ISSN 2618-1584 Vol. 4, Issue 15: 55-64, DOI: 10.25236/FMSR.2022.041509

Original article of prevalence, risk factors and clinical characteristics of constipation in Chinese patients with schizophrenia

Yan Kong[1], Jianjun Hu[1,*], Xirong Sun[1,*], Haiying Min[1], Ling Wang[1], Jie Yuan[1], Jiechun Zhang[1], Xiangyang Zhang[2,3]

[1]Clinical Research Center for Mental Illness of Tongji University, Shanghai Pudong New Area Mental Health Center and Affiliated Mental Health Center of Tongji University, Shanghai, China
[2]CAS Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China
[3]Department of Psychology, University of Chinese Academy of Sciences, Beijing, China
[*]Corresponding author

Abstract: *Background: The aim of study was to explore the prevalence and clinical characteristics of constipation in Chinese inpatients with schizophrenia and analyze its risk factors. Methods: 806 schizophrenic patients in Shanghai were recruited to analyze the prevalence of constipation and the clinical characteristics of schizophrenic patients. According to whether the patients had constipation, they were divided into constipation group and normal group. The living conditions of the two groups were compared, and the risk factors of constipation were analyzed. Finally, the ROC curve was used to determine the predictive efficacy of the related factors on constipation, and the utilization of the risk factors Logistic regression analysis was used to determine the important factors of constipation. Results: The prevalence of constipation in Chinese schizophrenic patients was higher than that in the general population. The prevalence of mild constipation was 32.5% in 806 schizophrenic patients, and the prevalence of severe constipation was 20.9%. There was also gender difference in the prevalence of constipation in schizophrenic patients, among which the prevalence of female constipation was 17.6%, and that of male constipation was 9.9%. The dietary habits of patients also had a significant impact on the prevalence of constipation (P=0.001). Conclusion: The risk of constipation in female patients with schizophrenia is significantly higher than that in male patients. The incidence of constipation is related to gender, age, education level, negative symptoms, PANSS total score, smoking, exercise and drinking water. Gender, education level and daily smoking are important predictors of constipation.*

Keywords: *China; schizophrenia; risk factors; regression analysis*

1. Introduction

Constipation is a common adverse symptom of human digestive system, which lasts for a long time, consumes a lot of medical and health care products, and will cause huge economic burden on patients. The most common symptoms of constipation are abdominal pain, hard stool, etc. at the same time, patients will feel anorectal obstruction, and also often have the feeling of incomplete emptying after defecation, and even need manual operation [1-2]. It has been reported that constipation not only causes troubles in patients' daily life, but also affects patients' emotional health, and then induces a variety of physical diseases [3]. Most studies have found that schizophrenic patients are more likely to have constipation symptoms than healthy people. The main reason is that schizophrenic patients can't control their living habits, and during hospitalization, they don't participate in activities for a long time, which leads to the decrease of body digestive function and eventually constipation [4-5]. Schizophrenia can be divided into positive symptoms and negative symptoms. Patients usually behave differently from ordinary people, and are more sensitive to things around them. They can't express their meaning clearly when they speak in simple sentences. They are extremely unstable, prone to anger and anxiety, and lack certain subjectivity [6-7]. And some studies have found that in addition to the living habits of patients with schizophrenia will lead to constipation, taking a large number of drugs during the hospital will also lead to constipation, because patients will have adverse reactions after taking some antipschotics, resulting in constipation, and then make patients appear hemorrhoids, intestinal obstruction and other symptoms, patients will also have irritable mood It has seriously affected the

ISSN 2618-1584 Vol. 4, Issue 15: 55-64, DOI: 10.25236/FMSR.2022.041509

treatment and rehabilitation of patients [8-9]. But at present, some studies can not show the related factors of constipation in patients with schizophrenia, so it is very important to analyze the causes of constipation in patients with schizophrenia, which will help to take measures in advance, help patients recover and reduce the pressure of life.

The underlying mechanism of constipation in patients with schizophrenia is not clear, but some studies have said that the pathogenesis of schizophrenia may indirectly lead to constipation [10-12], and the diet habits of patients with schizophrenia will also affect their body metabolic function [13]. In particular, the menu of patients with schizophrenia includes too much animal fat, while the intake of vegetables is lower than the normal level, which leads to metabolic syndrome in patients, and further increases the risk of constipation [14]. In the last century, olanzapine was introduced into China as an antipsychotic, which increased the treatment opportunities of schizophrenic patients in China. In this century, amisulpride was introduced into China as the second generation of atypical antipsychotic. Due to its effectiveness, tolerance and low price, it is widely used in China [15]. Clozapine is also an antipsychotic drug for the treatment of schizophrenia. However, some studies have found that about 70% of schizophrenic patients using clozapine have slow gastrointestinal transit, leading to potential complications such as constipation [16]. However, clozapine is a more effective drug in the treatment of schizophrenia, so the effect of clozapine in constipation of schizophrenia needs further study. After taking antipsychotic drugs, some patients with schizophrenia will have extrapyramidal adverse reactions, which are generally treated with anticholinergic drugs. However, relevant studies have found that anticholinergic drugs are related to other adverse reactions such as constipation and dry mouth [17]. Schizophrenia patients mainly take drugs, including a large number of antidepressants, such as bupropion, which will be metabolized into three active metabolites, and each has strong antidepressant activity. However, studies have found that bupropion in the treatment of depression in patients with other side effects, the more serious side effects are seizures, dry mouth and headache Side effects such as pain and constipation [18]. For the treatment of patients with constipation, cathartic and other drugs are generally used to promote the excretion of patients. Cathartic is usually divided into expansive agent, penetrant, lubricant and stimulant. However, some scholars found that while expansive agent increases intestinal motility, excessive use of expansive agent will lead to fecal inhalation or intestinal obstruction, thus aggravating constipation [19].

