Could the Type of Delivery Contribute to Clinical Features of Schizophrenia and Nicotine Dependence among Patients Who are not Under Antipsychotic Treatment?

Nadalin, Sergej; Peitl, Vjekoslav; Karlović, Dalibor; Dević Pavlić, Sanja; Škrobo, Mislav; Uremović, Melita; Zatković, Lena; Buretić-Tomljanović, Alena

Source / Izvornik: **Archives of Psychiatry Research : An International Journal of Psychiatry and Related Sciences, 2022, 58, 91 - 98**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.20471/may.2022.58.01.10

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:184:952247

Original paper

Archives of Psychiatry Research 2022;58:91-98
DOI:10.20471/may.2022.58.01.10
Received October 17, 2021, accepted after revision January 10, 2022

Could the Type of Delivery Contribute to Clinical Features of Schizophrenia and Nicotine Dependence among Patients Who are not Under Antipsychotic Treatment?

Sergej Nadalin[1], Vjekoslav Peitl[2,3], Dalibor Karlović[2,3], Sanja Dević Pavlić[4], Mislav Škrobo[2], Melita Uremović[3], Lena Zatković[5], Alena Buretić-Tomljanović[4]

[1]Department of Psychiatry, General Hospital "Dr. Josip Benčević", Slavonski Brod, Croatia, [2]Department of Psychiatry, University Hospital Center Sestre Milosrdnice, Zagreb, Croatia, [3]School of Medicine, Catholic University of Croatia, Zagreb, Croatia, [4]Department of Medical Biology and Genetics, Faculty of Medicine, University of Rijeka, Rijeka, Croatia, [5]Hospital Pharmacy, Clinical Hospital Center Rijeka, Rijeka, Croatia

Abstract - The type of delivery and antipsychotic medications could modulate clinical features of schizophrenia and nicotine dependence by affecting gut microbiota composition. In this study, we aimed to investigate whether the age of disease onset, severity of PANSS (Positive and Negative Syndrome Scale) psychopathology and nicotine dependence might be associated with the type of delivery among two groups of patients with schizophrenia without antipsychotic therapy: first-episode patients, and chronic patients, non-adherent to antipsychotic medications. Information regarding antipsychotic non-adherence, smoking status, and the type of delivery (vaginal delivery or caesarean delivery) was obtained from autoanamnestic and heteroanamnestic data. Age of disease onset was defined as age at the patient's first hospital admission due to a psychotic episode at which the diagnosis of schizophrenia was used. PANSS evaluation data was taken during the acute state of the illness at the most recent hospitalization. Values of the age of disease onset, PANSS score and PANSS factor and prevalence of early (≤ 26 years) and late (> 26 years) disease onset did not differ significantly between patients born by caesarean delivery and vaginal delivery ($p > 0.05$). The prevalence of smokers was significantly higher among patients born by caesarean delivery ($p = 0.012$). The caesarean delivery is associated with ~9%-fold greater risk of nicotine dependence. We did not find any associations of the age of disease onset and PANSS psychopathology with the type of delivery among patients without therapy, but our results implicate that caesarean delivery might be a risk factor for nicotine dependence in that patient group.

Key words: age of onset; caesarean delivery; schizophrenia; smoking

e-mail: apr.kbcsm@gmail.com • www.http://apr.kbcsm.hr

Correspondence to:
Sanja Dević Pavlić
Department of Medical Biology and Genetics
Faculty of Medicine, University of Rijeka
Braće Branchetta 20
51 000 Rijeka, Croatia
Phone: +385 51 651 246
Fax. + 385 51 678 89
E-mail: sanja.devic@uniri.hr

Introduction

According to the World Health Organization, the frequency of caesarean deliveries at the global level today is 21%, which is three times more than thirty years ago [1]. This frequency is even higher in the Republic of Croatia; according to the data from the report of

the Croatian Institute of Public Health, the share of such births was 26.6% in 2020 and represents an increase of as much as 1.3% compared to the previous 2019 [2].

