Autonomic control of asystolic vasovagal syncope

David L Jardine, Hamid Ikrar, Ian G Crozier

Abstract
A 30 year old woman with a lifelong history of severe, recurrent, vasovagal syncope became asystolic for 30 seconds after 37 minutes of 60° head-up tilt. During early tilt, sympathetic activity, heart rate, left ventricular contractility, and cardiac output increased. Mean blood pressure was initially maintained. Presyncope was associated with maximal contractility and bradycardia despite sustained sympathetic activity. Subsequently, asystole occurred associated with complete withdrawal of muscle nerve sympathetic activity. In asystolic vasovagal reactions, presyncope may be triggered by increased left ventricular contractility and is associated with increased levels of parasympathetic and sympathetic activity. Asystole and peripheral vasodilatation may be caused by sudden and complete withdrawal of the increased sympathetic activity.

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Keywords: head-up tilt; vasovagal syncope; asystole

Some patients with severe, recurrent, vasovagal syncope have been shown to become asystolic during tilt-table testing.1,2 Their syncopal episodes may be rapid in onset and prolonged, sometimes causing injury. It is generally believed that this condition does not carry an increased mortality despite occasional severe episodes which mimic sudden cardiac death.3 The term “malignant vasovagal syncope” has been used to convey the significant morbidity experienced by some patients.2

We present a patient with lifelong recurrent syncope and describe detailed haemodynamic and autonomic assessment during an episode of tilt-induced asystole. To our knowledge, this is the first microneurographic record of vasovagal asystolic syncope. Previous reports on similar patients have not included muscle sympathetic activity or heart rate variability.1,3 Others have recorded either heart rate variability4-6 or muscle sympathetic activity4-6 during vasovagal syncope but not simultaneously, and not during asystole in a patient with a “malignant history”. We also report the associated haemodynamic changes in an attempt to demonstrate how the autonomic nervous system controls the haemodynamics of an asystolic vasovagal reaction.

Case report
A 30 year old woman was referred for investigation after a postoperative cardiovascular collapse. She awoke on the recovery ward shortly after a general anaesthetic for a vaginal hysterectomy and suddenly lost consciousness while still in a horizontal position. She was found to be hypotensive with a pulse rate of 36/min. One minute later she became pulseless and apnoic. Cardiopulmonary resuscitation was initiated and she recovered within 3 minutes. Investigations after recovery showed no evidence of perioperative myocardial ischaemia or haemorrhage. She gave a lifelong history of fainting, her previous episodes being precipitated by illness, intense excitement, heat, cold, or venepuncture. On examination there was no evidence of postural hypotension, carotid hypersensitivity, or cardiac disease. Her electrocardiogram, electro-physiological studies, 24 hour Holter tape, and echocardiogram were normal.

Methods
The patient underwent 60° head-up tilt table testing to confirm the suspected diagnosis of malignant vasovagal syncope. After a light, caffeine-free lunch she was positioned horizontally and supine on the tilt table with foot support. Cutaneous electrodes for thoracic impedance and the electrocardiogram (ECG) were placed. Microneurography needles were inserted in the right leg to record post ganglionic sympathetic activity from the superficial peroneal nerve.10 The following variables were recorded continuously on computer for 15 minutes before tilt, 37 minutes during tilt until syncope, and 15 minutes after tilt during recovery: heart rate (HR) from the ECG; low frequency (0.06-0.1 Hz) heart rate variability (LFHRV) from a computer-stored tachogram using 256 beat samples for spectral analysis of sympathetic activity; intra-arterial systolic and diastolic blood pressure; total thoracic impedance and its first time differential from the
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Mean blood pressure (MBP) was derived from systolic and diastolic blood pressure. Stroke volume was derived from thoracic impedance using the Kubicek equation. Cardiac output (CO) was derived from stroke volume and HR. Left ventricular contractility was estimated using the Heather index (HI), derived from thoracic impedance and the systolic ejection time.

Results
Initially, when the patient was in the horizontal position, all haemodynamic variables were within normal limits for our laboratory. Immediately after tilt there was an increase in MSA, LFHRV, HI, and HR (figs 1 and 2). During tilt, MBP and CO were maintained for 30 minutes until HI became maximal and the patient began to feel unwell. At 30 minutes, presyncope began and HR and MBP began to fall despite sustained MSA, LFHRV, and CO. At 36 minutes, MSA surged and then rapidly fell over 60 seconds. Asystole developed lasting for 30 seconds and the patient became syncopal. She was immediately tilted back to the horizontal and the microneurographic recording field was lost during recovery.