The metabolic function of schizophrenics has a great influence on constipation. According to the relevant research, the gender of the patients will affect their energy metabolism. The main reason is that the differences of brain-derived neurotrophic factors between men and women are different. When the male schizophrenia patients have metabolic difficulties at the same time, the level of brain-derived neurotrophic factors in serum is significantly higher than that of other male patients, while female patients have higher levels of brain-derived neurotrophic factors than other men This is not the case with the comparison between [20]. However, there are also studies that women with schizophrenia are more likely to continue delusion disorders than men, so there is a greater risk of constipation in women with schizophrenia than in men, and the results are uncertain [21]. However, there are few studies on the correlation between the risk factors and clinical manifestations of constipation in schizophrenic patients. Therefore, there are still some questions about the conclusion of the risk factors of constipation in schizophrenic patients. Many studies have analyzed the risk factors of constipation in schizophrenic patients, but there are some limitations. For example, clozapine, a drug used for schizophrenia patients, few studies have been conducted to analyze the effect of clozapine on constipation in Chinese schizophrenics. Most of the studies only stop to detect the physical condition of patients, but ignore some external factors. Therefore, this study is mainly conducted from the following points. Firstly, the author investigates whether the constipation of Chinese schizophrenics patients is significantly higher than that of normal people. Secondly, the prevalence of constipation in Chinese schizophrenics is calculated. Finally, it analyzes whether antipsychotics are also Chinese schizophrenics patients besides the habits in daily life and the physical conditions of the patients themselves The risk factors of constipation.

2. Methods

2.1. General information

This study was conducted in Shanghai from July 1, 2019 to June 30, 2020. 806 schizophrenic patients were recruited, including 413 male patients and 393 female patients. All schizophrenic patients were diagnosed as schizophrenia by two psychiatrists according to the 10th edition of the international

ISSN 2618-1584 Vol. 4, Issue 15: 55-64, DOI: 10.25236/FMSR.2022.041509

diagnostic and classification standards for diseases, and a total of 110 patients developed constipation. Inclusive criteria: aged 18-75 years; no other mental diseases; no major diseases such as cancer or nervous system diseases; female patients were not pregnant or breast-feeding; the diagnosis met the chronic conditions for more than 2 years. Exclusion criteria: the patient had partial organ failure; the patient had other symptoms that could cause constipation; the patient was bedridden for a long time and could not move freely; the patient did not cooperate with the relevant medical staff. All patients were informed and signed informed consent, and the study was approved by the hospital ethics committee.

In addition, 50 control subjects were recruited, 50 male nurse attendants who lived for two months under the same conditions with patients were randomly selected in the hospital as a control group.and all the control subjects had normal physical functions.

2.2. Methods

After admission, all patients should have a balanced diet of three meals a day and take at least one hour of physical exercise every day. Record the medication time and drug types of all patients, arrange the patients to defecate at a fixed time every day, investigate the daily intake of fruits, vegetables and water, observe the constipation of patients, calculate the prevalence of constipation in patients with schizophrenia, and analyze the clinical manifestations, causes and related risk factors of constipation. Before the control group entered the test, some researchers conducted a questionnaire survey on the subjects to collect the general information of the subjects, including the subjects' smoking behavior, whether they have drug or alcohol abuse behavior, and whether they have physical abnormalities or medical diseases.

2.3. Diagnostic criteria

The frequency of active defecation was less than 4 times per week in schizophrenic patients, and the frequency of defecation exceeding the normal excretion time was more than 1 time. The patients' feces appeared hard ball or did not appear hard ball, but the frequency of hard feces was more than 1 time. After defecation, the patients still had the feeling of not excluding clean more than 1 time per week. Each group of patients completed excretion 2-3 times independently, and mild constipation was found to have no other adverse reactions after excretion; patients could only excrete 1-2 times a week, and it was slightly difficult to excrete. After excretion, there was a feeling of incomplete emptying, and the stool was dry, and slight adverse reactions occurred in the body, such as moderate constipation in patients with abdominal discomfort; patients defecated once a week or did not defecate, and Defecation can not be carried out autonomously, and serious adverse reactions occur in the body, such as severe abdominal pain and anal pain, which is called severe constipation.

