

Caffeine restriction has no role in the management of patients with symptomatic idiopathic ventricular premature beats

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Abstract

Objective—To assess the role of caffeine restriction in the management of patients with symptomatic idiopathic ventricular premature beats.

Design—A randomised, double blind, 6 week intervention trial incorporating dietary caffeine restriction, caffeinated coffee, and decaffeinated coffee.

Setting—Cardiac outpatient clinic.

Patients—13 patients with symptomatic frequent idiopathic ventricular premature beats.

Main outcome measures—Weekly measures of serum caffeine concentration, coffee consumption, visual analogue score of palpitations, and 24 hour ventricular premature beat frequency.

Results—The interventions achieved significant alterations in serum caffeine concentrations ($P < 0.001$) which correlated with coffee consumption ($r = 0.70$; $P < 0.001$). Visual analogue palpitation scores showed a small, but significant correlation with ventricular premature beat frequencies ($r = 0.34$; $P = 0.003$). However, there were no significant changes in palpitation scores or ventricular premature beat frequencies during the intervention weeks and no significant correlations were found between these variables and serum caffeine concentrations.

Conclusions—Caffeine restriction has no role in the management of patients referred with symptomatic idiopathic ventricular premature beats.

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Keywords: palpitations; caffeine; ventricular premature beats; dietary restriction

Although many clinicians believe that caffeine can induce or exacerbate the frequency of arrhythmias and ventricular premature beats (VPBs), the evidence for this view is anecdotal and tenuous. Caffeine, like theophylline, is a methylated xanthine. It has pharmacological actions as an adenosine receptor antagonist, and to a minor extent, a phosphodiesterase inhibitor.¹ It also induces catecholamine release, leading to a rise in blood pressure and reflex bradycardia. However, these humoral effects are only seen after acute administration in caffeine naive subjects and are not seen during chronic administration. Moreover, in vitro and animal experiments

have only demonstrated an arrhythmogenic effect of caffeine at supraphysiological concentrations.^{2,3}

Clinical studies of acute and subacute caffeine administration, have focused on electrophysiological approaches^{4,5} and ambulatory electrocardiographic monitoring⁶⁻⁹ in patients with malignant arrhythmias and ischaemic heart disease. Although some studies^{4,6} have suggested a possible link, there has been no conclusive evidence proving an association between moderate caffeine consumption and arrhythmogenesis.¹⁰

A large population screening of 7311 healthy men¹¹ demonstrated that the presence, but not the frequency, of VPBs is weakly associated only with extremes of coffee intake ($r = 0.1$; nine or more cups per day). The influence of chronic moderate caffeine exposure in the exacerbation of palpitations and VPBs has not been established.

The aim of this study was to determine whether caffeine restriction is of any value in the management of symptomatic palpitations associated with frequent VPBs in patients without evidence of underlying cardiac or metabolic disorders.

Patients and methods

SUBJECT SELECTION

Subjects with symptomatic palpitations and frequent ventricular premature beats were identified through the hospital records of the Royal Infirmary of Edinburgh. Screening was performed at the clinic with a physical examination, a resting and a 24 hour ambulatory electrocardiogram, echocardiogram, and venous blood sampling. Subjects entered the study if they had ongoing symptoms of palpitations that were attributable to frequent VPBs on the ambulatory electrocardiogram. They were excluded according to the criteria in table 1. The written informed consent of each subject was obtained and the study was approved by Lothian Research Ethics Committee.

MEASUREMENTS

Ambulatory electrocardiographic monitoring

Twenty four hour ambulatory electrocardiography was performed using a 3-channel electrocardiographic tape recorder (Tracker 3; Reynolds Medical, Hertford). VPB counts were determined using a Pathfinder 700 analyser (Reynolds Medical) with v3.993 software. Subjects were encouraged to maintain normal daily activities during ambulatory monitoring.

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Table 1 Exclusion criteria

| |
|--|
| Abnormal resting electrocardiogram including evidence of left ventricular hypertrophy (> 35 mm from the summation of the amplitude of S wave in V1 and the R wave in V5 or V6) |
| Echocardiography: |
| • Left ventricular hypertrophy (> 1.3 mm thickness of posterior wall of the left ventricle) |
| • Regional wall motion abnormalities |
| • Valvar heart disease (trivial mitral incompetence was permitted) |
| Electrolyte imbalance (including corrected calcium) |
| Renal impairment |
| Biochemical dysthyroidism |
| Raised random blood glucose |
| Hypercholesterolaemia (total cholesterol > 6.7 mmol/l) |
| Any history or physical findings consistent with hypertensive, cardiac, or thyroid disease |
| Inability to drink coffee |

Palpitations

Symptomatic palpitations were assessed on a linear visual analogue scale. Subjects were asked to grade the level of palpitations during the 24 hours of electrocardiographic monitoring by marking a 10 cm line graded from no palpitations to continuous palpitations.

