Impact of a Caffeine Restriction Policy on Inpatients With Schizophrenia

A Pre-Post Comparison Using Electronic Health Records

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Abstract:

Background/Purpose: Caffeine is the most commonly used psychostimulant worldwide. Although its large intake is suspected to worsen psychotic symptoms because of increasing dopamine neurotransmission, schizophrenic patients are heavier caffeine consumers than the general population. This study aims to assess the impact of a caffeine restriction policy in a psychiatric hospital on patient psychopathology, hospitalization characteristics, and psychotropic prescribing patterns.

Methods: It is a retrospective cross-sectional study based on electronic health records of a psychiatric hospital in the French-speaking area of Belgium. Two different periods were compared, the first (n = 142), in 2017, when caffeine was available in the institution and the second (n = 119), between November 2018 and November 2019 after the restriction of access to caffeine was implemented. Adult inpatients with schizophrenia or schizoaffective disorder admitted for an acute hospitalization were included. Antipsychotic exposure, benzodiazepine daily dose, Global Assessment of Functioning scores, length of hospital stay, and some other factors were tested for their potential association with the decaffeinated period.

Results: After adjusting for potential confounders, reduced caffeine availability inside the hospital was significantly associated with higher Global Assessment of Functioning scores at discharge (adjusted odds ratio [aOR] = 2.86, 95% confidence interval [CI] = 1.77–4.62) and shorter hospital stays (aOR = 0.68, 95% CI = 0.47–0.99) but was not associated with change in antipsychotic exposure at discharge (aOR = 1.04, 95% CI = 0.64–1.7) or benzodiazepine daily dose (aOR = 0.89, 95% CI = 0.61–1.29).

Conclusions: Limiting access to caffeine in psychiatric hospitals is a simple and inexpensive intervention that should be promoted, especially for patients with schizophrenia.

Key Words: schizophrenia, schizoaffective disorder, caffeine, antipsychotics, psychopharmacology, benzodiazepines

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Caffeine, the main active substance of coffee, tea, and cola sodas, is the most widely used psychostimulant drug worldwide.[1]

Although a similar proportion of the general population and the population with schizophrenia are regular caffeine consumers, caffeine intake is heavier among schizophrenic individuals.[2] Motivations evoked to underlie this large use among inpatients include boredom during hospitalizations and appetence for a stimulating effect to balance the sedative properties of most psychotropic drugs.[3]

The major mechanism of action of caffeine is the antagonism of adenosine receptors A_1 and A_{2A}. These receptors influence glutamatergic and dopaminergic neurotransmissions, the 2 main systems that are affected in schizophrenia. Caffeine increases dopaminergic transmission and might worsen symptoms of schizophrenia.[4]

Several cases have been reported on patients with stable schizophrenia who experienced worsening hallucinations or delusions after having increased their daily consumption of caffeine.[5–8] In a previous trial, the intake of 10 mg/kg of caffeine in stable schizophrenic patients resulted in worsening of symptoms.[6] In most cases, symptoms resolved by reducing the amount of caffeine intake without modifying the medication regimen.[5,7,8] In addition, de novo psychotic or manic symptoms have also been reported after excessive caffeine consumption in patients without any history of psychotic illness.[7,9]

Impact of reducing caffeine intake on symptoms of schizophrenia has received limited attention, and current evidence comes from small sample size studies.[10,11] To the best of our knowledge, no real-world observational study has never been described. Impact of caffeine reduction on the prescription of psychotropic medications, considering potential confounding factors, is unknown.

At Hôpital du Beau Vallon, a large Belgian psychiatric hospital, caffeinated sources have been replaced by decaffeinated beverages in the hospital in mid-2018. This context allows for a naturalistic evaluation of the impact of a caffeine withdrawal policy on inpatients experiencing schizophrenia or schizoaffective disorder.

The aim of this study was to investigate the evolution of patient symptoms, hospitalization characteristics, and psychotropic prescribing patterns after the withdrawal of caffeine availability inside a hospital.