Research into the implications of caesarean delivery is of growing scientific interest not only in physical but also in mental illnesses, such as schizophrenia [3-6]. No association was found between caesarean delivery and lifetime risk of schizophrenia but some studies suggest that caesarean delivery may contribute to an earlier onset of schizophrenia, although the results of the studies are not uniform [3-6]. In a recent study, Fond and associates compared various clinical features of schizophrenia between patients on antipsychotic therapy born by vaginal delivery and caesarean delivery [6]. Their results did not show a significant correlation between the type of delivery and the age of disease onset, the severity of the symptoms of the PANSS (Positive and Negative Syndrome Scale), the severity of depressive symptoms of the CDRS (Calgary Depression Rating Scale for Schizophrenia) and the severity of manic symptoms of the YMRS (Young Mania Rating Scale). Nevertheless, the results suggest that patients born by caesarean delivery may manifest poorer intellectual functioning before the onset of the first psychotic symptoms compared with patients born by vaginal delivery. This study also examined the association between the type of delivery and nicotine dependence and found no significant difference in the distribution of smokers and non-smokers between patients born by vaginal delivery and caesarean delivery. Furthermore, the association of the type of delivery with components of the metabolic syndrome, such as body mass index (BMI) values, waist circumference and plasma triglyceride and glucose concentrations, was investigated. Patients born by caesarean delivery were found to have significantly lower BMI and waist circumference values compared to the group of patients born by vaginal delivery, while triglyceride and glucose concentrations did not differ significantly between the two groups of subjects. In our recent study we compared BMI values, and plasma total cholesterol, LDL cholesterol (low density lipoprotein cholesterol), HDL cholesterol (high density lipoprotein cholesterol), triglyceride, and glucose concentrations among patients with schizophrenia without antipsychotic medications born by vaginal delivery and caesarean delivery [7]. Our results suggest that the effect of the delivery type on the components of the metabolic syndrome in patients without therapy could differ from that in chronic patients receiving therapy. In summary, we did not find an association of the type of delivery with BMI values (nor with cholesterol concentrations), but we did find an association of the type of delivery with triglyceride concentrations, with caesarean delivery being a risk factor for elevated triglyceride concentrations. However, we did not correlate the clinical features of schizophrenia and nicotine dependence with the type of delivery. To our knowledge we also found no study that correlated the clinical features of schizophrenia and nicotine dependence with the type of delivery in patients with schizophrenia without therapy.

During a caesarean delivery, the newborn is not exposed to the mother's vaginal and intestinal bacteria and has fewer specific bacteria in the intestinal microbiota, such as bacteria from the genera Bifidobacterium and Bacteroides. Studies in animal models suggest that these bacteria are involved in the synthesis of the neurotransmitters gamma-aminobutyric acid (GABA) and dopamine in the brain, whose role is implied in the clinical features of schizophrenia and nicotine dependence (in patients with schizophrenia and the general population) [8,9]. It has also been observed that caesarean delivery, probably due to hypoxia, modulates the expression of dopamine receptors in the mesocorticolimbic regions of the brain; increases the expression of dopamine receptors D1 and D4, and decreases the expression of dopamine receptors D2 [6,10].

Studies in patients with schizophrenia suggest that certain second-generation antipsychotic medications (so-called atypical antipsychotics), such as olanzapine and risperidone,

may decrease but also increase the number of bacteria from the genera Bifidobacterium and Bacteroides [11-13]. Since caesarean delivery has also been shown to be a modulatory factor in the composition of the intestinal microbiota investigating the association of clinical features of schizophrenia with the type of delivery in patients without antipsychotic therapy may be important when prescribing specific antipsychotic medications [8,9].

In patients with schizophrenia without antipsychotic therapy, it would also be important to investigate the association of nicotine dependence with the type of delivery. The modulatory effect of cigarette smoking on Bifidobacterium and Bacteroides has been observed in animal model studies and in the human population: cigarette smoking reduces the number of bacteria of the genus Bifidobacterium while increases the number of bacteria of the genus Bacteroides [14-16]. Furthermore, by induction of liver microsomal enzymes, cigarette smoke reduces the plasma concentrations of atypical antipsychotics olanzapine and clozapine, leading to the need for a higher therapeutic dose in smoking patients [17-19].

In this study, we examined the relationships between the age of schizophrenia onset, the severity of PANSS symptoms and nicotine dependence with the type of delivery in two groups of patients without therapy, in whom we previously investigated the association of metabolic syndrome components with the type of delivery [7]. Our study included patients with the first episode of schizophrenia and chronic patients non-adherent to antipsychotic medications in the appropriate period.