2.4. Statistical method

All the data were collected and analyzed by SPSS22.0. The counting data were described by percentage. Chi square test was used $\chi 2$. The measurement data were expressed by mean ($\overline{x} \pm s$) standard deviation. T test was used to analyze the related factors of constipation. $P < 0.05$ means the difference is statistically significant.

3. Result

3.1. General information of patients

Figure 1 shows the situation of constipation in healthy group and schizophrenic patients, 50 people in each group. Both groups lived for two months under the same conditions. Finally, the situation of constipation in the two groups was observed. It can be clearly seen that the health group had 1 case of constipation in the first month, and the constipation patients returned to normal after two months, while the schizophrenic patients had 7 cases of constipation after the first month, and 12 cases of constipation patients were observed on the 45th day. After two months, there were 11 cases of constipation, and the difference between the two groups was statistically significant ($P < 0.05$).

ISSN 2618-1584 Vol. 4, Issue 15: 55-64, DOI: 10.25236/FMSR.2022.041509

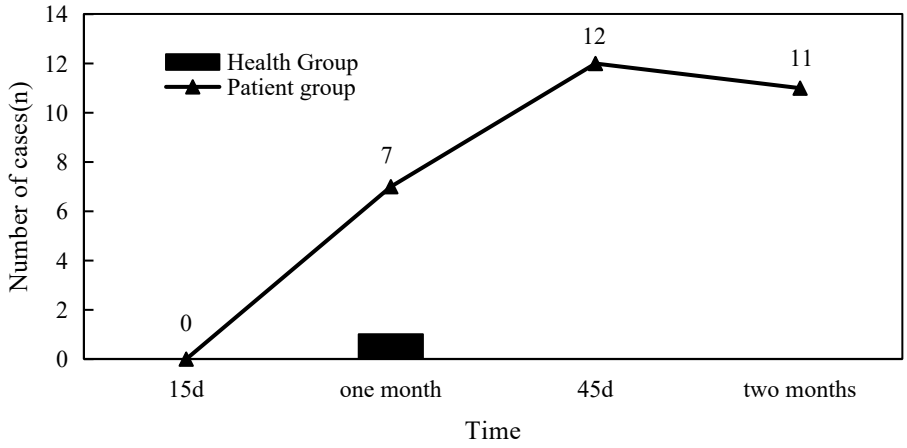

Figure 1: Comparison of constipation prevalence between healthy people and schizophrenic patients

The general information of 806 schizophrenic patients recruited this time is shown in Table 1. The number of female patients suffering from constipation is significantly larger than that of male patients, and the gender difference of schizophrenic patients has statistical significance in the prevalence of constipation ($\chi2$=9.9474，P=0.002). Besides, the age, length of stay, education level, smoking volume and antipsychotic drugs of schizophrenia patients will have certain effect on the incidence rate of constipation ($\chi2$=7.9604，P=0.005；$\chi2$=9.7073，P=0.001；$\chi2$=23.8632，P=0.001；$\chi2$=7.2193，P=0.007；$\chi2$=51.8661，P=0.000).

Table 1: General information of constipation in inpatients with schizophrenia(n, %)

Factor		Number of cases	Constipation group	Normal group	$\chi2$	P
Gender	Male	413	41(9.9%)	372(90.1%)	9.9474	0.002
	Female	393	69(17.6%)	324(82.4%)		
Age(year)	≥55	427	72(16.9%)	355(83.1%)	7.9604	0.005
	<55	379	38(10%)	341(90%)		
Length of stay(d)	≥21	409	71(17.4%)	338(82.6%)	9.7073	0.001
	<21	397	39(9.8%)	358(91.2%)		
Degree of education	High	325	21(6.5%)	304(93.5%)	23.8632	0.001
	Low	481	89(18.5%)	392(81.5%)		
Smoking volume	≤3/d	217	18(8.3%)	199(91.7%)	7.2193	0.007
	>3/d	589	92(15.6%)	497(84.4%)		
Medication	Old model	453	27(6%)	426(94%)	51.8661	0.000
	New model	353	83(23.5%)	270(76.5%)		

Table 2 shows the relationship between the use of different drug treatments and constipation in hospitalized schizophrenic patients. 51 schizophrenic patients with constipation used chlorpromazine, including 12 patients with mild constipation, 39 patients with moderate constipation, 28 patients with perphenazine, 8 patients with mild constipation, 20 patients with moderate constipation, and 20 patients with clozapine and risperidone There were 17 cases and 14 cases respectively. When comparing the differences of taking drugs in all patients with constipation, the p value was 0.001, indicating that different drugs have a significant impact on constipation in hospitalized schizophrenic patients.