MATERIALS AND METHODS

It is a retrospective cross-sectional study before and after the implementation of a caffeine withdrawal policy in a psychiatric hospital.

The exposed group includes all inpatients hospitalized in 2017 and entering the inclusion criteria. The year 2017 is the last year when caffeine was still available inside the hospital. The group without caffeine includes inpatients hospitalized in the same hospital between November 1, 2018, and November 1, 2019, and meeting the inclusion criteria. Inclusion criteria are adult inpatients (ie, 18–65 years

old) with a diagnosis of schizophrenia or schizoaffective disorder (ie, *Diagnostic and Statistical Manual of Mental Disorders*, *Fifth Edition*, 295.xx)[12] and admitted to the psychiatric hospital for an acute hospitalization (ie, less than 1 year). If a patient was hospitalized more than once during the study period, only data from the last hospitalization were collected.

Data collected in our previous study were used for the control group (ie, without caffeine available).[13] Data of the exposed group (ie, with caffeine available) were collected between January and April 2022 from electronic health records and the hospital prescribing software. The study protocol was approved by the ethics committee of the Beau Vallon hospital.

The GAF scores (ie, Global Assessment of Functioning scale) and mean length of hospital stays were tested for their potential association with caffeine withdrawal, after adjusting for potential cofactors. The GAF scale ranges from 0 to 100 and aims at evaluating the overall psychopathological state of mentally ill patients, with 0 being the most severe and 100 the best global functioning.[14] In Belgium, psychiatrists are required to assess each patient admitted to a psychiatric unit with the GAF scale, both on admission and at discharge, making these scores available in each patient's medical record.

Prescribing patterns of antipsychotics and benzodiazepine receptor agonists (BZRAs), prevalence of patients receiving an antipsychotic "as needed" during their hospitalization, and number of antipsychotics at discharge were also tested. Antipsychotic exposure is expressed as the ratio of the prescribed daily dose to the defined daily dose of the World Health Organization. Antipsychotics were identified using the Anatomical Therapeutic Chemical group N05A, with the exclusion of lithium (ATC N05AN01). The mean BZRAs daily dose during the stay was calculated using a lorazepam equivalent dose based on the Belgian official compendium (CBIP/BCFI).[15]

Type of potential confounders considered in the model include demographic and individual factors (eg, age, sex, smoking habits, intellectual disability), hospitalization characteristics (eg, involuntary admission), and pharmacologic treatment (eg, type and route of antipsychotics).

Multivariable logistic regression with multiple imputation for missing data was performed to detect factors associated with no availability of caffeine inside the hospital, in which *P* values less than 0.05 were considered statistically significant. The statistical analyses were performed using R software version 4.0.3.

RESULTS

Sociodemographic characteristics were similar between the group of patients with available caffeine (n = 142) and the group without caffeine (n = 119), with a mean age of 43 years (SD, 12 years) in both groups, 31.4% (n = 44) and 31.9% (n = 38) of the patients living in a residential facility ($P = 0.082$), and 56.9% (n = 74) and 59.7% (n = 59.7) having a legal guardian, respectively ($P = 0.701$; Table 1).

After adjusting for potential confounders, reduced caffeine availability inside the hospital was significantly associated with a higher GAF score at discharge (adjusted odds ratio [aOR] = 2.86,

TABLE 1. Characteristics of the 2 Populations, During the Period With Caffeine Fully Available and After the Restriction of Access to Caffeine

