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Psychopathological differences in schizophrenia associated with amphetamine use in a sample of male Saudi patients

Psychopatologiczne różnice w objawach schizofrenii związane z używaniem amfetaminy – badanie na próbie saudyjskich pacjentów płci męskiej

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Abstract

Introduction: Amphetamine use is a significant problem around the world and is common in psychiatric patients. Very few studies in Saudi Arabia have addressed the effect of amphetamine on the psychopathology of schizophrenic patients. The study aimed to assess any psychopathological differences in schizophrenia associated with amphetamine use in male Saudi patients at Mental Health Hospital, Taif, Saudi Arabia.

Material and methods: All male patients with schizophrenia admitted during a period of one year were assessed using the Positive and Negative Syndromes' Scale (PANSS). Means of syn-

Streszczenie

Wprowadzenie: Używanie amfetaminy stanowi poważny problem globalny i jest powszechne wśród pacjentów z zaburzeniami psychicznymi. Dotychczas w Arabii Saudyjskiej w bardzo niewielkim zakresie badano wpływ amfetaminy na objawy schizofrenii. Celem badania była ocena różnic w przebiegu schizofrenii, które wiązałyby się ze stosowaniem amfetaminy przez mężczyzn leczonych w szpitalu psychiatrycznym w Taif w Arabii Saudyjskiej.

Materiał i metody: Wszystkich mężczyzn chorych na schizofrenię, przyjętych do szpitala w ciągu jednego roku, oceniano za pomocą Skali Objawów Pozytywnych i Negatywnych (PANSS). Porównano

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dromes and subscales' scores for schizophrenic patients with recent amphetamine use (RAU) were compared with those with no recent use (NRAU). A χ^2 test was used on the associations.

Results: Among 199 schizophrenic male patients included in the study, 35 (17.5%) had amphetamine use over the last week prior to hospital admission. This is referred to as "recent amphetamine use" (RAU). No statistically significant differences in positive symptoms were found between schizophrenic patients of RAU and NRAU, except in excitement, which was higher in (RAU) (p = 0.028). The scores of negative symptoms were significantly higher in schizophrenic patients with NRAU (p = 0.002). Regarding risk behaviour, violence was more frequent in RAU patients (p = 0.037).

Discussion: Unlike some other studies, difference was mainly in excitement rather than in delusions or hallucinations, suggesting a trans-cultural issue which needs more exploration.

Conclusions: Amphetamine use is associated with psychopathological differences in schizophrenia requiring special consideration and safety measures and more studies of different design.

Keywords: Schizophrenia, Psychopathology, Saudi Arabia, Amphetamine use.

średnie natężenie objawów w grupie chorych, którzy niedawno używali amfetaminy (RAU), i tych, którzy jej ostatnio nie używali (NRAU). Przy ustalaniu zależności między grupami zastosowano test χ^2.

Wyniki: Do badania zakwalifikowano 199 mężczyzn z rozpoznaniem schizofrenii. Trzydziestu pięciu z nich (17,5%) używało amfetaminy w ostatnim tygodniu przed przyjęciem do szpitala, co określono jako „niedawne używanie amfetaminy" (RAU). Nie stwierdzono statystycznie istotnych różnic w objawach pozytywnych między chorymi na schizofrenię z grupy RAU i NRAU. Wyjątek stanowiło podniecenie, bardziej nasilone u pacjentów używających amfetaminy (RAU) (p = 0,028). Natężenie objawów negatywnych było istotnie wyższe u chorych na schizofrenię z NRAU (p = 0,002). Jeśli chodzi o zachowania ryzykowne, to przemoc występowała częściej u pacjentów z RAU (p = 0,037).

Omówienie: W naszych badaniach, w przeciwieństwie do niektórych innych, grupy różniły się raczej pod względem podniecenia, a nie urojeń lub halucynacji. Sugeruje to, że przyczyną tych rozbieżności są różnice kulturowe, które wymagają bardziej dokładnych studiów.

Wnioski: Używanie amfetaminy wiąże się z różnicami psychopatologicznymi w przebiegu schizofrenii, wymagającymi szczególnej uwagi i środków bezpieczeństwa i większej liczby bardziej zróżnicowanych badań.

Słowa kluczowe: schizofrenia, psychopatologia, Arabia Saudyjska, używanie amfetaminy.