Serum caffeine concentration

To assess dietary caffeine intake and compliance, a venous blood sample was withdrawn at 1700 hours.¹² Serum obtained was assayed for caffeine by high performance liquid chromatography with 8-chlorotheophylline as internal standard.¹³

STUDY DESIGN

Subjects were asked to follow a 6 week protocol (fig 1). On day 6 of each week an ambulatory electrocardiogram was applied at about 1700 hours and removed after 24 hours when venesection and an assessment of palpitations was undertaken. For the first two baseline weeks, each subject continued their normal diet and coffee intake. During weeks 3 and 4, jars of instant coffee (freeze dried and granulated), which contained either caffeinated or decaffeinated coffee, were provided weekly in a randomised double blind fashion. Each subject continued on their normal diet and received one jar of caffeinated and one jar of decaffeinated coffee over the two weeks. Subjects were instructed to consume at least three cups of coffee per day and the jars were weighed at the beginning and after completion of the study week. For weeks 5 and 6 the subjects adhered to a caffeine free diet, having been given both verbal and written instruction on caffeine-containing food products and pharmaceuticals. Jars of coffee were again provided at weekly intervals in an identical manner.

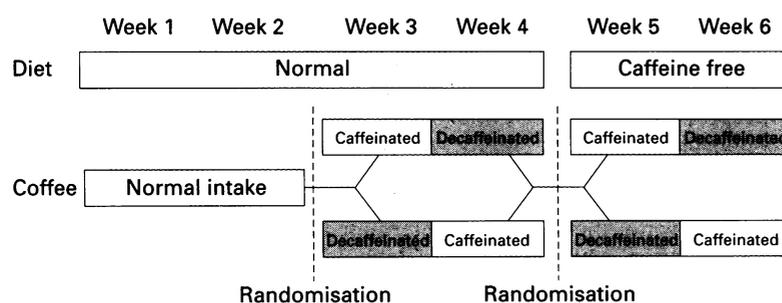


Figure 1 Six week treatment protocol.

DATA ANALYSIS

The VPB count was corrected to give an average count over 24 hours. Because of positive skew in the distribution of VPB counts and to achieve an approximately normal distribution, logarithmic transformation of counts was used in the subsequent analysis and discussion. The first two baseline VPB counts were used to determine repeatability as described previously.¹⁴

Data were analysed using Excel v5.0 (Microsoft). Where appropriate, correlation coefficients and two factor analysis of variance were determined for coffee consumption, serum caffeine concentrations, palpitation scores, and 24 hour VPB counts.

Statistical significance was taken at the 5% level and power calculations were determined for 90% probability. Where appropriate, results are expressed as the mean with standard errors of the mean in parentheses.

Results

Thirteen subjects were recruited into the study and their baseline characteristics are detailed in table 2.

CAFFEINE EXPOSURE

The mean weekly consumption of coffee was 50.1 (2.6) g. There was a significant correlation between coffee consumption and serum caffeine concentrations during the caffeinated coffee weeks ($r = 0.70$; $P < 0.001$). During the four intervention weeks, significant changes in serum caffeine concentrations were achieved ($P < 0.001$; fig 2). Two subjects had detectable caffeine concentrations during the caffeine-free diet/decaffeinated coffee week.

POWER AND REPEATABILITY OF BASELINE VPB COUNTS

The mean of the two baseline VPB counts was 2.63 (0.33). Excluding one outlier,¹⁴ the mean of the differences between the baseline counts was 0.00096 with a coefficient of repeatability of 1.0. This gives a 90% power of detecting a difference of 0.46 from the baseline mean of the VPB counts.

VPB COUNTS AND PALPITATION SCORES DURING THE INTERVENTION WEEKS

There were no significant differences across the four intervention weeks in the VPB counts, percentage change in VPB counts from the

Table 2 Baseline characteristics of study subjects

| Characteristic | Value |
|--------------------|-------------------------|
| Number | 13 |
| Sex | 12 f: 1 m |
| Age | 47.77 (3.46) yr |
| Coffee consumption | 3.96 (1.11) cups/day |
| Alcohol | 5.62 (2.38) units/wk |
| Smokers | 4 |
| Blood pressure | 135 (19)/79 (7.6) mm Hg |
| Serum cholesterol | 5.69 (0.24) mmol/l |
| Random glucose | 5.48 (0.30) mmol/l |
| Serum caffeine | 2.01 (0.35) mg/l |
| log [VPB count] | 2.63 (0.33) |

