± 19 years). A psychiatric disorder was diagnosed in 21 (81%) patients: 12 had depression, four panic attacks, two general anxiety, and three a somatization disorder. Only five patients showed normal psychosocial function. Of the patients with psychiatric disorders four accepted psychiatric care, such as psychotherapy and/or pharmacotherapy; 17 patients refused treatment. During 6 months of follow-up no patient under psychiatric care had syncope, while all patients without psycho- or pharmacotherapy had recurrent syncopal events. In these patients the median of syncopal episodes was three in a 6 months interval before and after clinical assessment. Patients who refused both psychiatric evaluation and therapy continued to experience syncope as before.

Conclusions In patients with recurrent unexplained syncope psychiatric alteration is common. However, patients seldom accepted a psychiatric evaluation and treatment.

Key Words: Recurrent unexplained syncope, psychiatric diseases.

Introduction

Recurrent syncope is a common clinical entity. Its aetiology is difficult to determine and unknown in 38% to 47% of the patients[1–6]. Diagnostic work-up of syncopal events is standardized[7–8]; head-up tilt testing has emerged as a routine diagnostic procedure to provide evidence of susceptibility to neurocardiogenic syncope[8–9]. More recently external or implantable loop recorders have increased the diagnostic yield[10–13]. Electrophysiological studies may also help to characterize the risk for future events, but fail to provide information about the aetiology of syncope[14]. Moreover, the relationship between syncope and psychiatric conditions is largely unexplored[15–17]. Although, the prevalence of psychiatric disease in patients with syncope is higher than average and may even play a role in predisposition to syncope, fewer than 5% of patients have been assigned a psychiatric diagnosis in cohort studies from the 1980s, probably because standardized assessment for psychiatric illness did not exist[15–18]. This study was designed to determine both prevalence of pathological psychiatric conditions and prognostic outcome in patients with recurrent unexplained syncope.

Methods

Patient selection and study inclusion criteria

Between July 1996 and October 1998, 220 patients were referred to our institution for investigation of syncope.
Fifty patients were consecutively enrolled in the present study after a non-diagnostic work-up, including head-up tilt testing, since they fulfilled the criteria of at least two syncopal episodes during the preceding 6 months in the absence of underlying cardiac or neurological disease. Patients with any structural heart disease and patients with abnormal physical test results or patients on medical therapy were not recruited.

**Routine assessment**

All screened patients underwent a detailed medical history, a laboratory analysis and a complete physical examination. An electrocardiogram, exercise electrocardiogram, ambulatory Holter monitoring of at least 24 h, carotid sinus massage, Schellong test, two dimensional echocardiography and head-up tilt testing were performed. Neurological examination included physical examination, electroencephalogram, carotid Doppler evaluation and cranial computerized tomography. Electrophysiological study and coronary angiography were not part of the standardized evaluation; however, an electrophysiological study was performed if the patient’s clinical history suggested an arrhythmia as the cause of syncope. All tests were normal and inconclusive in explaining syncope in patients enrolled in the present study.

**Head-up tilt testing**

Head-up tilt testing was regularly performed according to the Westminster drug-free protocol and consisted of 10 min in supine position prior to 60 min standing at 60 degree inclination on a tilt table with foot support, but no pharmacological provocation. A positive response to head-up tilt testing was defined as abrupt development of syncope or presyncope in association with hypotension or bradycardia, or both. Tilt table testing was negative in all study patients.

**Study design**

The patients, who met the inclusion criteria, were offered psychiatric evaluation by a psychosomatist. They were carefully informed about the possibility of a psychiatric aetiology of their syncope. If a patient was found to have a psychiatric disorder, specific therapy was recommended, including psychotherapy with optional adjunctive individually tailored pharmacotherapy. All patients were contacted after 6 months of follow-up for a structured interview.