Introduction

Drug use is on the rise and has become a global lifestyle trend affecting both the rich and poor communities [1]. The connection between mental illness and drug use is well established [2]. A challenging question of morbidity is whether the clinical characteristics were caused by the drug, or whether they were symptoms of the primary disease that were exacerbated by the substance, or whether they were a combination of both [3]. Globally, stimulants like amphetamine are the second most commonly used group of drugs after cannabis [4]. Amphetamine is widely used by both the general public and psychiatric patients, and its trafficking has increased in recent years especially since 2009 [4, 5].

Drug use is stigmatising and considered inappropriate activity in Saudi Arabian society, so it is often unreported, and its prevalence in the general population is still unknown [6]. According to some reports, about 7-8% of Saudis have used drugs, with 70% of drug users being between 12 and 22 years of age [7].

In recent years, studies have shown an increase in the use of amphetamine [8, 9]. It is currently the most common psychoactive substance, followed by cannabis and alcohol though the majority tend to use multiple substances [7]. The most common factors that may lead to substance use are peer pressure and psychosocial stressors [6]. De-

spite limited evidence, Saudi females use far fewer drugs than males. This may be due to prohibitions and the conservative culture, which makes psychoactive substances less available to them than to males [7]. Amphetamine in Saudi Arabia is usually available as white pills called Captagon, which is the brand name of fenethylline, an amphetamine connected to theophylline via an alkyl chain [10].

Amphetamine's stimulant effect is mainly achieved by increasing the availability of norepinephrine and dopamine in the central nervous system and this may result, at some levels, in euphoria and increased energy and concentration [11]. However, heavy use leads to excessive release of dopamine and glutamate in the cortex which causes psychotic symptoms like delusions and hallucinations even in the absence of a previous history of psychosis [11-14]. In contrast to the primary psychosis of schizophrenia, the psycho-pathological characteristics that arise with stimulant use are often referred to as secondary psychosis [15]. Schizophrenic patients may use substances and the prevalence of substance use among them is rather higher than in the general population [16-18]. It is thought that this high prevalence is partly because they want to reduce their symptoms or to counteract secondary side effects of antipsychotic drug treatment, which is referred to as the self-medication hypothesis [19].

The coexistence of substance use with chronic mental illness like schizophrenia is considered a double burden, which presents complex medical, financial and psychosocial problems [20]. It has been found that substance use is highly associated with treatment non-compliance [21-23] and longer duration of untreated schizophrenia [24]. It was suggested that patients with schizophrenia comorbid with substance use show more agitation, aggression [3], visual hallucinations and grandiosity [25, 26] with lower presentation of negative symptoms than that of schizophrenia alone [27, 28]. On the other hand, a previous study in Norway showed that positive symptoms were equal in both the schizophrenic and comorbid patients [3].

Although observational studies of amphetamine-induced psychotic disorders are common, few have examined the effect of amphetamine use on the clinical features of schizophrenic patients particularly in the Middle East and Arab world. Furthermore, comorbid amphetamine use, with its potential changes in schizophrenia psychopathology, may influence the course of the illness and its management, therefore we designed this study to observe any difference in the psychopathology of schizophrenic patients using amphetamine by assessing positive and negative symptoms and other related psychosocial factors.

■ Material and methods

It was a cross-sectional study conducted on patients at the Mental Health Hospital in Taif, a government unit serving mainly the local Taif population and other patients from the western region in Saudi Arabia. The hospital provides care for a variety of mental conditions, with the exception of childhood disorders, which are handled at the Children's Hospital.

The study was carried out from 2017 to 2019. The data collection period lasted a year and ended at the start of 2019. It included male patients of 18 years of age and more who were admitted during that year and who met the diagnostic criteria of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5). It was decided to include only male patients since amphetamine substance use is thought to be uncommon among females in Saudi Arabia [8, 29]. Recognised amphetamine-use patients were not included unless they had been diagnosed with schizophrenia or had developed psychotic features prior to the onset of substance use depending on the history or previous assessments and follow-up documented in their hospital records. Those who received the diagnoses of substance-induced psychosis, intellectual disability, mood disorders, or dementia were excluded from the study. In order to eliminate substance-induced psychosis, patients with substance-use associated new-onset psychosis were also excluded.