Table 2: Relationship between drug use and constipation

Medicine	Constipation	Degree of constipation		$\chi2$	P
		Light	Medium to severe		
Chlorpromazine	51	12	39	17.2131	0.001
Perphenazine	28	8	20		
Clozapine	17	5	12		
Risperidone	14	9	5		
Total	110	34	76		

The P values of positive symptoms, excitement and hostility, cognitive impairment and GAF score in constipation group were 0.060, 0.652, 0.264 and 0.917, respectively. There was no significant

ISSN 2618-1584 Vol. 4, Issue 15: 55-64, DOI: 10.25236/FMSR.2022.041509

difference between constipation group and normal group. The P values of total score, negative symptoms, anxiety and depression in PANSS evaluation were 0.001 between constipation group and normal group The total score, negative symptoms, anxiety and depression were statistically significant between the two groups (Fig 2).

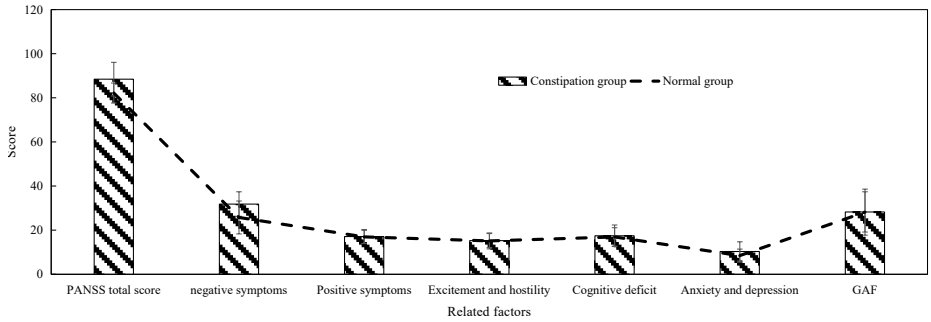

Figure 2: Comparison of mental symptoms between the two groups

3.2. Comparison of daily diet of patients

Table 3 shows the daily diet of all the schizophrenia patients in the study. It can be seen from the table that the intake of fruits, vegetables and daily drinking water of the constipation group are significantly lower than those of the normal group, and there are significant differences between the constipation group and the normal group(P=0.001)。

Table 3: Daily diet of the two groups($\bar{x} \pm s$)

Group	Number of cases(n)	Fruit intake(g)	Vegetable intake(g)	Water consumption(mL)
Constipation group	110	79.17±10.08	158.01±11.21	1648.14±210.63
Normal group	696	186.35±14.97	309.11±13.37	2397.42±220.75
t	/	96.0308	127.7377	34.4398
P	/	0.001	0.001	0.001

3.3. Prediction and analysis of risk factors

The influencing factors of constipation in schizophrenic patients were drug use, gender, age, education level, amount of smoking, negative symptoms, amount of exercise and drinking water. The ROC curve of main influencing factors and constipation in schizophrenic patients was drawn. The ROC curve of drug use, gender, age and amount of exercise with constipation in schizophrenic patients is shown in the figure. The curve areas of the four related factors were 0.89, 0.81, 0.59 and 0.67, respectively, which could be used to predict the constipation of schizophrenic patients (Fig 3).

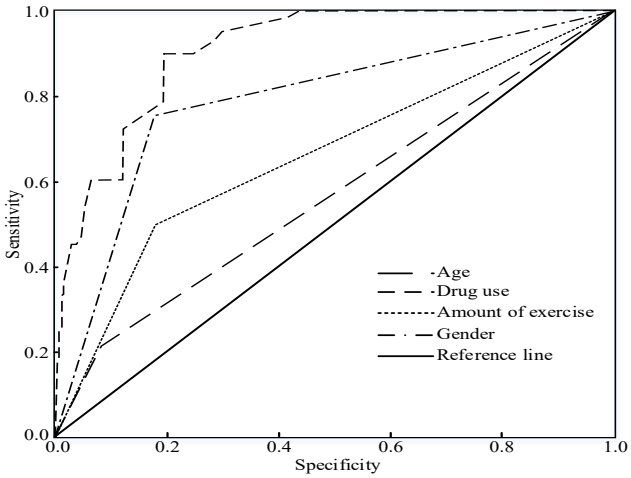

Figure 3: ROC curve of related factors

ISSN 2618-1584 Vol. 4, Issue 15: 55-64, DOI: 10.25236/FMSR.2022.041509

The ROC curve of education level, smoking amount, negative symptoms and drinking water amount with constipation of schizophrenic patients is shown in the figure. The curve areas of the four related factors were 0.82, 0.86, 0.66 and 0.79, respectively, indicating that education, smoking, negative symptoms and drinking water can predict the occurrence of constipation in patients with schizophrenia (Fig 4).

