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ORIGINAL ARTICLE

Health effects of kava use in an eastern Arnhem Land Aboriginal community

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Abstract

Background: Heavy kava use in Aboriginal communities has been linked to various health effects, including anecdotes of sudden cardiac deaths.

Aims: To examine associations between kava use and potential health effects.

Methods: A cross-sectional study was carried out within a kava-using east Arnhem Land Aboriginal community in tropical northern Australia. One-hundred-and-one adults who were current, recent or non-users of kava were enrolled in March 2000. Main outcome measures were physical, anthropometric, biochemical, haematological, immunological and neurocognitive assessments.

Results: Kava users more frequently showed a characteristic dermopathy ($P < 0.001$). They had increased levels of γ-glutamyl transferase and alkaline phosphatase ($P < 0.001$). Lymphocyte counts were significantly lower in kava users ($P < 0.001$). Fibrinogen, plasminogen activator inhibitor-1 and neurocognitive tests were not different between kava use categories. IgE and IgG antibodies were elevated across the whole group, as were C-reactive protein and homocysteine.

Conclusions: Kava use was associated with dermopathy, liver function abnormalities and decreased lymphocytes. If kava continues to be used by Aboriginal populations, monitoring should focus on the health consequences of these findings, including a possible increase in serious infections. The interaction between kava, alcohol and other substances requires further study. Although markers of cardiovascular risk are increased across the population, these were not higher in kava users, and this increase may be linked to the large infectious pathogen burden reflective of the socioeconomic disadvantage seen in many remote Aboriginal communities. (Intern Med J 2003; 33: 336–340)

Key words: Aboriginal people, C-reactive protein, immunoglobulins, kava, substance-related disorders.

INTRODUCTION

Kava, the intoxicating drink prepared from crushed roots of the plant *Piper methysticum*, is widely used in South Pacific countries on ceremonial occasions and in secular drinking.[1] Its effects on health became contentious when it was introduced to Arnhem Land Aboriginal communities in 1982.[2–4] In late 1999 there were perhaps 1050 people using kava in Arnhem Land in eight community areas (A. Clough, unpubl. data, 2000).

A survey on kava use in Arnhem Land conducted in 1987 suggested additional health burdens to Aboriginal populations. Kava use was associated with scaly skin and users were more likely to be underweight. Users also had decreased lymphocytes with increased γ-glutamyl transferase (GGT), high-density lipoprotein (HDL)-cholesterol levels and decreased total protein, albumin, urea and bilirubin.[5]

Recently it was suggested that kava use may be a risk factor for sudden cardiac deaths among young Aboriginal sportsmen in Arnhem Land populations, especially when coupled with heavy alcohol use.[6,7] Possible mechanisms include abnormal coagulation with enhanced thrombosis, dehydration or arrhythmias. Other health risks for kava users include acute neurological effects[8] and the infectious disease melioidosis, which may be greater among heavy users.[9,10] The aim of the present study was to further investigate health effects of kava consumption in an Arnhem Land community in tropical northern Australia.

METHODS

A memorandum of understanding between the local Aboriginal community Council and Menzies School of Health Research guided the research. The Institutional Ethics Committee of the Menzies School of Health Research and Royal Darwin Hospital granted approval. All participants gave written informed consent. Study procedures were explained with the assistance of

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Aboriginal health workers. Clinicians in the study were blinded to kava-using status of participants.

Community surveillance estimated that 75% of men and 25% of women were kava users. From a population of 150 men and 189 women, we were able to opportunistically recruit 101 consenting adults, a mix of male and female subjects, approximately half were kava users. Exposure to kava use was assessed by self-report in interview compared with consensus classification by community health workers along with health clinic records using procedures already validated.[11] These were 38 current kava users (34 men, four women) who reported using kava at least once in the month prior to interview; 27 recent users (18 men, nine women) who had had their last drink of kava prior to 'last month'; and 36 people (13 men and 23 women) who reported that they had never used kava. Information was also collected on other substance use including alcohol, tobacco, petrol sniffing and cannabis.

Subjects were examined for the presence of kava dermopathy (a rash characteristic of heavy use), scabies, skin sores (pyoderma) and tinea. Skin sores and tinea were assessed and scored by counting the sites present,[12] with maximum scores of 18 for skin sores and 41 for tinea. Skin sores and tinea scores were categorized, respectively, into mild (0–2) and (0–10); moderate (3–7) and (11–20); and severe (7+) and (20+). Height and weight were measured and body mass index (BMI) calculated.[13]

Electrolytes, full blood count, urea, creatinine, liver function tests, lipids (non-fasting), serum folate, iron studies, homocysteine, fibrinogen, C-reactive protein (CRP) and plasminogen activator inhibitor-1 (PAI-1) were measured along with immunoglobulins and IgG subsets. Eosinophilia was defined as an eosinophil count of $>0.6 \times 10^9$/L. Serum osmolality was calculated.[14] Urine was tested using Boehringer dipsticks. Samples 'positive' for blood were sent for microscopy after adding formalin. Numbers and percentages above and below the normal range were calculated for current kava users (Tables 1,2).