Subjects and Methods

The study included 131 patients (69 men and 62 women), whose clinical characteristics in relation to the type of delivery are shown in Table 1. All patients were hospitalized at the Department of Psychiatry of the University Hospital Center Sestre milosrdnice in Zagreb, in the period between 2015 and 2019. The Ethics committee of the said institution previously approved the research.

Data on the type of delivery, nicotine dependence and non-adherence to antipsychotic medications were collected from autoanamnesis and heteroanamnesis. Non-adherent patients were patients who had been off oral antipsychotic drugs for a month or more and had not been on long-term depot antipsychotic preparations.

The diagnosis of schizophrenia was confirmed by two specialists in psychiatry, according to the DSM-V classification (Diagnostic and statistical manual for mental disorders - DSM-V). Age of disease onset was defined as age at the patient's first hospital admission due to a psychotic episode at which the diagnosis of schizophrenia was used. Based on the median age at first hospitalization, which was 26 years for the entire sample, the age of disease onset was classified as early (patients were hospitalized at ≤ 26 years) and late (age at first hospitalization was > 26 years). In the acute phase of the disease, which required hospitalization, an evaluation of the symptoms of the PANSS rating scale was performed. The scale consists of 30 items, of which 7 measure positive symptoms, 7 negative symptoms, and 16 general symptoms. The values of all symptoms are rated from 1 (indicates the absence of symptoms) to 7 (indicates the strongest manifestation of a particular symptom), while the total symptoms of PANSS represent the sum of the established values of all positive, negative, and general symptoms [20]. By extracting the specific symptoms of PANSS and summing their values, the values of positive factor (P1, P3, P6 and O9), negative factor (N2, N3, N4, N6 and N7), depressive factor (G2, G3 and G6) and cognitive factor (G10 and G12) were calculated [21-23].

Statistical data processing

Median and interquartile scattering were used as central and scatter measures. Differences in the values of age, age at first hospitalization, PANSS score and PANSS factor between subjects born by vaginal delivery and caesarean delivery were tested using the Mann-Whitney U test. Differences in the frequency of early and late disease onset and differences in the frequency of smokers and non-smokers between the two groups of subjects were tested using the χ^2 test. The Odds ratio (OR) and the 95% Confidence interval (CI) were calculated to assess the strength of the association between caesarean delivery and nicotine dependence. Statistical data processing was performed using the computer program Statistica for Windows, version 13, (StatSoft, Inc., Tulsa, OK, USA), and *p* values less than 0.05 ($p < 0.05$) were considered as significant.

Table 1. Values of investigated clinical features according to the type of delivery

	Vaginal delivery (n = 120)	Caesarean delivery (n = 11)	z	p
Age (years)	33 (18 – 71)	27 (19 – 54)	1.67	0.093
Age at first hospitalization (years)	26 (14 – 57)	6 (19 – 34)	0.08	0.933
PANSS positive symptoms score	23 (7 – 39)	22 (11 – 35)	0.93	0.352
PANSS negative symptoms score	25 (10 – 48)	30 (17 – 39)	-1.28	0.199
PANSS general psychopathology score	49 (38 – 82)	47 (35 – 67)	0.71	0.478
PANSS total symptoms score	98 (63 – 159)	94 (75 – 141)	0.37	0.707
PANSS positive factor	13 (4 – 22)	11 (6 – 14)	1.63	0.102
PANSS negative factor	13 (5 – 32)	15 (7 – 22)	-1.03	0.303
PANSS depression factor	9 (4 – 19)	10 (7 – 14)	0.03	0.978
PANSS cognitive factor	6 (2 – 14)	4 (3 – 7)	1.57	0.116

PANSS = engl. Positive and Negative Syndrome Scale

Results

Only eleven out of one hundred and thirty - one respondents (8.4%) were born by caesarean delivery (Table 1). The trend towards younger age was observed in subjects born by caesarean delivery compared to subjects born by vaginal delivery (Table 1). No significant difference was found between the subjects born by vaginal delivery and caesarean delivery in the values of the age disease onset ($p > 0.05$) (Table 1) or in the frequency of early and late disease onset ($p > 0.05$) (Table 2). The values of the PANSS score and PANSS factor also did not differ significantly between the two groups of subjects ($p > 0.05$) (Table 1). However, a significantly higher frequency of smokers was found among subjects born by caesarean delivery than among those born by vaginal delivery (90.9% vs. 51.7%, $p = 0.012$) (Table 3). The caesarean delivery is associated with an approximately nine-fold greater risk of nicotine dependence: OR = 9.35 (95% CI = 1.2 - 75.4); $z = 2.10$, $p = 0.036$.