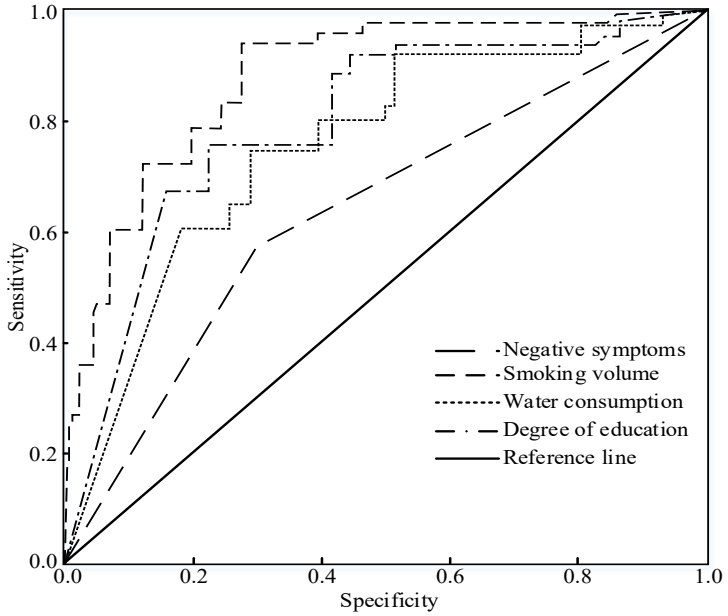

Figure 4: ROC curve of related factors

In order to further determine the important factors affecting the constipation of schizophrenic patients, taking the constipation of patients as the dependent variable and the factors with significant differences in single factor comparison as the independent variable, the multivariate logistic regression analysis was carried out, as shown in the table. It can be seen that among the five factors of age, gender, smoking amount, education level and drinking water amount, the gender, smoking amount and education level of patients are the important predictors of constipation (P=0.007; P=0.001; P=0.005) (Table 4).

Table 4: Logistic regression analysis of constipation risk factors in hospitalized schizophrenia patients

Variable	OR	P	95%CI
Age	1.06	0.017	1.03~1.08
Gender	1.62	0.007	1.13~2.34
Smoking volume	1.78	0.001	1.21~2.68
Educational level	3.27	0.005	2.09~6.54
Water consumption	7.04	0.038	3.51~14.13

4. Discussion

The cognitive and self-control of schizophrenics are far lower than that of ordinary people. Because of their poor mental state, they have very low psychological quality, strong sensitivity to the surrounding environment and are easily affected by the outside world. When stimulated, they will generate extreme ideas, even put them into action, and they will suffer from violence such as self injury and injury, which seriously endangers social security All, it can also have a significant impact on individuals and families [22]. Generally, mental patients are to improve their hospitalization, and then use drug treatment to alleviate the mental symptoms of patients. However, during hospitalization, the nursing staff is not properly operated or the patient has some conflict psychology. Then the patients will likely have other complications. The main reason is the side effects of the antipsychotic drugs and the patients can not follow the normal rules The plan developed by the nursing staff is ongoing [23-24]. Among the complications of schizophrenia patients during hospital., constipation has great influence on the patients' emotion and may aggravate the patients' condition. Therefore, the research and analysis of the relevant factors of schizophrenia patients is of great value for prevention and Nursing [25].

ISSN 2618-1584 Vol. 4, Issue 15: 55-64, DOI: 10.25236/FMSR.2022.041509

It is understood that there are few reports on the prevalence and clinical related factors of constipation in Chinese schizophrenic patients. This study found that the prevalence of constipation in schizophrenic patients is significantly higher than that in healthy normal people, which is consistent with the results of most previous studies [26]. In addition, relevant studies have found that some demographic and clinical characteristics of patients are verified to be important factors affecting constipation in patients with schizophrenia, including gender difference, age and medication during hospitalization [27]. This study found that female patients with constipation is significantly greater than male patients, and some studies said that most of the reports only focus on male patients with schizophrenia, less attention to women, but the study found that female patients with schizophrenia have a greater tendency of violence than the general population, and the ratio is higher than male patients, the reason is that female patients are more likely to be violent than male patients Sexual patients have more drug abuse, which also increases the risk of complications in female patients, which is consistent with the results of this study [28]. However, a study in rural China reported that the long-term prognosis of male schizophrenic patients in rural China is worse than that of female patients, which also leads to the fact that male schizophrenic patients in rural China are more likely to have complications than female patients [29]. Some studies have also reported the need to take special clinical intervention measures for female patients with schizophrenia. In the follow-up survey after the first hospitalization, it was found that about 70% of female patients still need secondary hospitalization, indicating that female patients with schizophrenia are more seriously affected than male patients [30]. This study shows that the risk of constipation in female patients with schizophrenia is significantly higher than that in male patients, which is roughly in line with previous research results. In addition to gender reasons, some studies have found that the education level of patients also determines the risk of constipation. Different education levels of patients generally lead to different self-control ability of patients. Studies show that most patients with higher education level have better self-control ability than those with lower education level [31]. The results of this study show that the prevalence of constipation is 6.5% in patients with higher education level, and 18.5% in patients with lower education level. It can be seen that education level is also an important factor of constipation in patients with schizophrenia, which is consistent with the relevant research results.