**Psychosomatic assessment**

Psychiatric assessment was performed by a board certified psychosomatist. All patients completed three standardized, self-administered questionnaires to evaluate their formal functional status such as the Symptom Check List 90 (SCL-90-R) and two established German questionnaires, the Giessen Complaint List and the Body Image Questionnaire. The Giessen Complaint List is generally used to evaluate patients with psychosomatic complaints and patients with somatic disease and psychosomatic processes. The Body Image Questionnaire is employed to assess disturbances concerning the patient’s image of the body. In addition, all patients underwent a semi-structured psychosomatic interview. Diagnoses were made by the psychosomatists on the basis of predetermined criteria from the international classification of diseases (ICD-10).

**Statistical analysis**

Data are presented as median and mean value ± standard deviation, median value or percentage of patient numbers. Comparisons were made using Statistics for Windows (version 5.5, StatSoft). Differences between patient groups were analyzed using the Student’s t-test for continuous and normally distributed variables, the Mann–Whitney U-test for continuous, non-parametric variables, and Fisher’s exact test for categorical variables. The number of syncopal events before and after study inclusion was compared using the Wilcoxon matched-pairs signed-ranks test. Values of P<0.05 were considered significant.

**Results**

**Patient characteristics**

The study population comprised 50 patients (35 female, 15 male) at age 43 ± 19 years (range 14 to 83). The median of syncopal events was six (range 2–112) and the median of the syncopal episodes during the last 6 months before study inclusion was three (range 2–23) (Fig. 1).
Acceptance of psychosomatic assessment

Of 50 patients included in the present study, 24 (48%) refused to undergo psychiatric evaluation. These patients were older than patients who accepted psychiatric evaluation (50 years vs 36 years; P = 0.009) and had less syncopal events, less prodromal symptoms and a shorter history of syncope. The median of syncopal events before study inclusion was significantly higher in patients who accepted psychiatric evaluation (9 vs 4.5 events; P = 0.036); 54% of patients who accepted and 25% of patients who refused psychiatric assessment reported symptoms over a period of 5 years or more (P = 0.048). Gender, presyncope, and frequency of body injuries did not significantly differ between these two patient groups (Table 1).

Results of psychosomatic assessment

Of 26 patients who underwent psychiatric evaluation 21 (81%) had a psychiatric condition. Twelve patients (46%) had major depression and four (15%) suffered from panic attacks. Three patients (12%) had a somatization disorder and two (8%) had a general anxiety disorder. None was drug dependent (Fig. 2). The assigned diagnosis (psychiatric condition) represented the most relevant aspect of their disease. Nine of the 21 (43%) patients had multiple pathological psychiatric conditions. Of the 12 patients with depression, three had an additional anxiety disorder, one had phobic disorder and three were neurasthenic. One patient with somatization disorder also showed phobic disorder, and one patient with panic attacks had personality disturbances.

Specific psychiatric therapy

All patients were informed about the diagnosis and therapeutic strategies were explained. However, only four of 21 patients (19%) with psychiatric alterations eventually accepted tailored psychotherapy and adjunctive pharmacotherapy. Baseline and demographic data

Follow up

Patients under psychiatric therapy experienced no more syncopal episodes. All four patients regularly attended psychotherapeutic sessions and two of them continued medical treatment. During the 6 months after medical assessment, all 17 patients with psychosomatic disorders, who refused psychiatric treatment, continued to have syncope with identical frequency as in the 6 months before (Fig. 3). The median of syncopal events did not change from the 6 months before to the 6 months after clinical evaluation. During follow-up, 16 (67%) of 24 patients who refused psychosomatic evaluation continued to experience syncope. The median value of syncopal events decreased from 3.0 in the 6 months before clinical assessment, to 1.5 during the following 6 months; 8 (33%) patients had no more syncope (Table 2).