The instrument used for this study consisted of two parts with the first part containing sociodemographic factors, pattern of substance use, if any and evidence of any recent risk-taking behaviour (i.e. suicidal attempts, violence or homicidal acts and arrests). Information was obtained from direct interview supported by recent patient records. The second part of the questionnaire consists of a Positive and Negative Syndrome Scale (PANSS), which is a rating scale used for measuring symptom severity of schizophrenia patients. It was published by Stanley Kay, Lewis Opler, and

Abraham Fiszbein in 1987, and since that time it has been used worldwide [3, 27, 28, 30]. Several studies have provided evidence of the criterion-related validity of the PANSS, its predictive validity, reliability and utility for both typological and dimensional assessment [30]. It includes positive, negative and general subscales. Only positive and negative subscales were used in our study. Patient assessment was conducted in the first week of hospitalisation.

The software employed for analysing collected data was the Statistical Package for Social Sciences (IBM® SPSS® Statistics) version 24, a property of International Business Machines Corp. (IBM) 2016. The software is compatible with Windows. Descriptive data were presented in numbers and percentages, means scores were calculated for syndromes' and subscales' and were compared between schizophrenic patients according to the factor of recent amphetamine use. We set a limit of one week of amphetamine use before admission to define the group of schizophrenic patients with recent amphetamine use (RAU). The other group; patients who had no recent use (NRAU), included every patient who did not used amphetamine within the last week before admission according to the history and a negative result based on urine drug screening. Chi-square test was applied to analyse the associations between PANSS scores of recent amphetamine user schizophrenic patients with the set level of significance at 0.05. Significant associations between recent amphetamine use and psychopathological features were then reanalysed with multiple linear regression to decide if these results were contradicted by other independent variables. Therefore only significant associations were selected for multiple linear regression. The coefficients, standard errors, significance and adjusted R squares of all included variables were presented. Multiple linear regression was applied because the dependent variables, PANSS scores, were continuous. This model of analysis presents the 'coefficient' for every independent variable, which estimates its effect on the dependent variables when other factors were adjusted.

Ethical approval for the study was obtained from the ethical committee of the Administration of Research and Studies, Ministry of Health, Taif, Saudi Arabia (IRB Registration Number with KACST, KSA: HAP-02-T-067). Required permission was gained from the hospital authorities, and consent to participate was obtained verbally from patients and their next of kin, after explaining the purpose and objectives of the study. The participants were assured that confidentiality and anonymity would be maintained, and their participation is entirely voluntary. This procedure was carried out by a licensed psychiatric specialist and was accepted by the ethical committee since the research poses only a minimal risk.

■ Results

A total of 199 patients were included in the study, all of whom were Saudi males. Almost half (49.5%) were between 35 and 50 years of age (n = 97), and 41.3% (n = 81) were between 20 and 34. Only 18.2% (n = 36) were married, another 18.2% were divorced and 63.6% (n = 126) were single. Most participants were unemployed 90.8% (n = 178). Regarding their educational level, 62.1% did not attend secondary school. The majority of the participants' families (72.1%) had 7 or more members. The sociodemographic characteristics are presented in more detail in Table I.

Among all participants, 96 (48.2%) had a history of amphetamine use at some stage in their life, and 35 (17.6%) had recent amphetamine use within the last week prior to hospital admission. It was decided to include this group with amphetamine use not more than one week prior to admission for comparison with other schizophrenic patients on the assumption that the psychiatric effects of amphetamine last for one week on average according to several previous observational and experimental studies [31-34].

More than half (56.6%) of the patients was ≥ 35 years of age and 126 (63.6%) were single as shown in Table I. Most of the patients (90.8%) were not in work (n = 178); other sociodemographic characteristics are presented in Table I.

Regarding sociodemographic factors, there were no statistically significant differences between schizophrenic patients with recent amphetamine use and those who did not except in educational level. Among those who are not current amphetamine users, 22 patients (13.8%) are university graduates, while secondary school was the highest educational level among the other group (Table I).