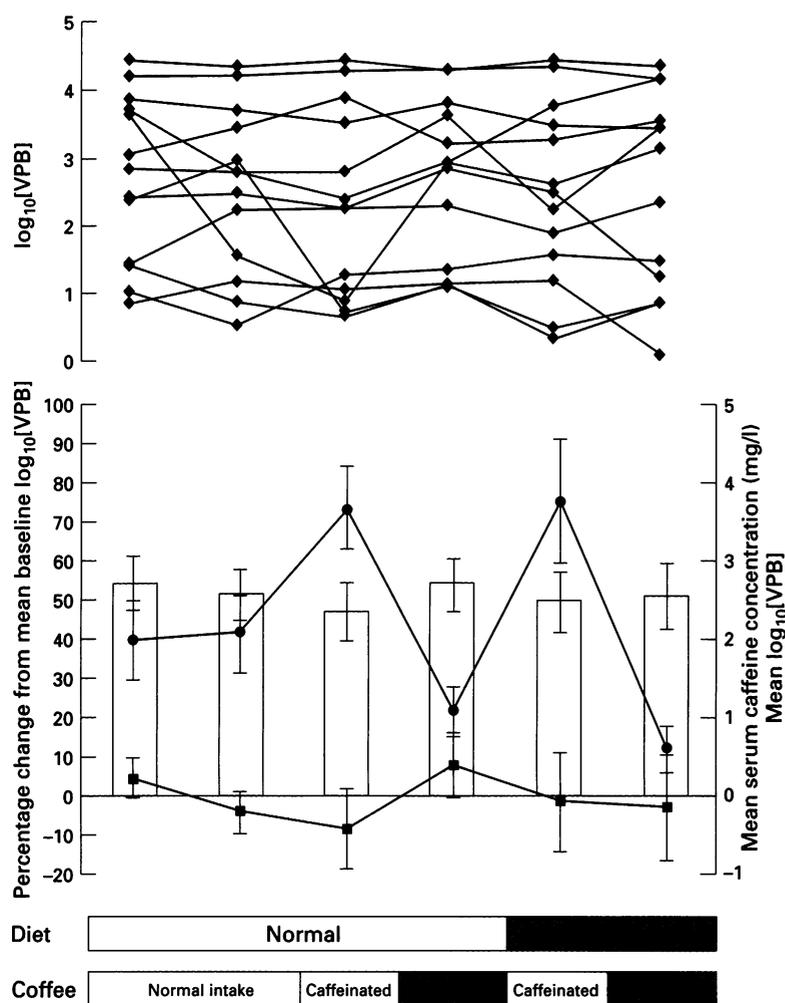


Figure 2 The upper panel shows individual VPB counts (diamonds) and the lower panel shows the mean VPB count (bars), the percentage change from the mean baseline VPB count (squares), and the mean serum caffeine concentration (circles) across the six week protocol.

baseline mean (fig 2), or palpitation scores. There were no significant correlations between serum caffeine concentrations and the VPB counts ($r = 0.04$; $P = 0.76$) or palpitation scores ($r = 0.07$; $P = 0.54$). However, the palpitation scores showed a significant correlation with the VPB counts ($r = 0.34$; $P = 0.003$).

Discussion

We believe that this is the first randomised, double blind trial which has assessed the efficacy of caffeine restriction in subjects with symptomatic palpitations secondary to idiopathic VPBs. The trial achieved effective and significant variations in serum caffeine concentrations and in agreement with Lelo *et al*,¹² showed a good correlation between serum caffeine concentrations and coffee consumption. Nonetheless we found no evidence to support an association between caffeine exposure and either the VPB frequency or the symptoms of palpitations.

The power of the study to detect a change of 0.46 (that is, 17.5%) in the mean VPB frequency refers to logarithmic data. This

equates to about a threefold shift in the mean of the arithmetic VPB counts which accords with earlier and much larger studies¹⁵ assessing the spontaneous variability of VPB frequency. The corollary of this is that we have achieved marked shifts in serum caffeine concentrations without a detectable effect on either the objective or subjective measures of palpitations. However, it must be conceded that a modest effect of caffeine on VPB frequency could pass undetected.

The exclusion of subjects with cardiac, hypertensive, and metabolic disorders (to define a precise study population) avoids potential confounding factors which could obscure an effect of caffeine on VPB frequency. Despite this, there remains a possible selection bias. Subjects referred to the clinic will tend to have more resistant and problematic palpitations; this could select against caffeine sensitive subjects. Nevertheless, this study has shown that in most patients referred to hospital with symptomatic idiopathic VPBs, caffeine restriction will result in no therapeutic benefit.

We therefore reject the rationale of curbing caffeine intake in these patients: to quote Graboys and Lown "The physician should take care not to diminish life's pleasures when there is no sound basis to do so, lest he or she be deemed a modern-day Savonarola".¹⁶

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