Some studies have investigated the correlation between smoking rate and quality of life of patients with mental illness, and found that the smoking rate of patients with schizophrenia is 5.3 times that of the general population, and the smoking rate of patients with schizophrenia is also higher than that of patients with other mental symptoms [32]. Some studies have also found that about one third of smokers are in China, and in China, schizophrenics believe that smoking has many benefits, which can effectively reduce the pain of disease [33]. The above two studies have found that smoking in patients with schizophrenia will have a greater impact on their body. At the same time, this study found that one of the important factors of constipation in patients with schizophrenia is the amount of smoking, which just confirms the previous research view. Some studies have shown that constipation is a common problem. First of all, constipation is a common problem in childhood. Problems during children's learning to defecate will affect their defecation function [34]. In addition, relevant studies have found that cancer patients often have constipation, and almost more than 60% of cancer patients have constipation, especially those who have used opioid analgesics or anticholinergic drugs in the course of treatment [35]. In this study, we found that the drugs taken by schizophrenic patients are an important factor of constipation, and some anticholinergic drugs are also one of the important factors, which just confirmed that anticholinergic drugs may modulate the constipation of patients. Clozapine is a kind of antipsychotic drug commonly used in medicine to relieve the anxiety of patients, and it is also the first choice for the treatment of schizophrenia. However, there are many adverse reactions in the use of clozapine. According to relevant studies, the use of clozapine can produce adverse reactions such as fatigue, dizziness, weight gain, tachycardia, headache, constipation and confusion, although it is not effective in this way, clozapine is still the best drug for the treatment of schizophrenia, and the use of clozapine is strictly controlled due to obvious side effects. In the UK, only 54% of patients can take clozapine under the conditions [36]. There is a report on the correlation between clozapine use and constipation in patients with schizophrenia. Among the patients who participated in the test, the prevalence of constipation in patients who used clozapine was 28%, which was much higher than 11% in the control group. In more than half of the patients who received clozapine treatment, most of them had constipation [37].

Incidence rate of incidence rate of constipation is generally different from that of the rest of the world. The incidence rate of constipation is different from that of the rest of the world. The lowest incidence is 4%, the highest incidence is 29%, and there is a great connection between body weight and constipation [38]. Studies have confirmed that the intake of gluten containing cereal products plays an

ISSN 2618-1584 Vol. 4, Issue 15: 55-64, DOI: 10.25236/FMSR.2022.041509

important role in the pathogenesis of schizophrenia, and considering its pathogenesis, the treatment methods of schizophrenia were analyzed [39]. At the same time, Brazilian scholars have reported that unhealthy food may be related to constipation in dietary analysis, and finally concluded that poor eating habits such as insufficient intake of vegetables and fruits are significantly positively correlated with constipation [40]. In addition, the study on the correlation between the diet and constipation of schizophrenic patients found that due to the lack of self-control ability of schizophrenic patients, the intake of fat and total sugar is high, which will have a certain impact on the health of patients. The study pointed out that the diet method of stopping hypertension should be adopted [41]. In this study, we found that the fruit intake, vegetable intake and water intake of patients with schizophrenia have a significant impact on the incidence of constipation. In addition to the dietary habits of patients, according to the relevant research of American scholars, sports and constipation are also related [42]. There are also studies that patients with constipation can be treated by exercise, which is a feasible and effective treatment for constipation, but the determination of exercise method is not clear [43]. The daily activity time of schizophrenic patients is generally planned by nursing staff. Some studies improve the gastrointestinal motility of schizophrenic patients by making joint exercise. The final results show that the colon transit time of patients participating in joint exercise is significantly reduced [44].

5. Conclusion

To sum up, the constipation of schizophrenic patients is affected by various factors. The influencing factors are gender, age, education level, drugs taken, negative symptoms, total PANSS score, smoking, exercise and drinking water. Gender, education level and daily smoking are important predictors of constipation. Therefore, in order to reduce the prevalence of constipation in patients with schizophrenia, we can take certain preventive measures to help patients with schizophrenia improve their living standards and change their lifestyle, such as making exercise plans or eating habits. In addition, the use of laxatives can accelerate the recovery of constipation to a certain extent, and the rational use of laxatives can also reduce the incidence of constipation. But,the Study of anticholinergic drugs are not included in this manuscript, which is our future research objective.The rationales for selection of the main observation indicators and the definition we selected are not explained clearly in the manuscript and indeed it is quite deficient， and in this manuscript, we have only focused on some of the studies of commonly used psychiatric drugs, ignoring the study of other new antipsychotic drugs, which is our future research objective.

Acknowledgements

1) Research on the effect of dance art therapy on cognitive function, clinical symptoms and BMI of hospitalized patients with chronic schizophrenia, Shanghai Pudong New Area Science and Technology Development Fund Public Institution People's Livelihood Scientific Research Special (Medical and He alth) Project (No.: PKJ2021-Y77);2) Diagnosis and Treatment Center of Integrated Traditional Chinese and Western Medicine, construction project of "Shanghai Pudong New Area National Comprehensive Reform Pilot Zone for the Development of Traditional Chinese Medicine" (No.: PDZY-2022-0501).