Discussion

Our analysis has revealed a close association of syncopal events and pathological psychiatric conditions; 21 of all 50 patients with recurrent unexplained syncope (after a complex battery of tests) were diagnosed as suffering from psychiatric conditions. The interesting finding of our interdisciplinary work was the abolition of all syncopal symptoms in those patients subjected to standard psychiatric care for their specific disorder. Conversely, patients without specific treatment continued to experience syncopal events.

Main findings

Psychiatric evaluation was accepted by 26 of 50 patients, leading to a diagnosis in 21 (81%). An intimate relationship between syncope and psychiatric disease was previously described by Linzer et al.[21,25–26] and by Kapoor.

Table 1 Descriptive data of patients who accepted and refused psychiatric evaluation

<table>
<thead>
<tr>
<th></th>
<th>Accepted n=26</th>
<th>Refused n=24</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>36 ± 16</td>
<td>50 ± 19</td>
<td>0.009</td>
</tr>
<tr>
<td>Female gender (%)</td>
<td>77</td>
<td>63</td>
<td>0.383</td>
</tr>
<tr>
<td>Syncopal episodes (median)</td>
<td>9</td>
<td>4-5</td>
<td>0.036</td>
</tr>
<tr>
<td>Presyncope (%)</td>
<td>50</td>
<td>50</td>
<td>1.000</td>
</tr>
<tr>
<td>Symptoms duration ≥ 5 yr (%)</td>
<td>54</td>
<td>25</td>
<td>0.048</td>
</tr>
<tr>
<td>Body injuries (%)</td>
<td>38</td>
<td>50</td>
<td>0.569</td>
</tr>
<tr>
<td>Prodromal symptoms (%)</td>
<td>88</td>
<td>63</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Data presented are mean values ± SD, median, or percentage of patients.

Figure 2 Spectrum and percentage of diagnoses at psychiatric evaluation in 26 patients.

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The question whether psychiatric disorders are cause or effect of syncope has not been resolved. In our patients the prevalence of psychiatric disease was 81 percent and thus higher than in patients with cardiac and non-cardiac syncope, or even unexplained syncope in patients not subjected to head-up tilt testing[16]. Conversely, Kapoor et al. showed in 1995, that the prevalence of psychiatric illness notably differs between patients with unexplained (24·5%), non-cardiac (19%) and cardiac (9·7%) syncope. The marked difference in the rate of psychiatric illness notably differs between patients with unexplained (24·5%), non-cardiac (19%) and cardiac (9·7%) syncope. The fact that the American Psychiatric Association’s DMS-IV (Diagnostic and Statistical Manual of Mental Disorders, fourth edition) includes syncope as manifestation of somatization, generalized anxiety and panic disorders reinforces this hypothesis[16,25–27]. In addition, our data corroborate previous findings by Kapoor et al. who identified the highest incidence of psychiatric illness in the subset with unexplained syncope; the difference in percentage may be explained by the fact that Kapoor et al. failed to exclude vasovagal syncope since tilt testing was not performed[16]. None of the 50 patients enroled in our study had structural heart disease and all had recurrent syncope with two or more syncopal events within the 6 months preceding and following recruitment. Furthermore, all patients underwent head-up tilt testing to exclude a predisposition to neurocardiogenic syncope. Kapoor et al. accepted just a single syncopal episode and did not offer head-up tilt testing to exclude vasovagal syncope[16].

Pathophysiological explanation

Several mechanisms have been proposed to explain how psychiatric disease could lead to syncope, among them hyperventilation, Valsalva manoeuvre, neurocardiogenic reactions and arrhythmias. Hyperventilation is a feature of some psychiatric disorders and may lead to cerebral vasoconstriction and thus syncope[28]. Valsalva manoeuvre in particularly emotional situations may impair venous return to the heart and reduce cardiac output leading to syncope[29]. Hyperventilation and Valsalva manoeuvre may be responsible for epidemic fainting[28]. Hyperventilation is also proposed as provocative manoeuvre for recognizing psychiatric syncope[17]. Another mechanism is the neurocardiogenic reaction to acute stress or phobia, such as fainting during blood drawing[29–30]. In addition, stress and psychological factors may predispose patients with underlying heart disease to malignant arrhythmias and sudden death[16].