Regarding psychopathology, a comparison was made between the two groups using the mean of each symptom in the PANSS. There was no sta-

Table I. Sociodemographic background of all participants

Sociodemographic factors	All patients		Schizophrenia with RAU (*n* = 35)	Schizophrenia with NRAU (*n* = 164)	*p*-value
	n	%			
Age					
< 20	4	2.0	1 (2.9%)	3 (1.9%)	0.758
20-34	81	41.3	17 (48.6%)	64 (39.8%)	
35-50	97	49.5	15 (42.9%)	82 (50.9%)	
> 50	14	7.1	2 (5.7%)	12 (7.5%)	
Marital status					
Single	126	63.6	20 (57.1%)	106 (65.0%)	0.647
Married	36	18.2	8 (22.9%)	28 (17.2%)	
Divorced	36	18.2	7 (20.0%)	29 (17.8%)	
Occupation					
Yes	18	9.2	3 (8.6%)	15 (9.3%)	0.595
No	178	90.8	32 (91.4%)	146 (90.7%)	
Education					
Illiterate	4	2.1	0	4 (2.5%)	0.016*
Primary	48	24.6	5 (14.3%)	43 (26.9%)	
Intermediate	69	35.4	19 (54.3%)	50 (31.3%)	
Secondary	52	26.7	11 (31.4%)	41 (25.6%)	
University	22	11.3	0	22 (13.8%)	
Family Members					
< 3	3	1.6	0	3 (2.0%)	0.154
3-6	49	26.3	5 (15.2%)	44 (28.8%)	
7-10	87	46.8	21 (63.6%)	66 (43.1%)	
> 10	47	25.3	7 (21.2%)	40 (26.1%)	

RAU – recent amphetamine use, NRAU – no recent amphetamine use
**Statistically significant – p < 0.05*

tistically significant difference between patients' groups in positive symptoms except in excitement. The severity of excitement was significantly higher among current amphetamine user schizophrenic patients (*p*-value = 0.028). On the other hand, the negative symptom subscale showed significant differences. Schizophrenic patients without current amphetamine use scored higher for Blunted affect (*p*-value = 0.001), Emotional withdrawal (*p*-value = 0.007), Poor rapport (*p*-value = 0.010), Difficulty in abstract thinking (*p*-value = 0.017), Lack of spontaneity (*p*-value = 0.024) and the overall negative symptom subscale (*p*-value = 0.002) (see Table II).

When the two groups of patients were compared regarding risk behaviour i.e. suicide, violence, arrest and sexual offenses, those behaviours seem to be more frequent in schizophrenic patients with current amphetamine use though the differences were not statistically significant except for violence (*p*-value = 0.037) as shown in Table III.

Table IV presents multiple linear regression results of psychopathological features of schizophrenia (manifested as PANSS scores). Except for 'recent amphetamine use', *p*-values were > 0.05, which indicates that none of the other independent variables were significantly associated with changes in dependent variables.

Discussion

The aim of this research was to observe the psychopathological differences between schizophrenia patients who used amphetamine versus those who did not. Thirty five patients (17.6%) of the 199 in the sample were found to have used amphetamines in the week prior to the study having either declared use or having tested positive

Table II. Positive and Negative Syndrome Scale (PANSS) scores of schizophrenic patients with recent amphetamine use compared with those without recent amphetamine use

Symptoms scores according to the PANSS	Schizophrenia with RAU (*n* = 35)		Schizophrenia with NRAU (*n* = 164)		*p*-value
	Mean	SD	Mean	SD	
Delusions	3.63	1.66	4.15	1.94	0.137
Conceptual disorganization	2.17	1.54	2.47	1.86	0.377
Hallucinatory behavior	3.00	1.65	3.52	1.95	0.143
Excitement	3.37	1.48	2.70	1.65	0.028*
Grandiosity	1.97	1.56	2.07	1.70	0.743
Suspiciousness/persecution	4.26	1.52	3.93	1.72	0.294
Hostility	3.20	1.68	3.10	1.82	0.777
Positive subscale scores	**21.6**	**5.83**	**21.97**	**6.13**	**0.745**
Blunted affect	1.57	0.95	2.48	1.57	0.001*
Emotional withdrawal	1.89	1.32	2.75	1.78	0.007*
Poor rapport	1.60	0.91	2.33	1.60	0.010*
Passive/apathetic	2.40	1.61	3.06	1.85	0.054
Difficulty in abstract thinking	1.97	1.34	2.80	1.92	0.017*
Lack of spontaneity	1.57	0.98	2.20	1.56	0.024*
Stereotyped thinking	1.29	0.83	1.71	1.37	0.083
Negative subscale scores	**12.29**	**6.36**	**17.37**	**8.89**	**0.002***