References

[1] Sharma A, Rao S. Constipation: Pathophysiology and Current Therapeutic Approaches. Handbook of Experimental Pharmacology, 2017, 239: 59-74.
[2] Kanaki AA, Singanal S. Efficacy and safety of prucalopride in the treatment of chronic constipation. International Journal of Basic & Clinical Pharmacology, 2018, 7(5):998.
[3] Jiang Y, Tang Y, Lin L. Clinical Characteristics of Different Primary Constipation Subtypes in a Chinese Population. Journal of Clinical Gastroenterology, 2019, 54(7):1.
[4] Alonso Y, Alba Valiente-Pallejà, Verge B, et al. High frequency of clinical conditions commonly associated with mitochondrial disorders in schizophrenia. Acta Neuropsychiatrica, 2020, 32(5):1-16.
[5] Bentsen H, Cuenod M, Do KQ. Glutathione related factors in two biotypes of schizophrenia. Schizophrenia Bulletin, 2019, 45(Supplement_2):S309-S309.
[6] Lin CH, Chan HY, Hsu CC, et al. Factors associated with laxative use in schizophrenia patients treated with second-generation antipsychotics. European Neuropsychopharmacology, 2021, 43:139-146.
[7] Yamada E, Namiki Y, Takano Y, et al. Clinical factors associated with the symptoms of constipation

ISSN 2618-1584 Vol. 4, Issue 15: 55-64, DOI: 10.25236/FMSR.2022.041509

in patients with diabetes mellitus: A multicenter study. Journal of Gastroenterology & Hepatology, 2018, 33(4):863-868.
[8] Oddur, Ingimarsson, James H, et al. Constipation, ileus and medication use during clozapine treatment in patients with schizophrenia in Iceland. Nordic journal of psychiatry, 2018,72(7):497-500.
[9] Chen HK, Hsieh CJ. Risk of gastrointestinal Hypomotility in schizophrenia and schizoaffective disorder treated with antipsychotics: A retrospective cohort study. Schizophrenia Research, 2017:396-409.
[10] Chih-Chieh Chang, Hsing-Kang Chen. The Prevalence of Constipation and Its Risk Factors in Patients with Schizophrenia. Taiwanese Journal of Psychiatry (Taipei) 2021; 35: 95-98
[11] Lu YS, Chen YC, Kuo SH, et al.: Prevalence of antipsychotic drugs related to constipation in patients with schizophrenia. Taiwan J Psychiatry 2016; 30: 294-9.
[12] Shirazi A, Stubbs B, Gomez L, et al.: Prevalence and predictors of clozapine-associated constipation: a systematic review and meta-analysis. Int J Mol Sci 2016; 17: 863.
[13] Kalinowska S, Trześniowska-Drukała, Beata, Safranow K, et al. Association between thyroid function and metabolic syndrome in male and female schizophrenia patients. Psychiatry Research, 2019, 274: 167-175.
[14] Adamowicz K, Kucharska-Mazur J. Dietary Behaviors and Metabolic Syndrome in Schizophrenia Patients. Journal of Clinical Medicine, 2020, 9(2):537.
[15] Peng Men, Zhanmiao Yi, Chaoyun Li et al. Comparative efficacy and safety between amisulpride and olanzapine in schizophrenia treatment and a cost analysis in China: a systematic review, meta-analysis, and cost-minimization analysis. BMC psychiatry, 2018,18(1):286.
[16] Every-Palmer S, Ellis PM, Nowitz M, et al. The Porirua Protocol in the Treatment of Clozapine-Induced Gastrointestinal Hypomotility and Constipation: A Pre- and Post-Treatment Study. CNS Drugs, 2017, 31(1):75-85.
[17] Pristed SG, Correll CU, Nielsen J. Frequency and correlates of anticholinergic use among patients with schizophrenia in Denmark: A Nation-wide pharmacoepidemiological study. Psychiatry Res, 2017:198-203.
[18] Schwasinger-Schmidt, Macaluso TE, Other Antidepressants. Handbook of experimental pharmacology, 2019, 250:325-355.
[19] Attard A, Iles A, Attard S, et al. Clozapine: why wait to start a laxative?. BJP sych Advances, 2019, 25(6):377-386.
[20] Lin CC, Hung YY, Tsai M C , et al. Increased serum brain-derived neurotrophic factor in male schizophrenic patients with metabolic syndrome. Medicine, 2017, 96(22):e7089.
[21] Petkari, Eleni & Mayoral., Fermín & Moreno-Küstner, Berta. Gender Matters in Schizophrenia-spectrum Disorders: Results from A Healthcare Users Epidemiological Study in Malaga, Spain. Comprehensive Psychiatry. 2017, 72. 136-143.
[22] Silva NLD, Galhenage J, Dayabandara M, et al. Sheehan Syndrome Presenting with Psychotic Manifestations Mimicking Schizophrenia in a Young Female: A Case Report and Review of the Literature. Case Reports in Endocrinology, 2020, 2020(5):1-6.
[23] Viswam S K, Maheswari E, Singh H, et al. Adverse drug reactions due to atypical antipsychotics in the absence of other centrally acting drugs among patients with mental illness. Archives of Pharmacy Practice, 2019, 10(2):105-109.
[24] Yen C C, Tze-Chun T, Tzu-Ting C, et al. Efficacy, tolerability, and safety of oral paliperidone extended release in the treatment of schizophrenia: a 24-week, open-label, prospective switch study in different settings in Taiwan. Neuropsychiatric Disease & Treatment, 2018, 14:725-732.
[25] Hideaki K, Masanori T, Shinpei K, et al. Safety and effectiveness of rapid-acting intramuscular olanzapine for agitation associated with schizophrenia – Japan postmarketing surveillance study. Neuropsychiatric Disease & Treatment, 2018, 14:265-272.
[26] Susanna Every-Palmer, Pete M Ellis. Clozapine-Induced Gastrointestinal Hypomotility: A 22-Year Bi-National Pharmacovigilance Study of Serious or Fatal 'Slow Gut' Reactions, and Comparison with International Drug Safety Advice. CNS Drugs, 2017, 31:699-709.
[27] Biagi E, Capuzzi E, Colmegna F, et al. Long-Acting Injectable Antipsychotics in Schizophrenia: Literature Review and Practical Perspective, with a Focus on Aripiprazole Once-Monthly. Advances in Therapy, 2017, 34(5):1036–1048.
[28] Wang J, Li C, Zhu XM, et al. Association between schizophrenia and violence among Chinese female offenders. Scientific Reports, 2017, 7(1):818.
[29] Mao Sheng, Ran WenJun, et al. Gender differences in outcomes in people with schizophrenia in rural China: 14-year follow-up study. British Journal of Psychiatry, 2018, 206(4):283-288.
[30] Sommer I E, Tiihonen J, Mourik AV, et al. The clinical course of schizophrenia in women and men—a nation-wide cohort stud. NPJ Schizophrenia, 2020, 6(1):12.