	Group With Caffeine (n = 142)		Group Without Caffeine (n = 119)		*P* Value
Characteristics	**n**	**%**	**n**	**%**	
Sociodemographic characteristics					
Male	9	6.3	13	10.9	0.263
Female	133	93.7	106	89.1	0.263
Age, mean (SD), y	43	12	43	12	
Living situation					0.082
Residential facility	44	31.4	38	31.9	
Homeless	2	1.4	8	6.7	
Living alone or with relatives	94	67.2	73	61.4	
Legal guardian	74	56.9	71	59.7	0.701
Unemployed	126	90	111	93.3	0.38
Comorbidities					
Tobacco smoking	68	49.3	70	58.8	0.134
Alcohol use disorder	56	40.3	22	18.5	**<0.001**
Substance use disorder	46	32.9	26	21.8	0.053
Intellectual disability	29	20.7	18	15.1	0.262
Hospitalization characteristics					
Involuntary admission	48	33.8	29	24.4	0.104
Length of hospital stay, median (IQR), d	42	17–95	42	18–83	0.739
GAF score admission, mean (SD)	36	13	33	12	0.107
GAF score discharge, mean (SD)	40	13	45	12	**0.005**
Primary diagnosis					0.599
Schizophrenia	102	71.8	81	68.1	
Schizoaffective disorder	40	28.2	38	31.9	

$P < 0.05$, in bold, are considered significant.

IQR, interquartile range.

95% confidence interval [CI] = 1.77–4.62) even though a lower GAF score on admission was significantly associated with the group with restricted access to caffeine (aOR = 0.42, 95% CI = 0.26–0.67).

A shorter length of hospital stay was also significantly associated with the decaffeinated period (aOR = 0.68, 95% CI = 0.47–0.99).

However, reduced in-hospital caffeine availability was not associated with a change in antipsychotic exposure at discharge (aOR = 1.04, 95% CI = 0.64–1.7) and BZRA daily dose (aOR = 0.89, 95% CI = 0.61–1.29).

Removing caffeinated beverages did not reduce the odds of receiving an "as needed" antipsychotic during the stay (aOR = 1.17, 95% CI = 0.46–2.97) or change the number of antipsychotics per patient at discharge (aOR = 0.67, 95% CI = 0.36–1.24; Table 2).

DISCUSSION

After adjusting for potential confounding factors, a higher GAF score at discharge, reflecting a better psychopathological state of patients, was significantly associated with the decaffeinated period. As this group was also significantly associated with a lower GAF score on admission, it reflects an even greater improvement in GAF scores over the course of hospitalizations in the decaffeinated group than in the caffeinated one. It confirms previous findings of improvement in symptoms of schizophrenia by reducing access to caffeine in a hospital.[10,11]

In addition, a shorter duration of hospitalization was also associated with the period of restricted access to caffeine, indicating that patients tend to show a more rapid symptom improvement when caffeine is not readily available in the hospital facility.

However, implementation of the decaffeinated beverage policy did not lead to a reduction in antipsychotic exposure at discharge. This finding is surprising, knowing that caffeine consumption is suspected to worsen symptoms of schizophrenia and that switching to decaffeinated beverages reduces psychotic symptoms.[6,10,11] Different hypotheses can be made. First, antipsychotics are seldom deprescribed during a hospital stay, as we have previously shown, and antipsychotic drug regimens at discharge might thus not thoroughly translate patients' symptoms severity.[13] Second, our methodology differed from previously published studies, which were interventional trials aimed at testing symptom changes with detailed scales (eg, Brief Psychiatric Rating Scale). Only one study also monitored prescribing patterns by recording changes in the number of "as needed" antipsychotics and anxiolytics. This study did not find any reduction in the use of psychotropic medication after caffeine withdrawal, although it did show a diminution of psychotic symptoms.[11] This finding confirms the existence of a gap between symptom modification and re-evaluation of prescribing patterns. Finally, our setting was different from the previously mentioned trials. Indeed, one study was conducted in a closed ward only, where no supply of caffeine coming from outside could occur, whereas our study included both open and closed wards.[10] Assuming that only high quantities of caffeine can change the severity of symptoms sufficiently to result in a revision of the daily dose of antipsychotics at discontinuation, and that heavy consumers presumably find

TABLE 2. Factors Associated With Reduced Caffeine Availability Inside the Psychiatric Hospital in Patients With Schizophrenia, in a Multivariable Regression Model