**Statistically significant – p < 0.05*

Table III. A comparison between schizophrenic patients with recent amphetamine use vs. those without recent amphetamine use regarding risk behaviour (using Fisher's Exact Test)

Risk behaviour	Schizophrenia with RAU (*n* = 35)		Schizophrenia with NRAU (*n* = 164)		*p*-value
	n	%	*n*	%	
Suicidal attempt	7	20.0	31	18.9	0.522
Violence	18	51.4	55	33.5	0.037*
Self-neglect	16	45.7	89	54.3	0.231
Arrest	14	40.0	61	37.2	0.449
Homicidal act	1	2.9	16	9.8	0.160
Sexual offence	4	11.4	10	6.1	0.216

**Statistically significant – p < 0.05*

for amphetamines in urine analysis. A comparison between the two groups proved no significant differences in sociodemographic features, which supports the aim of the study. The only exception was at the educational level, when a significant part of schizophrenic patients who were not current amphetamine users, were university graduates, while no one from the other group of patients reached this educational level. This may support the association between amphetamine use and lower educational levels, which is similar to results from several previously published studies. A cross-sectional study conducted on male truck drivers in Sao Paulo found that education levels below nine years were significantly associated with using amphetamines compared to higher education levels [35]. Another cross-sectional survey on northern Thai youth showed that non-methamphetamine users were 1.3 times more likely to be better educated (95% CI: 1.06-1.62) [36]. In a systematic review of risk factors for methamphetamine use in young people, non-methamphetamine users had more years in education than methamphetamine users [37-39]. Despite the significant association

between amphetamine use and lower education levels, our study cannot prove a causal relationship or decide which of the two factors might have affected the other.

Regarding psychopathology, our study showed that the severity of excitement, according to PANSS, was significantly higher among patients with schizophrenia comorbid with amphetamine use. This association was examined by multiple linear regression (Table IV) to exclude the effect of other variables. This finding is supported by a follow-up study by Rebecca McKetin *et al.*, who found that the excitement increased significantly with methamphetamine use [40]. Several studies related stimulant drugs to the excitement and violent behaviour [41-46]. Both animal and human studies concluded that amphetamine has some pharmacological effects on the dopaminergic and serotonergic systems leading to aggressive behaviour [47]. Regarding our study design, there is still no conclusion on whether amphetamine caused excitement in those patients, or they might have used amphetamine because they were excited, or other certain circumstances might have increased the chance of both amphetamine use and excitement [48].

As we concluded, there were no statistically significant differences in other PANSS positive symptoms of schizophrenic patients according to recent amphetamine use. This is unlike the observations that amphetamine exacerbates delusions, suspiciousness, and hallucinations in underlying psychotic disorders, which may be mediated by an increase in monoamines reported by other studies [22, 49, 50]. On the other hand, some studies reported no significant difference in positive symptoms between schizophrenia and stimulant-induced psychosis [3]. This is consistent with the results of a randomised controlled studies on the effect of amphetamine on schizophrenic patients, as results indicated that the administration of amphetamine had no significant effect on positive symptoms of delusions and hallucinations compared with placebo [51]. This disparity in results may be due to transcultural issues suggesting more exploration, or due to different settings and designs of studies; in our study, all patients were in the acute phase of illness, which is most likely to be very similar in both groups [3].

Comorbidity between schizophrenia and amphetamine use was linked to less extreme negative

Table IV. Regression results of psychopathological features of schizophrenia (PANSS scores)

