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POSSIBLE CORRELATION BETWEEN CHRONIC TRAMADOL ADMINISTRATION AND DISTURBANCES IN TESTICULAR ACTIVITY AND FERTILITY IN MALE

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ABASTRACT: The purpose of this study was used to detect the possible correlation between chronic tramadol administration used at least within the past 12 months and disturbances in testicular activity and fertility in male. The study was involved 100 cases who recruited from toxicological units of Al-Azhar University Hospital (New Damietta). In addition to 20 subjects as a control group. After free informed consent. Extraction of tramadol using a high performance liquid chromatography (HPLC), other blood investigations including semen analysis and finally clinical examination to all groups.

Results: There is significant and marked increased in viscosity in (70.0%) and decreased in some semen parameter as (volume, count, motility and progression) were it is (49.0%), (88.0%), (77.0%) and (77.0%) respectively, especially on long term tramadol administration as compared with control group. **Conclusion:** Significant correlation between tramadol administration and impaired sperm quality parameters in adult males especially on long term tramadol administration as compared with control group. **Recommendation:** All husband who taken tramadol for a long period especially for premature ejaculation must be recognize about effects of tramadol on fertility as the opposite is true on a long run.

Key words: Tramadol, semen, reproductive function, HPLC

INTRODUCTION

Tramadol, synthetic codeine analog, is a weak μ-receptor agonist and centrally acting analgesic. It has received widespread acceptance in human medicine since it was first introduced in 1977 in Germany. The analgesic potency of tramadol is equal to meperidine and 5 to 10 times less than morphine in humans [1]. It was synthesize tramadol in 1962. It is registered for use in Germany since 1977, UK since 1994, Egypt since 1995, USA since 1995 and France since 1997 [2.] At the first, this new opioid painkiller medication was known as having safe and low abuse liability and widely used throughout the world. After a while, it shows significant risk when overdose occurs and the Food and Drug Administration (FDA) has received hundreds of reports of tramadol-associated abuse, dependence and withdrawal [3]. The analgesic action mechanism of tramadol is complex. Most reports suggest that the analgesic action and other clinical effects of tramadol are due to both opioid and non-opioid mechanisms [4]. Tramadol acts as serotonin-norepinephrine reuptake inhibitors (SNRIs). This increases the levels of these two neurotransmitters in the synapse and tends to elevate mood. It is

thought that these effects on central catecholaminergic pathways contribute significantly to the drug's analgesic efficacy [5]. Several studies have demonstrated that long-term administration of tramadol had dose dependent adverse effects on testicular tissues [6]. Other studies showed that rats received subcutaneous injections of tramadol (40mglkg body weight) three times per week for 8 weeks showed reduced plasma levels of luteinizing hormone, follicle-stimulating hormone [7]. The effect of chronic tramadol use on testicular tissue in wistar albino rats was evaluated by [8]. The testis showed seminiferous tubules disorganization with almost missing of sperm and comparatively reduced spermatogenic cells. Flow cytometric analysis revealed apparent elevation of apoptotic spermatogenic cells. So, tramadol decreased the fertility of male wistar albino rats. These findings need to be confirmed in human as well as its safe and effective minimum daily dose and the long-term effects and side effects [9]. The present work aimed to detect the possible correlation between chronic tramadol administration used at least within the past 12 months and the disturbances in testicular activity and fertility in male in toxicology units, in Al-Azhar University Hospital (New Damietta) from the 1st of December 2016 to 1st of August 2017.

PATIENTS and METHODS

It involved 100 cases who recruited from toxicological units in Al-Azhar University Hospital (New Damietta) between 1st of December 2016 to 1st of August 2017. In addition to 20 subjects as a control group. The purpose of selecting healthy controls were to provide a comparison group of subjects who are representative of the general population with no experience of any chronic diseases, alcoholism and diabetes [10].

The questionnaire contained inquiries about the following topics:

A. Social and demographic factors (sex, age and, region of current residence "urban or rural",
B. personal habits (current smoking and alcohol administration within the last 30 days),
C. history of positive tramadol exposure within at least the past 12 months,
D. medical history (especially history of diabetes, varicose vein, oral anti-thyroid therapy, bilharzial antibody, or autoimmune diseases, immunological causes of infertility, bacterial infection, TORCH infections (toxoplasmosis, rubella, chlamydia, herpes), renal disease, heart disease, tuberculosis, chronic drug abuse administration other than tramadol (for exclusion).