Variables	aOR	95% CI	*P*
Patients characteristics			
Age	0.82	0.5–1.33	0.415
Female	0.38	0.12–1.15	0.087
Tobacco smoking	2.87	1.44–5.72	**0.003**
Alcohol use disorder	0.22	0.10–0.47	**<0.001**
Substance use disorder	0.5	0.22–1.15	0.101
Intellectual disability	0.77	0.33–1.79	0.544
Unemployed	2.02	0.69–5.97	0.202
Legal guardian	1.18	0.6–2.32	0.638
Homeless	9.36	1.42–61.58	**0.02**
Antipsychotic treatment			
Antipsychotic exposure* at discharge	1.04	0.64–1.7	0.863
At least one LAI at discharge	2.32	1.22–4.42	**0.01**
At least one FGA at discharge	1.57	0.69–3.55	0.279
As needed antipsychotic during the stay	1.17	0.46–2.97	0.742
No. antipsychotics at discharge	0.67	0.36–1.24	0.202
Hospitalization			
Involuntary admission	0.47	0.23–0.97	**0.04**
GAF score admission	0.42	0.26–0.67	**<0.001**
GAF score discharge	2.86	1.77–4.62	**<0.001**
Length of hospitalization	0.68	0.47–0.99	**0.045**
Cotreatment			
Daily dose of BZRAs	0.89	0.61–1.29	0.53
Diagnosis			
Schizoaffective disorder	1.27	0.66–2.46	0.479

$P < 0.05$, in bold, are considered significant.

*Antipsychotic exposure is expressed as the ratio of the prescribed daily dose to the defined daily dose of the World Health Organization.

FGA, first-generation antipsychotic(s); LAI, long-acting injectable antipsychotic(s).

their way to caffeinated beverages even when not available in the hospital, this may have overshadowed the effect.[2]

Exposure to BZRA during the stay was also not significantly reduced by the new decaffeination policy. As caffeine has an anxiogenic effect, the administration of anxiolytics was expected to be lowered by its eviction.[16] However, acutely admitted patients with schizophrenia are often agitated and require sedative medications such as short-term benzodiazepines.[17] The effect of caffeine withdrawal on anxiety might therefore be more visible in stable patients without acute exacerbations.

Potential limitations may be considered for the interpretation of these findings. Daily caffeine intake could not be monitored, as caffeine plasma concentrations are not routinely measured. However, it has been previously demonstrated that restricting access to caffeine inside a hospital lessened the daily intake of patients.[11] In addition, it cannot be excluded that shorter hospital stays are the result of a new healthcare policy, but the 2 periods were chosen very close to each other to avoid a possible bias induced by a change in hospital policy. Finally, although caffeine is a potential competitive inhibitor of CYP1A2, the effect of caffeine withdrawal on plasma concentrations of antipsychotics could not be quantified because of lack of availability. Indeed, in Belgium, therapeutic drug monitoring of antipsychotics is not performed in clinical routine. However, only clozapine and olanzapine are primary metabolized by the CYP1A2,[18] which does not affect the pharmacokinetics of all other antipsychotics investigated. Furthermore, removal of this potential drug-drug interaction would have lifted the inhibition, which could have lowered the plasma concentration of clozapine and olanzapine[19] and, if clinically significant, resulted in worsening of patients' symptoms. Despite this, as higher GAF scores were significantly associated with the decaffeinated period, this reflects a potentially even stronger pharmacodynamic effect of caffeine suppression on patients with schizophrenia, and further supports our results.

In conclusion, improvement in the psychopathological state of patients and reduction of the length of hospitalization supports the limitation of caffeine availability inside psychiatric hospitals, especially for patients suffering from schizophrenia spectrum disorders.

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AUTHOR DISCLOSURE INFORMATION

M.F. is currently an employee of UCB Pharma S.A., which had no role in the study design, collection, analysis or interpretation of the data, writing the manuscript, or the decision to submit the manuscript for publication. The other authors declare no conflicts of interest.

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The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available because of privacy and ethical restrictions.

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