Discussion

To date, only few studies have investigated the association of clinical features of schizophrenia and nicotine dependence with the type of delivery; their results were not uniform, and studies primarily included chronic patients taking antipsychotic therapy [3,6]. In this study, we included a population of patients without

Table 2. Frequency of early and late disease onset according to the type of delivery

	Disease onset (≤ 26 years), n (%)	Disease onset (> 26 years), n (%)	χ^2	df	p
Vaginal delivery (n = 120)	61 (50.8)	59 (49.2)	0.66	1	0.416
Caesarean delivery (n = 11)	7 (63.6)	4 (36.4)			

Table 3. Frequency of smokers and non-smokers according to the type of delivery

	Smokers, n (%)	Non-smokers, N (%)	χ^2	df	p
Vaginal delivery (n = 120)	62 (51.7)	58 (48.3)	6.27	1	0.012
Caesarean delivery (n = 11)	10 (90.9)	1 (9.1)			

therapy; these were patients with the first episode of schizophrenia who had never been prescribed antipsychotic therapy and chronic patients non-adherent to antipsychotic therapy.

Similar to a recent study conducted by Fond and associates our results did not show a significant association of specific symptoms of the PANSS score with the type of delivery [6]. The values of individual PANSS factor, including the depressive factor, also did not show significant variations depending on whether patients were born by vaginal delivery or caesarean delivery (Table 1). It should be noted that Fond and associates in their study did not use the depressive factor of the PANSS to assess depressive symptoms, as was the case in our study, but the CRDS [6]. This scale has a higher specificity for the assessment of depressive symptoms in schizophrenia and includes nine items, in contrast to the depressive factor, which considers only three items [21-24]. Our results, suggesting that there is no significant association between the age of schizophrenia onset and the type of delivery, also coincide with the results of research by Fond and associates [6]. However, such results do not coincide with the results of a meta-analysis that included 854 patients with schizophrenia from different populations, conducted several years ago by Verdoux and associates [3]. Their study examined the relationship between the age of disease onset divided into early (≤ 22 years) and late (> 22 years), with 14 birth complications, and one of the categories was complicated caesarean delivery. The results showed that patients born by a complicated caesarean delivery have a ten times higher risk of developing schizophrenia before the age of 22. The inconsistency of the results on the association of the age of disease onset with caesarean delivery could, at least to some extent, stem from the fact that Verdoux and associates included patients with complicated caesarean delivery in the study [3]. On the other hand, Fond and associates in their research do not state whether caesarean delivery was complicated, and such data do not exist for our patients either [6].

The results of our study suggesting a positive association between caesarean delivery and nicotine dependence (Table 3) do not coincide with the results of research by Fond and associates in which no correlation was found between the type of delivery and the smoking status of the respondents [6]. This difference could be because the respondents included in our study have currently been off antipsychotic medications while in the study of Fond and associates subjects were on stable antipsychotic therapy for at least 4 weeks [6]. Since persons born by caesarean delivery are more prone to infections, especially during childhood, the composition of their intestinal microbiota could be further determined by the interaction of antibiotics and antipsychotic medications [6,25]. Furthermore, it is possible that patients on antipsychotic therapy smoke more often than patients who are off antipsychotic medications, precisely to alleviate extrapyramidal symptoms and cognitive deficits that occur due to dopamine receptor blockade by antipsychotic medications [19,26,27]. Research suggests that nicotine, a major component of cigarette smoke that leads to addiction, has a positive effect on dopaminergic neurotransmission in the brain: it stimulates nicotinic

acetylcholine receptors, promoting increased dopamine release and inhibiting monoamine oxidase, an enzyme involved in breaking down dopamine [28-30]. Literature data show that as many as 60-90% of patients with schizophrenia smoke and that approximately 30% of smokers with schizophrenia belong to the group of heavy smokers (smoke more than 20 cigarettes a day), which is three times more than in general population [31-35].

