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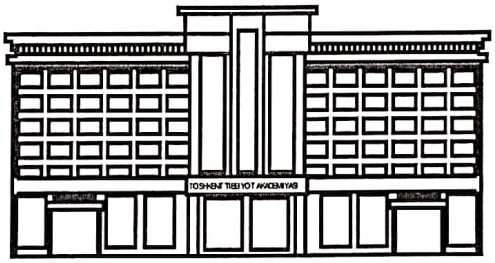

ВЕСТНИК

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EFFICACY AND SAFETY OF FLUOXETINE IN PATIENTS WITH UROLOGIC DISEASE: A COMPARATIVE TREATMENT ANALYSIS

Allaeva M.J., Achilov D.D., Abdurakhmanov F.F., Askarov O., Kholmatov J.A., Sultanov S.A.

ЭФФЕКТИВНОСТЬ И БЕЗОПАСНОСТЬ ФЛУОКСЕТИНА У ПАЦИЕНТОВ С УРОЛОГИЧЕСКИМИ ЗАБОЛЕВАНИЯМИ: СРАВНИТЕЛЬНЫЙ АНАЛИЗ ЛЕЧЕНИЯ

Аллаева М.Ж., Ачилов Д.Д., Абдурахманов Ф.Ф., Аскаров О., Холматов Ж.А., Султанов С.А.

UROLOGIK KASALLIGI BO'LGAN BEMORLARDA FLUOKSETINNING SAMARADORLIGI VA XAVFSIZLIGI: QIYOSIY DAVOLASH TAHLILI

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Аннотация.

Актуальность: *Преждевременная эякуляция (ПЭ) остается сложным поли этиологическом заболеванием, дестабилизирующим половую функцию мужчин. Его распространенность оценивается в 20-40%. Диагноз ТЭЛА затруднен, поскольку его симптомы в значительной степени субъективны и плохо определяются в клиническом контексте. В качестве основного метода терапии используется фармакотерапия.*

Цель: *Сравнительная оценка эффективности и безопасности кломипрамина гидрохлорида (назальный спрей 2,5 мг) и флуоксетина (капсулы 20 мг) при лечении пациентов с преждевременной эякуляцией.*

Методы. *Обследовано 672 мужчины в возрасте от 18 до 60 лет (средний возраст 36,4±3,7 года) с жалобами на ТЭЛА. Респонденты были опрошены с помощью опросника «Узбекский индекс ЛЭ» (UIPE). Для оценки эффективности и безопасности назального спрея, содержащего кломипрамина гидрохлорид, методом случайной выборки был отобран 101 пациент. Обследованы и получали лечение флуоксетином 103 пациента. Группа плацебо.*

Результаты: *у пациентов с преждевременной эякуляцией, получавших кломипрамин, LIVIA увеличивается по сравнению с пациентами, получавшими флуоксетин.*

Ключевые слова: *сексуальная дисфункция, преждевременная эякуляция, флуоксетин, кломипрамин, эффективность.*

Annotatsiya.

Mavzuning dolzarbligi: *Erta eyakulyatsiya (EE) erkaklarning jinsiy faolligini beqarorlashtiradigan murakkab polietiologik kasallik bo'lib qolmoqda. Uning tarqalishi 20-40% ni tashkil qiladi. EE tashxisi qiyin, chunki uning belgilari asosan subyektivdir va klinik kontekstda kam aniqlangan. Terapiyaning asosiy usuli sifatida farmakoterapiya qo'llaniladi.*

Tadqiqot maqsadi: *Erta eyakulyatsiya bilan og'rigan bemorlarni davolashda klomipramin gidroxlorid (2,5 mg burun spreyi) va fluoksetin (20 mg kapsulalar) samaradorligi va xavfsizligini solishtirish.*