ISSN 2618-1584 Vol. 4, Issue 15: 55-64, DOI: 10.25236/FMSR.2022.041509

[31] Hui Wen, Yenju Huang, et al. Nursing Experience with Reconstructing Self-Control Using Rational-Emotive Behavior Therapy on a Patient with Schizophrenia and Obsessive-Compulsive Symptoms. Hu li za zhi The journal of nursing, 2018, 65(5):112-119.
[32] Li X H, An F R, Ungvari G S, et al. Prevalence of smoking in patients with bipolar disorder, major depressive disorder and schizophrenia and their relationships with quality of life. Rep, 2017, 7(1):8430.
[33] Mak Y W, Chiang VCL, Loke A Y. Experiences of Tobacco Use among Chinese Individuals with Schizophrenia in Community-Based Residential Settings: A Qualitative Study. International Journal of Environmental Research and Public Health, 2020, 17(1):321.
[34] Tongu, Utku, Ylmaz, et al. Relationship of functional constipation and anal-retentive behavior features. Turkish journal of surgery, 2018:1-5.
[35] Aocn R J W, R. Managing Constipation in Adults with Cancer. Journal of the Advanced Practitioner in Oncology, 2017, 8(2):149-161.
[36] Iqbal E , Govind R , Romero A , et al. The side effect profile of Clozapine in real world data of three large mental health hospitals. PLOS ONE, 2020, 15(12):1-20.
[37] Chougule A , Praharaj S K , Bhat S M , et al. Prevalence and Factors Associated With Clozapine-Related Constipation: An Observational Study. J Clin Psychopharmacol, 2018, 38(1):42-46.
[38] Sayed T , Dalia K , Walid A B , et al. Effects of a proposed physical activity and diet control to manage constipation in middle-aged obese women. Diabetes Metab Syndr Obes, 2017, 10:513-519.
[39] Tomaka J , Karaku?A-Juchnowicz H , Morylowska-Topolska J , et al. Review paper. Gluten-related disorders and schizophrenia - potential linking mechanisms, diagnostic and therapeutic challenge[J]. Current Problems of Psychiatry, 2017, 18(1):9-24.
[40] Andreoli C S , Ribeiro-Vieira S A , Fonsca P C D A , et al. Markers of healthy eating habits, water intake, and constipation in children between 4 and 7 years of age. Revista de Nutrio, 2018, 31(4):363-372.
[41] Sori T , Mavar M , Rumbak I . The Effects of the Dietary Approaches to Stop Hypertension (DASH) Diet on Metabolic Syndrome in Hospitalized Schizophrenic Patients: A Randomized Controlled Trial. Nutrients, 2019, 11(12):2950.
[42] Wilson P B . Associations between physical activity and constipation in adult Americans: Results from the National Health and Nutrition Examination Survey. Neurogastroenterology and Motility, 2020(1):e13789.
[43] Gao R, Tao Y, Zhou C, Li J, Wang X, Chen L, Li F, Guo L. Exercise therapy in patients with constipation: a systematic review and meta-analysis of randomized controlled trials. Scand J Gastroenterol. 2019 ;54(2):169-177.
[44] Song BK, Kim YS, Kim HS, Oh JW, Lee O, Kim JS. Combined exercise improves gastrointestinal motility in psychiatric in patients. World J Clin Cases. 2018;6(8):207-213.