Neuropsychological assessments utilized the touch-screen-based Cambridge Neuropsychological Test Automated Battery featuring minimum reliance on verbal skills.[15,16] Data were recorded as the proportion of correct responses. Ocular motor function was assessed with measures of latency and accuracy for prosaccades (towards target) and antisaccades (away from target) and an antisaccade error rate was calculated.

Statistical methods

Data were analysed using intercooled STATA (version 7; Stata Corporation, College Station, TX, USA). Variables were compared across the three groups using one way ANOVA or χ^2 (exact) tests. Positively skewed data were log-transformed before analysis.

RESULTS

A rash consistent with kava dermopathy was present in 45% of current kava users, 11% of recent users and 6%

Table 1 Kava use (parametric tests): laboratory findings, comparison of mean, low and high values

Blood tests	Current user Mean (SD)	Recent user Mean (SD)	Non-user Mean (SD)	*P*	*n* (%) below lower level Current user	*n* (%) above upper level Current user
Haemoglobin (g/L) M(132–170) F(115–155)	148 (13)	143 (15)	138 (15)	0.02	1 (3%)	1 (3%)
Haematocrit (PCV) (0.34–0.49)	0.5 (0.04)	0.4 (0.05)	0.4 (0.05)	0.04	0	7 (19%)
White cell count ($\times 10^9$/L) (4.0–11.0)	7.0 (2.8)	7.3 (2.4)	8.4 (2.1)	0.05	3 (8%)	4 (11%)
Lymphocytes ($\times 10^9$/L) (1.5–4.0)	1.6 (0.6)	1.8 (0.6)	2.2 (0.7)	<0.001	18 (51%)	0
Neutrophils ($\times 10^9$/L) (1.8–7.5)	4.6 (2.3)	4.5 (1.7)	4.9 (1.8)	0.60	3 (8%)	5 (13%)
Platelets ($\times 10^9$/L) (150–400)	246 (70)	242 (55)	285 (79)	0.02	1 (3%)	1 (3%)
Creatinine (μmol/L) M (<120) F (<95)	103 (16)	96.5 (15)	93 (20)	0.06		4 (11%)
Potassium (mmol/L) (3.4–5.5)	4.0 (0.3)	3.8 (0.2)	3.8 (0.3)	0.04	1 (3%)	0
Iron (μmol/L) M (12–31) F (11–27)	13.6 (6.4)	13.8 (5.5)	10.6 (4.9)	0.04	17 (47%)	1 (3%)
Osmolality (mmol/L) (280–300)	282 (6.4)	285 (5.3)	285 (5)	0.08	6 (17%)	0
Cholesterol total (mmol/L) (<5.5)	5.1 (0.9)	4.6 (0.8)	4.2 (0.7)	<0.001		10 (26%)
Low-density lipoproteins (mmol/L) (<3.4)	3.4 (0.9)	3.2 (0.7)	2.9 (0.8)	0.03		17 (57%)
Alanine transaminase (U/L) (<40)	24 (7)	29 (16)	27 (13)	0.15		0

†Not all parameters available for all subjects.
M, male; F, female; PCV, packed cell volume.

Table 2 Kava use (non-parametric tests): laboratory findings, comparison of median, low and high values

Blood tests†	Current user Median (range)	Recent user Median (range)	Non-user Median (range)	*P*	*n* (%) below lower level Current user	*n* (%) above upper level Current user
C-reactive protein (mg/L) (<10)	8 (2–34)	6 (0–20)	8 (3–38)	0.37		14 (37%)
δ-glutamyl transferase (U/L) M (<60) F (<40)	75 (14–257)	44 (16–195)	34 (7–184)	<0.001		23 (61%)
Alkaline phosphatase (U/L) (35–135)	133 (86–212)	113 (77–166)	109 (61–240)	<0.001	0	18 (47%)
Ferritin (ug/L) M (20–300) F (15–200)	105 (0–318)	94 (1–376)	70 (11–769)	0.16	2 (5%)	2 (5%)
Eosinophils ($\times 10^9$/L) (<0.6)	0.29 (0–1.4)	0.27 (1–1.8)	0.27 (0.1–2.3)	0.24		9 (24%)
IgE total (kU/L) (<20)	2439 (1498–8464)	2689 (1595–3010)	1786 (364–9784)	0.02		28 (100%)
IgG total (g/L) (6.1–13.0)	18.1 (14–27)	19.5 (14–27)	20 (16–30)	0.54	0	33 (100%)
IgG1 (g/L) (4.9–11.4)	13 (8–19)	14 (11–23)	13 (11–20)	0.27	0	22 (79%)
IgG2 (g/L) (1.5–6.4)	2.1 (0.9–3.8)	1.7 (0.9–3.3)	2.3 (0.3–4.1)	0.65	6 (22%)	0
IgG3 (g/L) (0.2–1.1)	0.3 (0.2–0.6)	0.2 (0.2–0.9)	0.3 (0.1–1.1)	0.88	4 (20%)	0
IgG4 (g/L) (0.08–1.4)	1.3 (0.1–6.5)	1.2 (0.1–1.6)	1.1 (0.4–4.7)	0.44	1 (3%)	11 (42%)
Homocysteine (μmol/L) (6.0–15.0)	10 (5–95)	10 (4–32)	11 (4–42)	0.50	1 (3%)	8 (22%)
HDL (mmol/L) M (>0.9) F (>1.1)	1 (0.6–2.1)	1 (0.6–1.8)	0.9 (0.5–1.4)	0.01	18 (47%)	
Triglycerides (mmol/L) (<2.0)	2.4 (0.9–6)	1.9 (1–4.9)	2.3 (0.6–5.4)	0.30		25 (66%)