Tadqiqot usullari: *Biz 18 yoshdan 60 yoshgacha bo'lgan (o'rtacha yoshi 36,4±3,7 yosh) PE shikoyatlari bilan 672 nafar erkakni tekshirdik. Respondentlar bilan intervyu Uzbek LE ko'rsatkichi' (UIPE) so'rovnomasi yordamida o'tkazildi. Klomipramin gidroxlorid burun spreyi samaradorligi va xavfsizligini baholash uchun 101 bemor tasodifiy tanlangan. 103 bemor tekshirildi va fluoksetin bilan davolandi. Plasebo guruhi.*

Natijalar: *Klomipramine bilan davolashgan erta eyakulyatsiya bilan og'rigan bemorlarda LIVIA fluoksetin bilan kasallangan bemorlarga nisbatan oshadi.*

Kalit so'zlar: *jinsiy disfunksiya, erta eyakulyasiya, fluoksetin, klomipramin, samaradorlik.*

Relevance: Premature ejaculation (PE) remains a complex, polyetiological disease that destabilizes the sexual function of men. Its prevalence is estimated at 20-40%. The diagnosis of PE is difficult because it is largely subjective and poorly defined in the clinical context [1-3].

Almost every third man between the ages of 18 and 59 has this disorder accompanied by negative consequences, such as lack of self-confidence, anxiety, depression and dissatisfaction in relationships between men and their partners [4-5]. The main emphasis in the treatment of this group of patients is on psycho- and use are considered to be a first-line treatment option for PE. However. There is no FDA-approved drug for the treatment of PE on the market in the United States [6]. Currently, the use of selective serotonin reuptake inhibitors, which include fluoxetine and clomipromine, is of particular interest.

THE PURPOSE OF THE STUDY:

Comparative evaluation of the efficacy and safety of Clomipramine hydrochloride (2.5 mg nasal spray) and Fluoxetine (20 mg capsules) in the treatment of patients with premature ejaculation.

MATERIALS AND METHODS

This study was conducted at the Republican specialized, Scientific and Practical Medical Center of Urology, Ministry of Health of the Republic of Uzbekistan (RSNPMC of Urology).

A retrospective, prospective, randomized, blind, placebo-controlled study design was developed and applied to obtain data in the time period from 21.01.2012 to 01.03.2019.

The study was conducted in accordance with Protocol No. 11 / 8 of 07.09.2010 of the Ethics Committee of the Ministry of Health of the Republic of Uzbekistan, and the permission of pharm. Committee of the Republic of Uzbekistan No. 02 / 88 dated 12.05.2005.

The study involved 672 men aged 18 to 60 years (average age 36.4±3.7) with complaints of PE, who were examined using the questionnaire "Uzbek PE Index (UIPE)" (7).

LIVIA was also determined during each sexual act using a stopwatch.

Inclusion criteria

Practically healthy men who have been in a stable, heterosexual, monogamous sexual relationship (more than 6 months) who have been complaining about PE for at least 3 months. In all cases, informed consent to participate in the study was obtained.

Exclusion criteria

Patients with:

- hypogonadism;
- coronary heart disease (CHD according to anamnesis) and taking nitrates;
- deformities of the penis;
- with liver and kidney diseases in the decompensation stage; - alcohol abusers and drug addicts;
- patients with diabetes mellitus;
- who underwent ONMC within 6 months before the study;
- with uncontrolled arterial hypertension (systolic blood pressure above 170 mmHg or diastolic blood pressure above 100 mmHg), with arterial hypotension (blood pressure < 90/50 mmHg);
- patients with rhinitis and diseases of the paranasal sinuses and inflammatory diseases of the MVP.

Taking into account the inclusion and exclusion criteria, 303 patients with complaints of PE were selected for further study.

101 patients were selected by random sampling to evaluate the efficacy and safety of a nasal spray containing Clomipramine hydrochloride (2.5mg). 103 patients were examined and treated with the drug fluoxetine, in a dosage regimen of 20 mg.

In addition, 99 patients were in the placebo group.

Methods of statistical analysis

The research materials were subjected to statistical processing using parametric analysis methods.

Accumulation, correction, systematization of initial information and visualization of the results were carried out in Microsoft Office Excel 2016 spreadsheets.

Statistical analysis was carried out using the IBM SPSS Statistics v. 22 program (developed by IBM Corporation).