The small sample of respondents, the unbalanced number of patients born by vaginal delivery and caesarean delivery, as well as the fact that data on non-adherence to antipsychotic medications were collected from autoanamnesis and heteroanamnesis, are important limitations of our study. Subsequent studies in patients without antipsychotic therapy should investigate association of other clinical features of schizophrenia with the type of delivery, such as depressive symptoms of the CDRS and manic symptoms of the YMRS [6]. Furthermore, more complete anamnestic data on nicotine dependence should be collected, such as the number of cigarettes smoked per day, a Fagerstrom test to assess nicotine dependence, etc.

Finally, in the context of the intestinal microbiota, it should be mentioned that some other bacteria whose variations in numbers have been shown to be less dependent on the type of delivery, such as bacteria of the genus Lactobacillus, could be relevant in the clinical features of schizophrenia and/or nicotine dependence [8,36]. For example, studies in animal models suggest an important role of these bacteria in the synthesis of the neurotransmitters GABA, glutamate, and acetylcholine [8,37].

In conclusion, our results did not show an association between the investigated clinical features of schizophrenia (age of disease onset and severity of PANSS symptoms) with the type of delivery in patients without antipsychotic therapy. These results, together with the fact that neither in the research of the Fond and associates conducted on patients who were on antipsychotic therapy, was found an association of PANSS psychopathology with the type of delivery, imply that when prescribing antipsychotic medications data on the type of delivery should not actually be of greater importance for further clinical presentation [6]. On the other hand, we found that caesarean delivery increases the risk of developing nicotine dependence in patients without antipsychotic therapy, which in turn does not coincide with the research of Fond and associates in which no association between the type of delivery and smoking status in patients on antipsychotic therapy was found [6]. We are of the opinion that the same does not exclude that patients born by caesarean delivery may be at higher risk of developing nicotine dependence after the introduction of antipsychotic therapy compared to patients born by vaginal delivery or that, for example, they could smoke more cigarettes. Since the literature suggests that cigarette smoking reduces the concentration of certain antipsychotic medications in plasma, subjects born by caesarean delivery should certainly be closely monitored after the introduction of antipsychotic therapy to prevent undertreatment [17-19].

Acknowledgements

None.

Conflict of interest

None to declare.

Funding Sources

None.

