Case Report

Caffeine and clinical change in a patient with schizophrenia on a long-stay ward

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Abstract

We report a case of a 33-year-old male patient with schizophrenia, who showed significant and persistent changes in psychotic and mood symptoms relating to his caffeine intake.

Key words: Caffeine; Schizophrenia; Psychosis; Affect.

Introduction

Caffeine is the most widely consumed psychoactive substance in the world with mean daily consumption in the UK at 350-620mg. It is estimated that over 80% of adults consume caffeine regularly throughout the world.[1] Amongst psychiatric population, caffeine intake was highest in those with schizophrenia and lowest in anxiety and depression.[2,3] Its general physiological effect on central nervous system is well recognised and studied, however studies of caffeine's clinical effect on patients with schizophrenia has produced mixed results. Here we present a case of a 33-year-old male with schizophrenia who showed significant and persistent changes in his clinical state which were closely related to his caffeine intake.

Case report

Mr JM is a 33-year-old male whose current involuntary admission dates from April 2004. He has a diagnosis of paranoid schizophrenia (F20.1), which was made in 1998. His schizophrenia is treatment resistant. He remains in a floridly psychotic state. He has a medical history of obesity, hypertension, hypercholesterolemia, angina – with numerous positive exercise tolerance tests – and an adverse reaction (pseudophaeochromocytoma-like-reaction) to clozapine in 2005. His forensic history includes a two-year probation order for drunk and disorderly behaviour aged 14 and a serious assault on both parents in 2001. This assault was driven by his delusions and command hallucinations. In addition to his medications for his medical conditions, he is currently prescribed risperidone, sodium valproate, and procyclidine. He smokes on average 15 cigarettes a day with no alcohol intake. He has past history of substance abuse with alcohol, magic mushroom, amphetamine, and heroin but most notably with cannabis. However, he has no current illicit substance consumption as confirmed by regular urine drug screening on the ward.

His caffeine intake has always been noted to be high on the ward. Patient and collateral history indicates at least six litres of diet coke and nine to 10 cups of tea a day (equivalent to approximately 1050mg of caffeine intake a day).

While Mr JM was consuming such amounts of caffeine daily, he was noted to be floridly psychotic with marked positive symptom along with hypomanic traits. His typical mental state examination was described in terms such as "laughs inappropriately", "over-talkative at times with some flight of ideas", "irritable", "mood objectively mildly hypomanic", "bizarre delusions such as believing he can see the devil who he calls 'Stretch' and his imaginary girlfriend 'Maria'", "active visual and auditory hallucinations", and "ideas of reference also noted" by nurses and doctors alike.

Due to his morbid obesity (BMI of about 40) and high cardiovascular risk, a dietary advice and behavioural programme was instituted. Subsequently he completely stopped his intake of soft drinks and put in place regular exercise routines in the form of brisk walks around the hospital grounds.

After this change he continued to drink moderate amount of tea – around five to six cups a day (equivalent to estimated 165mg of caffeine intake a day). This was an almost 85% reduction in his daily caffeine consumption.

Coinciding to this change, there was significant changes in his mental state. The most notable change in his clinical presentation was the dramatic reduction in irritability and psychotic symptoms. He still reported ongoing hallucinatory experiences but they were less intense and frequent, stating "I still hear voices sometimes but I just let them talk and I ignore them", and he stated delusions were much weaker. In regard to his beliefs about 'Stretch' and 'Maria', he reported "they don't bother me anymore". Mr JM is noted to be overall much calmer and more settled on the ward. Over this period there was no change in his medications or other significant changes in his social and personal circumstances. The only other variables were a reduction in his weight and an increase in exercise.

This change in his clinical presentation has been consistent to this date in that he is noted to be more 'irritable', 'hypomanic', and 'psychotic' when he relapses into excessive caffeine consumption, and symptoms ameliorate once again with reduction in caffeine intake.

Objective with a literature review

We made a literature search to find out if there was any well established evidence for observations made in this patient case. We searched MEDLINE with full text, CINAHL Plus with Full Text and PsycINFO on June 3, 2009, using terms 'psychosis', 'schizophrenia', 'schizoaffective disorder', 'caffeine' with limits of 'English language', 'case reports', 'clinical trials' 'reviews', 'randomised control trial' and 'meta analysis'. This search produced 15 articles. Out of these 15

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articles, one was a duplication result, another was a general psychiatry textbook, one was a case report of use of caffeine in idiosyncratic reaction to morphine in a patient with schizophrenia and lastly a case series of use of caffeine in patients with schizophrenia to test role of narcosis in projective tests. Out of the remaining eleven articles, six were case studies and three were review articles. There was only one double-blind placebo-controlled clinical trial. There was also one cross-sectional survey. Some of the referenced materials in these articles that were deemed pertinent were also sought for closer inspection.