Descriptive analysis was used to obtain initial data, such as mean, standard deviation, and others.

The t-test of paired samples was used to evaluate the results before and after treatment with each drug (fluoxetine and clomipramine nasal spray).

In accordance with modern directions of pharmacotherapy, when studying the problem of PE, the safety profile was measured, and the effectiveness of each drug during treatment was evaluated in all patients. For each patient, measurements were performed twice, before and after treatment.

An independent t-test of the sample was used to evaluate the comparative values of the efficacy and safety of drugs used for the treatment of PE.

An independent sample t-test (sometimes also called the t-test for two criteria) was used to determine whether there were statistically significant differences in values between the two groups.

The chi-square criterion was used to compare the side effects of each drug and to compare the onset and duration of their duration of action. The chi-squared test was used for independence tests to determine whether the distributions of results for each drug differ from each other.

Conditionally, the patients were divided into four age groups: group 1 (from 18 to 29 years); group 2 (from 30 to 39 years); group 3 (from 40 to 49 years) and group 4 (from 50 to 59 years).

RESULTS:

The statistical results of placebo-controlled studies of the use of nasal spray containing clomipramine hydrochloride (abbreviated clomipramine) and fluoxetine are shown in Tables 1 and 2.

Table 1 presents statistical results of comparing the effects of drugs in four age groups.

Table 1.

Results of treatment of patients with Fluoxetine (20 mg) compared with Clomipramine hydrochloride nasal spray (2.5mg) depending on age

Age	Before treatment						After treatment					
	Fluoxetine		Clomipramine		Placebo		Fluoxetine		Clomipramine		Placebo	
	ILVE (min)	UIPE (mark)	ILVE (min)	UIPE (mark)	ILVE (min)	UIPE (mark)	ILVE (min)	UIPE (mark)	ILVE (min)	UIPE (mark)	ILVE (min)	UIPE (mark)
18-29	1.4±0.6	25.8±4.5	1.4±0.6	26±4.0	1.3±0.6	25±4.0	3.9±1.8*	16.6±4.4	6.0±1.4*	15±3.6	1.3±0.6	24.9±3.5
30-39	1.3±0.6	24.9±4.1	1.2±0.6	25±4.1	1.3±0.6	25±4.8	4.4±1.8*	15.9±3.8	5.9±1.4*	16±3.9	1.3±0.6	24.6±4.1
40-49	1.2±0.6	25.0±3.9	1.6±0.5	26±3.0	1.2±0.4	26±4.8	3.7±1.8*	15.5±3.8	5.3±1.1*	16±3.9	1.3±0.5	26.2±4.8

In all age groups of patients treated with fluoxetine, a t-test was performed for paired samples to compare LVIE.

There was a significant difference in the time estimates of the condition of patients before (M = 1.40, SD = 0.62) and after treatment (M = 3.89, SD = 1.76) among the 1st age group; t (44) = - 8.89, p <0.001.

In the 2nd age group, there was also a significant difference in time estimates before (M = 1.26, SD = 0.60) and after treatment (M = 4.39, SD = 1.84), t (40) = - 10.18, p <0.001.

A significant difference in the time before (M = 1.23, SD = 0.54) and after treatment (M = 3.69, SD = 2.05) was observed in group 3; t (12) = - 4.45, p = 0.001; In the 4th age group it was up to (M = 1.62, SD = 0.75) and after treatment (M = 4.00, SD = 1.63). t (3) = - 4.28, p = 0.02.

These results show that when treating patients with PE fluoxetine 20 mg, their LVIE time increases.

a t-test for paired samples to compare the UIPE scores in conditions before and after fluoxetine treatment for each age group showed that in the 1st age group there was a significant difference in scores before (M = 25.82, SD = 4.50) and after treatment (M = 16.64, SD = 4.35); t (44) = 10.40, p <0.001.

In the 2nd age group, there was also a significant difference in scores before (M = 24.90, SD = 4.09) and after treatment (M = 15.98, SD = 3.80); t (40) = 9.43, p <0.001.