†Not all parameters available for all subjects.

M, male; F, female; HDL, high-density lipoprotein.

of non-users ($P < 0.001$; Table 3). The two non-users with such a rash probably reflect incorrect clinical assessment rather than incorrect ascertainment of kava consumption. Scabies, skin sores and tinea were higher in current kava users but this was not statistically significant ($P = 0.52$, $P = 0.11$ and $P = 0.53$, respectively). Mean BMI was lower among kava users and a greater proportion of kava users (32%), compared with recent users (15%) and non-users (14%) had a BMI < 18.5, but more of the non-users were female. When female subjects were excluded there was still a trend for kava users to have lower BMI ($P = 0.062$).

There were no differences in neutrophils, monocytes and eosinophils across the categories of kava use. Of the group as a whole 25% had an eosinophilia. Lymphocyte numbers were significantly lower (Tables 1,2) in current and recent kava users ($P < 0.001$), with 51% of users having a level below the normal range.

Creatinine levels tended to be higher among kava users ($P = 0.06$) but there was no difference in calculated glomerular filtration rate (data not shown). The following parameters showed no association with kava use: urea, sodium, bicarbonate, chloride, inorganic phosphate, calcium, uric acid, serum folate, fibrinogen and PAI-1 (data not shown).

Cholesterol was significantly higher for current kava users: 28% were over 5.5 mmol/L compared with 11% for recent users and 11% for non-users. This remained significant when comparing only male subjects. Interestingly both HDL and low-density lipoprotein (LDL) were significantly higher in current kava users. Triglycerides were not significantly different between the groups.

Serum osmolality was not significantly different across the kava categories, although 17% of current kava users had values lower than normal. The presence of dipstick positive 'blood' was confirmed as true haematuria by microscopy in only one of 24 cases.

Levels of GGT and alkaline phosphatase (ALP) were above the normal range in 61% and 50% of kava users, respectively. When data were log-transformed current users had significantly higher GGT and ALP than recent users and non-users (Tables 1,2). However there were no differences between the groups in alanine transaminase (ALT), bilirubin, albumin or total protein.

IgE was elevated in every individual tested from the community and levels were significantly higher in current and recent kava users ($P = 0.02$). Total IgG levels (median: 18.1 g/L) were also all above normal but were not different between the groups. Elevated IgG1 and IgG4 were responsible for the high levels (Tables 1,2).

CRP and homocysteine were elevated in 36% and 16% overall, with no difference across the categories of kava use. No significant differences were found for any of the ocular motor or neuropsychological assessments across the groups.

Kava use was associated with alcohol use ($P < 0.001$), cannabis use ($P < 0.001$) and a history of petrol sniffing ($P = 0.035$). Both cannabis and alcohol use remained significant when comparing only male subjects. There

Table 3 Kava use: demographic characteristics

Outcome measure	Current user $n = 38$	Recent user $n = 27$	Non-user $n = 36$	*P*	*n* (%) below lower level Current user	*n* (%) above upper level Current user
F/M	4/34	9/18	23/13			
Physical assessments						
Age: mean (SD)	35.2 (9.3)	37.6 (11.8)	36.5 (13.5)	0.72		
Kava dermopathy (%)	17 (45%)	3 (11%)	2 (6%)	<0.001		
Scabies: median (range)	3 (0–11)	2 (0–6)	2.5 (0–8)			
Tinea score: median (range)	14.5 (2–30)	13 (1–27)	11 (0–25)	0.56		
Skin sores score: median (range)	3 (0–11)	2 (0–6)	2.5 (0–8)	0.12		
Body mass index (kg/m^2): mean (SD)	20.8 (4.2)	21.6 (3.3)	23.4 (4.8)	0.02	12 (32%)	3 (8%)
Other substance use						
Tobacco	31 (82%)	21 (78%)	22 (61%)	0.07		
Alcohol	17 (45%)	11 (41%)	0 (0%)	<0.001		
Cannabis	14 (37%)	13 (48%)	3 (8%)	<0.001		
Petrol sniffing history	14 (37%)	9 (33%)	4 (11%)	0.03		

F/M, female/male.

was a trend for kava users to be tobacco smokers ($P = 0.076$).