Discussion
The vasovagal response is defined as the development of arteriolar dilatation and inappropriate bradycardia leading to hypotension and loss of consciousness. The vasodilatation is thought to be due to sympathetic withdrawal and the bradycardia to simultaneous parasympathetic activation, although in humans the exact sequence and the relative importance of these mechanisms remains unclear. The response may be triggered in the brainstem by a paradoxical increase in baroreceptor firing rate from the heart or by emotional stress in the cortico-hypothalamic centres of the brain. In some patients the resulting transient autonomic imbalance is severe and reversible asystole may develop in the absence of sinus node disease or carotid hypersensitivity. We recorded autonomic activity continuously dur-
ing an episode of haemodynamiclly moni-
tored vasovagal asystole, in an attempt to
determine the control mechanisms respon-
sible.

The onset of presyncope coincided with the
peak level of left ventricular contractility. This
lends support to a proposed trigger mecha-
nism for vasovagal syncope, namely the para-
doxal stimulation of the central low pressure
baroreceptors when left ventricular contractil-
ity increased in the setting of a low cardiac
volume. However, recent experiments on
anaesthetised dogs did not demonstrate this
reflex and vasovagal syncope has been in-
duced in cardiac transplant recipients by
head-up tilting. Some of these patients had
no evidence of cardiac reinervation which
argues against the importance of a cardiac
reflex in vasovagal reactions.

Presyncope was associated with a gradual
fall in heart rate, blood pressure, and total
peripheral resistance despite sustained sympa-
thetic activity. The inappropriate bradycardia
can only be explained by an increase in
parasympathetic activity occurring at the same
time. Therefore both components of the au-
tonomic nervous system were activated simulta-
aneously, rather than sequentially as
hypothesised in the diphasic model of vasovagal
syncope. This has not been previously
demonstrated and contrasts with other reports
of vasovagal reactions which show tachycardia
in association with increased MSA during pre-
syncope. The progressive fall in blood pres-
sure despite increased MSA may have been
due to an active cholinergic vasodilatory
mechanism or the release of adrenaline.

Alternatively the splanchnic circulation, under
separate sympathetic control, may have been
relatively more vasodilated at this time. When
sympathetic withdrawal did occur, asys-
tole and severe vasodilation were observed,
resulting in prolonged syncope. This is consis-
tent with previous demonstrations of vasodi-
latation triggered by a sudden fall in MSA
suggesting a passive mechanism. Similarly,
the onset of asystole was related to the sudden
withdrawal of sympathetic activity, which
allowed the unopposed parasympathetic
activity to dominate. The reciprocal nature of
the autonomic balance between parasympathetic
and sympathetic action was therefore restored.

In this study we have attempted to docu-
ment as accurately as possible the autonomic
differences during tilt-induced asystolic syncope.
In the intact human it is not possible directly
to measure parasympathetic activity or global
sympathetic activity but MSA and low fre-
quency heart rate variability currently provide
the best dynamic measures of sympathetic
activity. Unfortunately neither forearm (mus-
cle) nor splanchnic blood flow were measured.
Stroke volume and left ventricular contractility
were measured indirectly via impedance car-
diography, a technique that has been validated
for detecting rapid changes in these variables.

In summary, we observed the autonomic and
haemodynamic changes that accompanied
tilt-induced asystolic vasovagal syncope. We
found there was an appropriate increase in
sympathetic activity in response to tilt, with
cardiac output and blood pressure initially
being maintained. The bradycardia and
hypotension of presyncope were associated
with maximal left ventricular contractility
and were due to increased parasympathetic activity
occurring on a background of increased sympa-
thetic activity. The usual reciprocal relation
between parasympathetic and sympathetic
activity was therefore disturbed and the result
was prolonged asystole associated with sudden
withdrawal of sympathetic activity. This loss of
reciprocity, preceding an episode of asystole
has not been previously demonstrated but has
been implicated as a mechanism for sudden
cardiac death.

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D. L. Jardine, H. Ikram and I. G. Crozier

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