In the 3rd age group, a significant difference in scores was before (M = 25.00, SD = 3.87) and after treatment (M = 15.54, SD = 3.76); t (12) = 5.84, p <0.001.

In the 4th age group, the difference in scores was up to (M = 26.25, SD = 6.95) and after treatment (M = 14.25, SD = 0.50); t (3) = 3.59, p = 0.04.

These results show that, in patients with PE, when receiving fluoxetine, UIPE scores improve.

Fluoxetine versus Clomipramine

To compare the therapeutic effect of fluoxetine and clomipramine drugs in the treatment of PE, a t-test of independent samples was conducted in four age groups to compare LVIE.

A significant difference in time indicators was in the treatment with fluoxetine (M = 3.89, SD = 1.76) and with clomipramine nasal spray (M = 6.00, SD = 1.37) in the 1st age group; t (93)=-6.55, p<0.001.

In the 2nd age group, the time difference was in fluoxetine treatment (M = 4.39, SD = 1.84) and treatment with clomipramine nasal spray (M = 5.87, SD = 1.40); t (77) = - 3.99, p <0.001.

In the 3rd age group, significant the difference in time parameters during treatment with fluoxetine (M = 3.69, SD = 1.84) and clomipramine nasal spray (M = 5.30, SD = 1.06) t (21) = - 2.46, p = 0.02.

It should be noted that in the 4th age group, the difference in time indicators during treatment with fluoxetine (M = 4.00, SD = 1.63) and clomipramine nasal spray (M = 6.67, SD = 1.15) was insignificant.

The results obtained indicate that in patients with premature ejaculation, when using a nasal spray - clomipramine, LVIE increases in comparison with that when using fluosetine.

The data of the t-test of independent samples when comparing the results of UIPE in the treatment with fluoxetine and clomipramine nasal spray are shown in Table 2.

Table 2.

Comparative evaluation of the effectiveness of the use of drugs Clomipramine and Fluoxetine

Groups	Before treatment		After treatment		Side effects of the drug*	Time before the start of the drug (in minutes)*
	ILVE (min)	UIPE (mark)	ILVE (min)	UIPE (mark)		
Clomipramine (N=101)	1.30±0.6	25.40±4.2	5.90±1.4*	15.70±3.7	1.60±0.6	12.90±1.80
Fluoxetine (N=103)	1.30±0.6	25.40±4.3	4.10±1.8*	16.10±4.0	2.70±0.6	218.9±20.6
Placebo (N=99)	1.30±0.6	25.44±4.3	1.32±0.6	25.14±4.0	1.62±0.56	12.89±1.82

Note: * In all comparison groups after treatment, p<0.05;

To compare RES and UIPE in conditions before and after treatment with fluoxetine and clomipramine, a paired t-test was performed.

Data analysis of patients receiving nasal spray (imitation of clomipramine) in the placebo group

For each age group of patients taking placebo (nasal spray distal water), the t-criterion of paired samples was determined to compare LVIE in conditions before and after treatment.

In all age groups, there was a slight, but significant difference in the studied doses in patients with placebo (Table 1)

. These results indicate that the use of nasal spray in the form of placebo in patients with PE does not really have a long-term time indicator.

In all age groups of patients receiving placebo, when conducting a paired t-test to compare the indicators of UIPE and LVIE in conditions before and after treatment, there were no significant differences between them.

There was a significant difference in time before (M = 1.33, SD = 0.61) and after treatment with fluox-

<0.001; The results showed that the use of fluoxetine really increases the duration of LVIE in patients with PE.

There was also a significant difference in UIPE scores before (M = 25.37, SD = 4.33) and after fluoxetine treatment (M = 16.15, SD = 3.97); t (102) = 15.78, p <0.001; which resulted in an increase in UIPE scores in patients with PE.

The use of clomipromine led to an increase in LVIE from (M = 1.34, SD = 0.61) to (M = 5.90, SD = 1.35); t (100) = - 34.04, p<0.001;

There was also a significant difference in the indicators of UIPE scores before (M = 25.49; SD = 4.15) and after treatment with clomipramine (M = 15.73; SD = 3.71); t (100) = 19.22, p<0.001;

A t-test of independent samples to compare LVIE after fluoxetine treatment and after clomipramine use (Table 2) revealed a significant difference in time indicators, respectively (M = 4.07, SD = 1.79) and (M = 5.90, SD = 1.35); t (202) = - 8.23, p <0.001.