References

1. Betran AP, Ye J, Moller AB, Souza JP, Zhang J. Trends and projections of caesarean section rates: global and regional estimates. BMJ Glob Health. 2021;6:e005671.
2. Rodin U, Cerovečki I, Jezdić D .Hrvatski zavod za javno zdravstvo. Izvješće za 2020. Porodi u zdravstvenim ustanovama u Hrvatskoj 2020. godine [Internet]. 2021 [cited 2021 August 16] Available from: https://www.hzjz.hr/wp-content/uploads/2021/07/PORODI_2020.pdf
3. Verdoux H, Geddes JR, Takei N, Lawrie SM, Bovet P, Eagles JM, et al. Obstetric complications and age at onset in schizophrenia: an international collaborative meta-analysis of individual patient data. Am J Psychiatry. 1997;154:1220-7.
4. Cannon M, Jones PB, Murray RM. Obstetric complications and schizophrenia: historical and meta-analytic review. Am J Psychiatry. 2002;159:1080-92.
5. O'Neill SM, Curran EA, Dalman C, Kenny LC, Kearney PM, Clarke G, et al. Birth by caesarean section and the risk of adult psychosis: A population-based cohort study. Schizophr Bull. 2016;42:633-41.
6. Fond G, Bulzacka E, Boyer L, Llorca PM, Godin O, Brunel L, et al. Birth by cesarean section and schizophrenia: results from the multicenter FACE-SZ data-set. Eur Arch Psychiatry Clin Neurosci. 2017;267:587-94.
7. Nadalin S, Dević Pavlić S, Peitl V, Karlović D, Zatković L, Buretić-Tomljanović A. Vrsta poroda i komponente metaboličkog sindroma u bolesnika sa shizofrenijom koji ne primaju terapiju. Medicina Fluminensis. 2021;57:437-43.
8. Agustí A, Campillo I, Balzano T, Benítez-Páez A, López-Almela I, Romaní-Pérez M, et al. Bacteroides uniformis CECT 7771 modulates the brain reward response to reduce binge eating and anxiety-like behavior in rat. Mol Neurobiol. 2021;58:4959-79.
9. Chen Y, Xu J, Chen Y. Regulation of Neurotransmitters by the Gut Microbiota and Effects on Cognition in Neurological Disorders. Nutrients. 2021;13:2099.
10. El-Khodor B, Boksa P. Caesarean section birth produces long term changes in dopamine D1 receptors and in stress-induced regulation of D3 and D4 receptors in the rat brain. Neuropsychopharmacology. 2001;25:423-39.
11. Johnsen E, Jørgensen HA. Effectiveness of second generation antipsychotics: a systematic review of randomized trials. BMC Psychiatry. 2008;8:31.
12. Liu JCW, Gorbovskaya I, Hahn MK, Müller DJ. The Gut Microbiome in Schizophrenia and the Potential Benefits of Prebiotic and Probiotic Treatment. Nutrients. 2021;13:1152
13. Kang DY, Li SJ, Liu CC, Wu RR. Gut Microbiota and antipsychotics induced metabolic alteration. Glob Clin Transl Res. 2019;1:131-44.
14. Tomoda K, Kubo K, Asahara T, Andoh A, Nomoto K, Nishii Y, et al. Cigarette smoke decreases organic acids levels and population of bifidobacterium in the caecum of rats. J Toxicol Sci. 2011;36:261-6.
15. Lee SH, Yun Y, Kim SJ, Lee EJ, Chang Y, Ryu S, et al. Association between cigarette smoking status and composition of gut microbiota: population-based cross-sectional study. J Clin Med. 2018;7:282.
16. Huang C, Shi G. Smoking and microbiome in oral, airway, gut and some systemic diseases. J Transl Med. 2019;17:225.
17. van der Weide J, Steijns LS, van Weelden MJ. The effect of smoking and cytochrome P450 CYP1A2 genetic polymorphism on clozapine clearance and dose requirement. Pharmacogenetics. 2003;13:169-72.
18. Nozawa M, Ohnuma T, Matsubara Y, Sakai Y, Hatano T, Hanzawa R, et al. The relationship between the response of clinical symptoms and plasma olanzapine concentration, based on pharmacogenetics: Juntendo University Schizophrenia Projects (JUSP). Ther Drug Monit. 2008;30:35-40.
19. Sagud M, Mihaljević-Peles A, Mück-Seler D, Pivac N, Vuksan-Cusa B, Brataljenović T, et al. Smoking and schizophrenia. Psychiatr Danub. 2009;21:371-5.
20. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull. 1987;13:261-76.
21. Wallwork RS, Fortgang R, Hashimoto R, Weinberger DR, Dickinson D. Searching for a consensus five-factor model of the Positive and Negative Syndrome Scale for schizophrenia. Schizophr Res. 2012;137:246-50.
22. Jiang J, See YM, Subramaniam M, Lee J. Investigation of cigarette smoking among male schizophrenia patients. PLoS One. 2013;8:e71343.
23. Misiak B, Kiejna A, Frydecka D. Assessment of cigarette smoking status with respect to symptomatic manifestation in first-episode schizophrenia patients. Compr Psychiatry. 2015;58:146-51.
24. Addington J, Shah H, Liu L, Addington D. Reliability and validity of the Calgary Depression Scale for Schizophrenia (CDSS) in youth at clinical high risk for psychosis. Schizophr Res. 2014;153:64-7.
25. Hoang DM, Levy EI, Vandenplas Y. The impact of caesarean section on the infant gut microbiome. Acta Paediatr. 2021;110:60-7.
26. Zhang XY, Chen DC, Tan YL, Luo X, Zuo L, Lv MH, et al. Smoking and BDNF Val66Met polymorphism in male schizophrenia: a case-control study. J Psychiatr Res. 2015;60:49-55.
27. Laruelle M, Kegeles LS, Abi-Dargham A. Glutamate, dopamine, and schizophrenia: from pathophysiology to treatment. Ann N Y Acad Sci. 2003;1003:138-58.
28. Dani JA. Roles of dopamine signaling in nicotine addiction. Mol Psychiatry. 2003;8:255-56.
29. Drew AE, Derbez AE, Werling LL. Nicotinic receptor-mediated regulation of dopamine transporter activity in rat prefrontal cortex. Synapse. 2000;38:10-6.
30. Fowler JS, Logan J, Wang GJ, Volkow ND. Monoamine oxidase and cigarette smoking. Neurotoxicology. 2003;24:75-82.
31. de Leon J, Diaz FJ. A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. Schizophr Res. 2005;76:135-57.
32. Levin ED, Rezvani AH. Nicotinic interactions with antipsychotic drugs, models of schizophrenia and impacts on cognitive function. Biochem Pharmacol. 2007;74:1182-91.
33. Zhang XY, Liang J, Chen DC, Xiu MH, He J, Cheng W et al. Cigarette smoking in male patients with chronic schizophrenia in a Chinese population: prevalence and relationship to clinical phenotypes. PLoS One. 2012;7:e30937.
34. Kelly C, McCreadie R. Cigarette smoking and schizophrenia. Adv Psychiatr Treat. 2000;6:327-31.
35. Salokangas RKR, Honkonen T, Stengård E, Koivisto AM, Hietala J. Cigarette smoking in long-term schizophrenia. Eur Psychiatry. 2006;21:219-23.
36. Dinan TG, Cryan JF. The microbiome-gut-brain axis in health and disease. Gastroenterol Clin North Am. 2017;46:77-89.
37. Bäuerl C, Collado MC, Diaz Cuevas A, Viña J, Pérez Martínez G. Shifts in gut microbiota composition in an APP/PSS1 transgenic mouse model of Alzheimer's disease during lifespan. Lett Appl Microbiol. 2018;66:464-71.