Clinical examination

After free informed consent to participate in this study and within one hour after arrival to toxicological units, clinical examination to all groups including vital signs with a special attention to; central nervous system (CNS) manifestations & Glasgow Coma Scale, gastrointestinal (GIT) manifestation and ECG changes to assess any cardiac abnormalities especially after overdoses of tramadol; it include QRS prolongation, non-specific T-wave and ST-segment changes, first-degree atrioventricular block, prolonged corrected QT intervals, atrial fibrillation and ventricular dysrhythmias [11]. Then 10 mL of blood was separated and collected in EDTA containing test tubes. Immunoassays were used as a preliminary tests for drug of abuse analysis then positive results of drug abuse residues were confirmed by using a high performance liquid chromatography (HPLC). The serum was used for extraction of tramadol residues especially when used at least within the past 12 months by using (HPLC) [12.13]. One mL of blood was put in a 50 mL flask for extraction of of tramadol residues .Hexane (6 mL) and acetone (3 mL) were added and the contents were shaken at room temp for 30 min in a mechanical shaker. The extract was centrifuged for 10 min at 2000 rpm and the clear top layer of hexane was collected in a clean test tube. The remaining portion was again extracted twice using same process and the hexane fractions were added to the previous solvent fractions. Clean up of the samples was done by column chromatography. Elute was collected in a 100 mL beaker and hexane was evaporated to concentrate the samples. The concentrated residues were dissolved in hexane for further analysis [14]. The other blood samples was stored at -8C and the following assays to all subjects; Fasting blood sugar, serum electrolytes, Hb levels, serum creatinine phosphokinase (CPK), renal function tests; serum creatinine concentration and blood urea nitrogen (BUN), liver enzymes; serum alanine transaminase "ALT" and aspartate transaminase "AST" levels, thyroid hormones levels and serum lipid profile; triglyceride (TG), total cholesterol (TC), high density lipoprotein (HDL) and low density lipoprotein (LDL) were measured using kits of Pars Azmoon Company.

According to the American Association for Clinical Chemistry (AACC), semen analysis to all subjects, also known as a sperm count test, analyzes the health and viability of a man's sperm [15].

Semen sample collection: According to the American Association for Clinical Chemistry (AACC)**:** [15, 16, 17.]

- Avoid ejaculation for 24 to 72 hours before the test.
- Avoid alcohol, caffeine and drugs such as cocaine and marijuana two to five days before the test.
- Stop taking any herbal medications, such as Echinacea, as instructed by your healthcare provider.
- Avoid any hormone medications as instructed by your healthcare provider.

Masturbation is considered the preferred way to get a clean sample in this study and the results should be ready within 24 hours to one week, depending on the laboratory you go to.

Analysis will include:

1- Volume: All results are read *per cc* not *per ejaculate*.
2- Morphology describes the shape and size of sperm.
3- Viscosity is the rate at which semen liquefies. The desired viscosity is +1 on a scale of +1 to +4, with liquefaction complete within 10-30 minutes.
4- pH: Semen is an alkaline body fluid, with a normal pH in the range of 7.2 to 8.0.
5- Sperm Count measures the actual number of both motile and non-motile sperm in every 1 cc of semen.
6- Motility expresses the percent of motile sperm compared to total sperm in the entire ejaculate. Normal motility is 50% or higher.
7- Progression is the rate and speed of forward movement. The desired progression is +2 or higher on a scale of +1 to +4.
8- White blood cells: It is normal to find 5 - 10 white blood cells per high power field. More than 10 could indicate a bacterial or viral infection of the reproductive tract.

STATISTICAL ANALYSIS

The collected data were organized, tabulated and statistically analyzed using SPSS software computer package version 16 (SPSS Inc. Chicago, IL). For quantitative data, all the values were expressed as mean ± standard deviation (SD) that the values $P<0.05$ were considered statistically significant. For comparison between the two groups, the students (t) test was used. For qualitative data, number and percent distribution were calculated and Chi square test (X2), was used for comparison between two groups.

RESULTS

1- Social and demographic data:

As regarding demographic data of the studied cases. The mean ages of the studied groups were (15.10±11%) in study group and (20.05±03%) in control group. The prevalence of alcohol administration, were 4 cases (4.0%) in the study group.

It is statistically insignificant as regarding male, prevalence of alcohol administration ($P> 0.05$) in the studied groups.

As regarding residence distribution in the study group, urban were 55 cases (55.0%) and rural were 45 cases (45.0%) while in control group both urban and rural are 10 cases (50.0% each). As regarding the smoker index in the study group; The number of non-smokers were 4 cases (4.0%), mild in 20 cases (20.0%), moderate in 32 cases (32.0%) and heavy smokers in 44 cases (44.0%) while smoker index in the control

group, number of non-smokers were 17 cases (85.0%), mild in 2 cases (10.0%) and moderate in 1 cases (5.0%) with no heavy smokers cases. In the study group, positive history of tramadol administration is 95 cases (95.0%),with no history of positive of tramadol administration.

It is statistically significant as regarding age distribution, residence distribution, smoker index and positive history of tramadol administration between the studied groups (P< 0.05) (Table 1).

2- Clinical data:

As regarding the clinical data, there is no significant difference between cases and controls as regard systolic and diastolic blood pressure, temperature, respiratory, heart rates and GIT manifestations (P>0.05).

As regarding CNS manifestations, depression was 40 cases (40.0%), seizures was 20 cases (20.0%), confusion was 10 cases, (10.0%), trouble in concentrating was 50 cases (50.0%) and irritability was 30 cases (30.0%), while in control group CNS manifestations of depression and confusion were positive in one case each (5.0%). As regarding Glasgow Coma Scale, mild was 3 cases (3.0%), moderate was one case (1.0%). ECG abnormalities were positive in 10 cases (10.0%).