Acceptance of psychiatric assessment and therapy

Although offered to all 50 patients, 24 (48%) refused to undergo psychiatric evaluation perhaps in expectation or fear of a psychiatric diagnosis; others seemed to consider recommendations not important or not serious. Of 21 patients with a psychiatric diagnosis, 17 (81%) refused the recommended psychiatric therapy. Thus, compliance in this highly selected group of patients is low as is well known[31]. Particularly in Europe, patients are reluctant to be exposed to psychiatric evaluation.

Table 2 Syncopal events during 6 months before and after clinical evaluation

<table>
<thead>
<tr>
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<td>Refused evaluation</td>
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<td>0·0001</td>
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<tr>
<td>Refused therapy</td>
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<td>0·33</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Accepted therapy</td>
<td>8·0</td>
<td>0·0</td>
<td>a</td>
<td>4 (100%)</td>
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Figure 3 Number of syncopal events during 6 months before and after evaluation of syncope in patients who refused psychiatric therapy. The frequency of syncope is unchanged ($P = 0·33$). Each point in the picture represents one patient.

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Moersch et al. reported that of 100 patients after myocardial infarction only six patients accepted psychiatric evaluation and of them only one consented to psychotherapy[31]. We believe that the principal factor for low compliance is the anticipation of a psychiatric diagnosis, although psychiatric evaluation was offered after completion of an extensive battery of tests with completely non-diagnostic results. A perception of psychiatric evaluation as a routine in the diagnostic work-up is likely to improve acceptance.

**Psychosomatic therapy**

Similarly, of 21 patients, in whom a psychiatric diagnosis was made, only four accepted to undergo psychiatric therapy. Specific therapy was successful in all four patients; none had syncope during follow-up, whereas patients who refused therapy continued to experience syncope with identical frequency (*P* = 0.33), and none had spontaneous remission of symptoms. Interestingly, 67% of those who even refused psychiatric evaluation continued to have episodes of syncope suggesting a relatively high percentage of psychiatric conditions among them (Table 2). However, these patients were older (50 ± 19 vs 36 ± 16 years) but less symptomatic than those who accepted evaluation for psychiatric disorders (Table 1), confirming previous findings of both a high rate of recurrence in patients with psychiatric conditions, and the need for specific treatment[16–17].

**Study limitations**

Our study was executed in a highly selected group of patients with recurrent unexplained syncope, no structural heart disease or neurological disorder, and a negative head-up tilt test; this cohort is more likely to be associated with psychiatric alterations than any other subset of patients with syncope. The Westminster Protocol was shown to have a positive yield of 27% to 75%[32]. Thus, it cannot be excluded that a neuromediated origin of syncope was present in some patients and that in these patients psychiatric conditions were not the cause but the consequence of the frequently recurrent syncopal spells. The systematic inclusion of patients with vasovagal syncope (with a positive tilt test) would possibly shed some more light onto the complex interaction between neurocardiogenic syncope and psychiatric illness. Moreover, although compliance with psychiatric evaluation and especially treatment is inherently low, a 52 percent recruitment for psychiatric evaluation is higher than average, and the response to specific psychiatric treatment is dramatic once a psychiatric disorder was diagnosed.

**Conclusions**

In patients with recurrent unexplained syncope, no structural heart disease, and negative head-up tilt testing, the incidence of psychiatric disorders is high suggesting an intimate relationship between unexplained syncope and psychiatric illness. Particularly in patients with a long clinical history and numerous syncopal and presyncopal events, psychiatric evaluation should be encouraged, since psychiatric therapy is effective, although the compliance with psychiatric evaluation and treatment is still low. Future studies on the efficacy of psychiatric treatment should have a randomized design.

**References**