Discussion

There have been studies indicating that schizophrenic patients on average have higher caffeine intakes than other psychiatric patients.[2,3] Different hypothesis are present to explain such observations. These include ideas such as schizophrenic patients may use caffeine to combat apathy or boredom or to offset the sedating effects of antipsychotic medications.[4] This pattern of high caffeine usage in schizophrenic patients is particularly worrying as it is well recognised that caffeine produces de novo psychotropic effects, and based on this, it is postulated that caffeine may worsen various existing psychiatric illnesses.[5,6]

The exact mechanism of the physiological effects of caffeine on the human body continues to be explored. It is postulated that it possibly acts on benzodiazepine receptors[7] as well as inhibits phosphodiesterase and catecholamine metabolism.[5,8] But the most notable effects are through competitive antagonism at adenosine A1 and A2A receptors.[9-11] Hyperdopaminergic effect of caffeine is modulated, in part, by caffeine acting as a competitive antagonist at the A2A adenosine receptor on the same postsynaptic neurons as the D2 dopamine receptor whereby it decreases the adenosinergic tone, which in turn increases the affinity of D2 receptors for dopamine.[9] Furthermore this state is enforced by increased release of dopamine in striatal area where it is normally under tonic inhibition by adenosine acting on presynaptic A1 receptors.[10]

The double-blind placebo-controlled study of behavioural effects of caffeine in 13 schizophrenic patients by Lucas et al[12] shows how this physiological finding may be converted into our clinical settings in our patient group. Hence it is not surprising to find that there are many case reports of caffeine consumption precipitating psychotic symptoms in schizophrenic patients as well as subjects with no previous psychiatric history.[13-15]

Nevertheless this finding has not been consistently replicated in slightly bigger clinical studies. Hughes et al[4] cites three cross-over studies which looked at the relationship between caffeine consumption and psychotic symptoms in schizophrenic inpatients. Findings in these three studies were not consistent and all of them failed to show any clinically significant changes. However there are many confounding factors that may have obscured the results in these studies, including caffeine's interaction with antipsychotics and cigarette smoking – both interact with P450 CYP1A2 isoenzymes.[4,16]

Caffeine can increase the serum levels of antipsychotics like olanzapine and clozapine whose metabolism is mostly dependent on CYP1A2 and UGTs (UDP-glucuronosyltransferases). Caffeine is also mainly metabolised by CYP1A2 thus by means of competitive inhibition, caffeine consumption can increase serum levels of some antipsychotics, which in turn would produce clinical improvement and/or exacerbate side-effects of these medications. Thus depending on the antipsychotics patients were on, the clinical picture may have been influenced indirectly by this drug-caffeine interaction. On the other hand, this interaction may also have influenced medication dosage in certain patients – due to more pronounced side effects – therefore making them more prone to changes in clinical states with fluctuating levels of caffeine depending on their daily consumption. However this is probably less likely to occur with olanzapine than clozapine as it has a wider therapeutic window.

Cigarette smoking may also have confounded their results as by-products of smoking – particularly the polycyclic aromatic hydrocarbons – are inducers of CYP1A2 and UGTs. Therefore increased level of cigarette smoking can reduce serum level of caffeine as well as some of the atypical antipsychotics, which consequently may influence a patient's clinical state.

Interpersonal variability in sensitivity to caffeine consumption cannot be underestimated either. In fact, a recent study showed that genetic influence on caffeine metabolism accounted for about 70% of the variability.[17]

Therefore it is plausible that there is a subgroup of patients who are particularly vulnerable to the effect of caffeine – both due to environmental factors and genetic predisposition. This may explain why many of the cross-over studies show inconsistent findings. Such studies would have contained heterogeneous groups of patients with variable vulnerability to the effects of caffeine thus reducing the power to detect any differences.

Another important confounding factor is the effect of other licit and illicit substance misuse by patients with schizophrenia. The ECA study had revealed that 47% of patients with schizophrenia misuse substances.[18] Nicotine was the most commonly used substance – caffeine use was not measured in this study – followed by alcohol, cannabis and cocaine. It is postulated that there will be a mixture of common and drug-specific factors that would explain the association between schizophrenia and substance misuse. It is also widely accepted that acute psychotic symptoms are frequently observed in intoxication states with certain substances such as cocaine, methamphetamine, and cannabis. Amphetamine-type stimulants are now used to help researchers to understand the neurobiological process that underlie psychosis.[19]

Longitudinal studies have now established that the early heavy exposure to cannabis as an independent risk factor for developing schizophrenia.[20,21] Numerous reviews have also consistently shown that there are increased rates of relapse and non-adherence in patients with schizophrenia who use cannabis. Nevertheless there is insufficient evidence to support the notion that these outcomes were specifically due to cannabis use.[21,22] Moreover there is limited understanding of neuropathological relationship between cannabis and schizophrenia although it is believed that there is a significant gene-environment interplay.[23,24] Vulnerability factor(s) that may mediate these effects await further investigations.

In the case of Mr JM, we were reasonably confident that

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he had no current illicit substance use problems which could confound the clinical picture, as this was corroborated by general observation, collateral history and frequent urine drug screening. Of note, his last positive urine drug result was in 2004.

Reduction in caffeine intake was not the primary goal in his management plan. His withdrawal from caffeine was achieved with relative ease through implementation of an effective behavioural programme to lose weight through diet control and physical activation. Mr JM did not have any withdrawal symptoms and it is interesting to note that in many of the case reports, significant reductions in caffeine intake were achieved with no apparent complications in most cases.[13-15] This may be explained by the fact that caffeine appears to be mildly addictive at best, unlike other truly addictive substances such as alcohol and heroin.[25,26]

Conclusion

The remarkable change in mental state we observed in Mr JM has been similarly replicated in many other case reports. Although higher level clinical evidence is lacking, many studies have provided insights into possible physiological basis for the putative action of caffeine in patients with mental illness as well as in healthy subjects. Therefore we suggest that caffeine intake should be questioned routinely as with other substance uses in all psychiatric assessments.

As caffeine continues to be the most widely used and most widely available psychoactive substance in the world,[1,25] with particularly high usage noted in psychiatric patients,[2,3] its psychotropic effects in schizophrenic patient deserves further evaluation.

Future studies should consider the importance of genetic polymorphism in its study design. A randomised double-blind placebo-controlled study design would be preferred to cross-over study design as this may help to overcome many of the confounding factors discussed above.

Declaration of Interest: None.

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