DISCUSSION

The study community is nominally 'dry' (alcohol is prohibited), although retail outlets are located nearby so illicit drinking occurs. There is concern that poly-substance abuse is increasing in many Aboriginal communities. In the present study, 82% of current kava users smoked tobacco, 45% drank alcohol, 37% used cannabis and 37% had a history of sniffing petrol. In the study by Mathews *et al.* alcohol was a confounding factor,[5] which may have contributed to the abnormal liver function tests. However, in the present study there was a lack of association between alcohol use and GGT and ALP (data not shown). Furthermore, several people with abnormal liver function were heavy kava consumers but did not drink alcohol.

Although there is currently no evidence for long-term liver damage in regular kava users, this requires assessment over longer periods, especially in heavy users. Furthermore, the nature of the abnormal liver function tests we observed remains to be elucidated. Elevated GGT and ALP suggests the possibility of an obstructive rather than an inflammatory pattern of response. In Aboriginal people who cease kava drinking, abnormal liver function tests return to normal after 1–2 months of abstinence from kava use[17] (B. Currie, unpubl. data, 2002). Importantly, the absence of an elevated ALT suggests that in contrast with alcohol, acute inflammation may not be occurring with kava use. However, recent case reports of fulminant liver failure associated with use of commercially available kava-based anxiety treatments in Europe[18] have resulted in kava-based herbal products being withdrawn from sale in several countries. This supports the need for further research into the effects of kava on the liver.

The more frequent occurrence of abnormally low lymphocyte levels coupled with higher IgE levels in current and recent kava users are suggestive of an immune system response. Elevated IgE and IgG levels in the whole population are likely to reflect recurrent and chronic bacterial and parasitic infections. The increases in IgG1 and IgG4 are consistent with combined bacterial and parasitic burdens, and elevated IgE levels and eosinophil counts in the whole group are likely to reflect the burden of intestinal parasites seen in remote Aboriginal communities.[19] It is possible that the association of heavy kava use with melioidosis[9,10] may reflect increased exposure to the wet season environmental pathogen *Burkholderia pseudomallei* during prolonged sessions of sitting in a kava circle consuming kava. Increased parasite exposure in kava drinkers could also explain higher IgE levels if they reflect a larger burden of geohelminths such as *Ancylostoma duodenale* and *Strongyloides stercoralis*. But the consistently lower lymphocyte counts in kava drinkers in this and the previous study[5] warrant concern about a kava-related immunological predisposition to certain infections such as melioidosis,

for which diabetes and alcohol excess are known major risk factors.[8,10]

Functional equivalence of neurocognitive assessments across the groups suggests little if any deleterious effect on the central nervous system. This is in contrast to abnormalities found in petrol sniffers[16] and heavy alcohol users.[20]

Fibrinogen and PAI-1 are considered important markers of potential thrombotic predisposition. There was no association of these parameters with kava usage. In addition, lipid profile was not clearly suggestive of increased atheroma risk, with HDL being elevated as well as cholesterol and LDL. The generally elevated levels of CRP across the population studied suggest a chronic systemic inflammatory response, possibly reflecting increased exposure to various infectious pathogens. CRP is now recognized as an important marker of cardiovascular risk and reflects possible pathogenetic processes, which may relate to specific organisms or to general pathogen burdens.[21,22] However, the CRP was not related to kava use and neither were homocysteine levels, another cardiovascular risk marker, which were also generally elevated.

In conclusion, some health effects of kava use such as abnormal liver function, kava dermopathy and decreased lymphocytes were observed in the present study. Monitoring these parameters will be useful as changes occur in licensing and distribution of kava. Further research is required to address concerns about possible associations of heavy kava use in Arnhem Land with various infectious diseases, especially melioidosis. Some of our results were confounded by concomitant alcohol use and the effects of using kava in combination with other substances requires further analysis. The general increase in IgE and IgG levels and CRP reflect the burden of infectious pathogens associated with the continuing socioeconomic disadvantage of those living in remote Aboriginal communities. Elevated CRP is increasingly recognized as a marker of risk for cardiovascular disease, and the generally high levels of CRP and homocysteine across all groups in this Aboriginal community are of great concern.

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