Može li tip poroda pridonjeti kliničkim karakteristikama shizofrenije i ovisnosti o nikotinu u pacijenata koji nisu liječeni antipsihoticima?

Sažetak - Vrsta poroda i antipsihotični lijekovi mogli bi modulirati kliničke značajke shizofrenije i ovisnost o pušenju djelovanjem na sastav crijevne mikrobiote. Istražili smo povezanost dobi nastupa bolesti, težine simptoma psihopatologije PANSS-a (engl. Positive and Negative Syndrome Scale) i ovisnosti o pušenju, s vrstom poroda, u dvije skupine bolesnika sa shizofrenijom bez terapije: u bolesnika s prvom epizodom shizofrenije i kroničnih bolesnika neadherentnih prema antipsihotičnoj terapiji. Podaci o vrsti poroda (vaginalni porod ili porod carskim rezom), ovisnosti o pušenju i neadherentnosti prema antipsihotičnoj terapiji prikupljeni su iz autoanamneze i heteroanamneze. Dob pri prvoj hospitalizaciji zbog psihotičnog ponašanja u sklopu koje je postavljena dijagnoza shizofrenije uzeta je u obzir kao približna dob nastupa bolesti. U akutnoj fazi bolesti koja je zahtijevala hospitalizaciju realizirana je evaluacija simptoma psihopatologije PANSS-a. Između ispitanika rođenih vaginalnim porodom i carskim rezom nije nađena značajna razlika u vrijednostima dobi nastupa bolesti, simptoma ljestvice PANSS-a i faktora PANSS-a te u učestalosti ranog (≤ 26 godina) i kasnog nastupa bolesti (> 26 godina) ($p > 0,05$). Ipak, nađena je značajno veća učestalost pušača među ispitanicima rođenim carskim rezom nego među onima rođenim vaginalnim porodom ($p = 0,012$). Porod carskim rezom povezuje se s približno devet puta većim rizikom za pojavu ovisnosti o pušenju. Nije pronađena značajna povezanost između dobi nastupa bolesti i težine PANSS psihopatologije s vrstom poroda u bolesnika koji nisu na terapiji antipsihotičnim lijekovima, ali bi porod carskim rezom mogao predstavljati rizični čimbenik za pojavu ovisnosti o pušenju u navedenoj skupini bolesnika.

Ključne riječi: carski rez; dob nastupa bolesti; pušenje; shizofrenija