These The results show the advantage of using clomipramine compared to fluoxetine in patients with PE.

t-test of independent samples conducted to compare the indicators of UIPE. There was no significant difference in scores after treatment with fluoxetine (M = 16.15, SD = 3.97) and clomipramine (M = 15.73, SD = 3.71). These indicate that there are no differences in the effect of these drugs on UIPE.

a t-test of independent samples conducted to compare the side effects of fluoxetine and clomipromine in the treatment of PE revealed a significant difference in the incidence of side effects of fluoxetine (M = 2.72, SD = 0.58) and clomipramine (M = 1.61, SD = 0.62) under conditions t (202) = 13.14, p <0.001, which also proves in favor of the latter.

According to the results of treatment with clomipramine, 94 out of 101 patients were registered and documented without any side effects. Two had a headache, one case of drowsiness, dizziness, one case of nausea and three cases of vomiting and nasal congestion.

According to the results of fluoxetine treatment, 87 out of 103 patients were registered and documented without any side effects, five had headache, seven cases of drowsiness and dizziness, and four cases of vomiting and nasal congestion.

Table 3.

Side effects of fluoxetine and clomipramine hydrochloride

Side effects	Fluoxetine (n=103)		Clomipramine (n=101)*		Placebo group (n=99)	
	n	**%**	**n**	**%**	**n**	**%**
Headache	5	4.8	2	1.98	2	2.02
Dizziness	7	6.7	1	0.99	0	0
Nausea	4	3.8	1	0.99	0	0
Vomiting. Nasal congestion	0	0	3	2.97	4	4.04
Total phenomenon	**16**	**15.3**	**7**	**6.93**	**6**	**6,06**

** Note:* $\chi^2 = 10.84$; $p<0.05$

The statistical independence or relationship between the side effects of drug treatment and therapeutic drugs (clomipramine and fluoxetine) in violation of PE was measured using the chi-square criterion.

Based on the statistical results of the chi-square test, a significant relationship was revealed between medications for treatment and side effects of medications (X2(4) =10.84; p=0.02).

a t-test of independent samples conducted to compare the time of action of fluoxetine and clomipromine revealed a significant difference in time estimates for treatment conditions with fluoxetine (M = 218.93, SD = 20.58) and clomipramine (M = 12.91, SD = 1.81); t (202) = 100.25, p <0.001.

Discussion

The results show that the nasal spray of clomipromine hydrochloride increases the average time of LVIE by 4 times and improves the indicators of UIPE among patients with PE.

Comparison of conditions before and after treatment with this drug showed a statistically significant improvement with a high degree of drug effect on patients of the experimental group.

The confidence interval of the difference is 95%. This statistically significant improvement varies among the age groups of patients with PE.

Nasal spray of clomipromine hydrochloride showed a slight difference between the age groups of patients with PE (p> 0.05), where it has a positive effect on increasing the duration of LVIE among young age groups.

Independent t-tests were conducted to compare the effectiveness of the corresponding medications in the treatment of PE. Statistically significant indicators of LVIE were revealed, side effects of medications, duration of action of clomipramine and fluoxetine were evaluated. According to the results of statistical analysis, the use of clomipramine is more effective than fluoxetine.

The results of the statistical comparison of the

a significant difference in the indicators of LVIE and UIPE before and after its use. These results show that when patients with PE use clomipramine, their scores of the Uzbek PE index (UIPE) improve and the duration of LVIE increases.

Chi-squared results indicate a statistically significant association between the side effects of drug treatment with clomipramine and fluoxetine. Since the p value is less than p = 0.05, it can be concluded that there is a connection between medications (clomipramine and fluoxetine) and the occurrence of side effects such as headache, drowsiness, dizziness, nausea, vomiting, nasal congestion.