Independent variables	Dependent variables (psychopathological features of schizophrenia assessed by PANSS)															
	Excitement		Blunted affect		Emotional withdrawal		Poor rapport		Difficulty in abstract thinking		Lack of spontaneity		Negative subscale			
	Coefficient (Std. Error)	Sig.	Coefficient (Std. Error)	Sig.	Coefficient (Std. Error)	Sig.	Coefficient (Std. Error)	Sig.	Coefficient (Std. Error)	Sig.	Coefficient (Std. Error)	Sig.	Coefficient (Std. Error)	Sig.		
Constant	3.039 (1.432)	0.035	1.020 (1.281)	0.427	2.483 (1.472)	0.093	0.873 (1.309)	0.506	1.453 (1.552)	0.351	1.569 (1.295)	0.228	8.538 (7.355)	0.247		
Age	0.144 (0.209)	0.494	–0.170 (0.187)	0.366	–0.036 (0.214)	0.865	–0.150 (0.191)	0.433	–0.405 (0.227)	0.076	–0.048 (0.189)	0.799	–0.461 (1.071)	0.667		
Marital status	–0.188 (0.167)	0.263	0.068 (0.150)	0.648	0.056 (0.173)	0.744	–0.029 (0.153)	0.849	0.175 (0.181)	0.335	–0.104 (0.151)	0.492	0.037 (0.864)	0.966		
Occupation	0.241 (0.419)	0.566	0.503 (0.375)	0.182	0.318 (0.430)	0.460	0.630 (0.383)	0.102	1.067 (0.455)	0.020	0.268 (0.379)	0.482	3.462 (2.149)	0.109		
Education	0.008 (0.129)	0.954	–0.101 (0.116)	0.384	–0.122 (0.133)	0.361	–0.148 (0.118)	0.211	–0.167 (0.140)	0.236	–0.128 (0.117)	0.276	–0.560 (0.664)	0.401		
Recent Amphetamine use	–0.668 (0.311)	0.033*	0.867 (0.279)	0.002*	0.794 (0.320)	0.014*	0.687 (0.285)	0.017*	0.759 (0.338)	0.026*	0.627 (0.282)	0.027*	4.679 (1.597)	0.004*		
Adjusted R^2	0.005		0.049		0.068		0.029		0.065		0.016		0.057			

**Statistically significant – p < 0.05.*
Multiple linear regression is applied.

symptoms, especially blunted affect, emotional detachment, poor rapport, difficulty in abstract thought and a lack of spontaneity. Again, this association was confirmed by multiple linear regression (Table IV) which showed no confounding effect from age, marital status, occupation or education. This is consistent with some clinical research findings [52-54], however some researchers consider this to be related to the premorbid personality of drug-using schizophrenia patients. These suggest that they were more functional and have better interpersonal skills than the other group [55]. Some interventional studies examined the effect of amphetamine on schizophrenic patients and found that it resulted in a reduction of negative symptoms [51]. This can be interpreted by the relation between negative symptoms of schizophrenia and decreased dopaminergic activity in the frontal lobes [56] and so increasing the activity of dopamine by amphetamine use results in decreasing negative symptoms, which may support the self-medication hypothesis of drug use [57], when schizophrenic patients are inclined to use amphetamine to alleviate negative symptoms like especially apathy [51].

The last result to be discussed in this study is that recent amphetamine-user schizophrenia patients reported more risk behaviour, i.e. violence in their present history. This is consistent with the result of PANSS scores of this group which showed a significant increase in excitement compared with schizophrenics without recent amphetamine use. This finding needs more attention in the risk assessment of patients with schizophrenia comorbid with substance use, especially amphetamines.

The current study has some limitations; it did not include a scale to diagnose amphetamine use disorder, and rather applied the recent use as the main factor in comparison. So, there was a possibility for some amphetamine users to be missed out if they, for one reason or another, had not used in the week prior to the study. Another limitation is that no causal relationship between different variables can be concluded since it was a cross-sectional study. Results of this study can be generalised to the population of interest: male schizophrenic patients with or without amphetamine use especially in the hospital setting, since the study sample was representative and covered all admitted male patients with schizophrenia over a whole year.

■ Conclusions

Patients with schizophrenia comorbid with amphetamine use have more violence and excitement and less negative symptoms compared with patients who only have schizophrenia. This notion suggests that considerable observations and more safety measures are required for those patients. Meanwhile, further studies are needed to explore the causal relationship in this association.

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Conflict of interest/Konflikt interesów

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Ethics/Etyka

The work described in this article has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) on medical research

involving human subjects, Uniform Requirements for manuscripts submitted to biomedical journals and the ethical principles defined in the Farmington Consensus of 1997.

Treści przedstawione w pracy są zgodne z zasadami Deklaracji Helsińskiej odnoszącymi się do badań z udziałem ludzi, ujednoliconymi wymaganiami dla czasopism biomedycznych oraz z zasadami etycznymi określonymi w Porozumieniu z Farmington w 1997 roku.

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