Conclusions

The results of studies in clinical practice revealed the effect of the nasal spray of clomipramine from 10 minutes of use, Whereas the encapsulated forms of the drug fluoxetine began to act from 210 minutes of use.

The developed new method allowed to reduce the number of side effects of clomipramine, such as nausea, vomiting, dry mouth, decreased libido, dizziness by 45% when using this method of treatment. Thus, the use of nasal spray allows you to minimize the dose of the drug while maintaining the effect of its effects, which is of great socio-economic importance.

The results of the study show that the new method has two times fewer side effects than other widely used (Fluoxetine, etc.) methods of treatment. Just as the results of comparing the duration of the drug show that a nasal spray containing clomipramine hydrochloride with a drug duration of 10-15 minutes can make it the most convenient and effective drug among other widely used drugs for the treatment of PE.

Literature.

1. Butcher. M.J.. et al.. Topical Agents for Premature Ejaculation: A Review. Sex Med Rev. 2020. 8(1): p. 92-99.

2. Forbes. C.M. R. Flannigan. and D.A. Paduch. Perineal Ultrasound: a Review in the Context of Ejaculatory Dysfunction. Sex Med Rev. 2018. 6(3): p. 419-428.

3. Kalejaiye. O.. et al.. Premature ejaculation: challenging new and the old concepts. F1000Res. 2017. 6: p. 2084

4. Nutritional and biological value of natural-bio shoots mung bean "Mungoltin". Food and biological values.

Javokhir B. Khayitov, Guli I. Shaikhova, Dilshod D. Achilov, Munira J. Allaeva / Cardiometry | Issue 21. February 2022 // №6 // 78-84.

5. Olivier, J.D.A., Olivier, B. Antidepressants and Sexual Dysfunctions: a Translational Perspective. Curr Sex Health Rep 11, 156–166 (2019). https://doi.org/10.1007/s11930-019-00205-y

6. Russo, G.I., Serefoglu, E.C. Premature Ejaculation: 2020 Update. Curr Sex Health Rep 11, 411–420 (2019). https://doi.org/10.1007/s11930-019-00232-9

5. Russo, G.I., Serefoglu, E.C. Premature Ejaculation: 2020 Update. Curr Sex Health Rep 11, 411–420 (2019). https://doi.org/10.1007/s11930-019-00232-9

8. Современная концепция консервативного лечения ПЭ / А. Д. Нисанбаев, А. А. Нисанбаева, Д. И. Сенгирбаев [и др.] // Вестник Казахского национального медицинского университета. – 2021. – № 3. – С. 372-376. – EDN MVAUDJ.

EFFICACY AND SAFETY OF FLUOXETINE IN PATIENTS WITH UROLOGIC DISEASE: A COMPARATIVE TREATMENT ANALYSIS

Allaeva M.J., Achilov D.D., Abdurakhmanov F.F., Askarov O., Kholmatov J.A., Sultanov S.A.

Resume. Relevance: *Premature ejaculation (PE) remains a complex polyetiological disease destabilizing the sexual function of men. Its prevalence is estimated at 20-40%. The diagnosis of PE is difficult because its symptoms are largely subjective and poorly defined in the clinical context. Pharmacotherapy is used as the main method of therapy.*

Objective: *Comparative evaluation of the efficacy and safety of Clomipramine hydrochloride (2.5 mg nasal spray) and Fluoxetine (20 mg capsules) in the treatment of patients with premature ejaculation.*

Methods: *The study involved 672 men aged 18 to 60 years (average age 36.4±3.7 years) with complaints of PE. The respondents were surveyed using the questionnaire "Uzbek PE Index" (UIPE). 101 patients were selected by random sampling to evaluate the effectiveness and safety of a nasal spray containing Clomipramine hydrochloride. 103 patients were examined and treated with fluoxetine. 99 patients were in the placebo group.*

Results: *in patients with premature ejaculation treated with clomipramine, LIVIA increases compared to patients treated with fluoxetine.*

Keywords: *sexual dysfunction, premature ejaculation, fluoxetine, clomipramine, efficacy.*