There is a statistically significant difference between cases and control groups as regard CNS manifestations, Glasgow Coma Scale and ECG abnormalities (P<0.05) (Table 2).

3- Investigation finding in the study groups.

As regarding Investigation finding, there is no significant difference between cases and controls groups as regard; fasting blood sugar, serum electrolytes (potassium), Hb levels, liver enzymes (AST and ALT), and renal function tests (P>0.05). As regarding investigation finding, there is a significant difference between cases and controls groups as regard; electrolytes (sodium, chloride and bicarbonate), CPK, lipid profile (serum triglyceride, serum cholesterol, high density lipoprotein and low density lipoprotein), thyroid hormones (T3 , T4 & TSH) and plasma tramadol level (P<0.05) (Table 3).

4- Results of semen analysis in the study groups (Table 4).

As regarding volume of semen analysis in the study group, normal volume of semen was 50 cases (50.0%), decreased in 49 cases (49.0%) and increase in one case(1.0%) while in control group normal volume of semen was 18 cases (90.0%), decreased and increased were in one case (5.0% each).

As regarding results of semen viscosity in the study group, normal viscosity of semen was 11 cases (11.0%), decreased in 19 cases (19.0%) and increase in 70 cases (70.0%) while in control group normal viscosity of semen was 19 cases (95.0%) and decreased in one case (5.0%). As regarding results of spermatic count in the study group, normal count of semen was 11 cases (11.0%), decreased in 88 cases (88.0%) and

increase in 1 case (1.0%) while normal count of semen in all control group. Abnormal spermatic motility and abnormal spermatic progression were detected in 77 cases (77.0% each) and in control group abnormal spermatic motility and abnormal spermatic progression were detected in 10 cases (50.0% each). There is a statistically significant difference between cases and control groups as regarding semen (volume, viscosity), spermatic count abnormal spermatic motility and abnormal spermatic progression) (P<0.05).

Abnormal morphology was positive in 70 cases (70.0%), while in control group was positive in 5 cases (25.0%). The mean pH changing in of the studied group was (7.10±10%) and in control group was (7.5.05±4%). The mean white blood cells in semen in the studied group was (8.10±10%) and in control group was (6.5.05±4%). There was a non-significant difference between cases and controls as regard abnormal morphology, mean pH changing and mean white blood cells (P>0.05).

Table (1): Comparison between cases and controls as regard demographic and social data, (n=120).

Studied parameters		Study group (n=100)	Control group (n=20)	P value
Sex n. (%)	Male	100 (100.0%)	20 (100 %)	0.699 (NS)
Age (mean ± SD) in years . (%)		(15.10±11%)	(20.05±03%)	0.020 (S)
Region of current residence n. (%)	Urban	55 (55.0%)	10 (50.0%)	P< 0.05 (S)
	Rural	45 (45.0%)	10 (50.0%)	
Smoker index n. (%)	Non	4 (4.0%)	17 (85.0%)	P< 0.05 (S)
	Mild	20 (20.0%)	2 (10.0%)	
	Moderate	32 (32.0%)	1 (5.0%)	
	Severe	44 (44.0%)	0 (0.0%)	
Alcohol administration n. (%)		4 (4.0%)	0 (0.0%)	0.820 (NS)
Positive history of tramadol administration n. (%)		95 (95.0%)	0 (0.0%)	0.001 (S)

S = Significant. NS = Non-significant. Significant at P< 0.05. Non-significant difference at P>0.05

Table (2): Clinical manifestation of the study groups, (n = 120).

Studied parameters		Study group (n=100)	Control group (n=20)	*P value*
Vital signs	Systolic blood pressure (mean±SD)	100.80±10.71	110.56±6.53	0.047 (S)
	Diastolic blood pressure (mean±SD)	60.07±7.16	80.25±6.05	0.118 (NS)

Studied parameters			Study group (n=100)	Control group (n=20)	*P value*
	Temperature °C		36.11±1.06	37.53±1.11	0.123 (NS)
	Respiratory rate/min		16.32±1.06	18.23±1.61	0. 13 (S)
	Heart rate beats/min		90.97±5.70	61.33±9.04	0.112 (NS)
CNS manifestations n. (%)		Depression	4 0 (40.0%)	1 (5.0%)	P< 0.05
		Seizures	20 (20.0%)	0 (0.0%)	
		Confusion	10 (10.0%)	1 (5.0%)	
		Trouble in concentrating	50 (50.0%)	0 (0.0%)	
		Irritable	30 (30.0%)	0 (0.0%)	
Glasgow Coma Scale		Mild	3 (3.0%)	0 (0.0%)	P< 0.05
		Moderate	1 (1..0%)	0 (0.0%)	
		Severe	0 (0.0%)	0 (0.0%)	
GIT manifestations n. (%)		Anorexia	85 (85.0%)	2 (10.0%)	P> 0.05
		Nausea	85 (85.0%)	0 (0.0%)	
		Vomiting	65 (65.0%)	0 (0.0%)	
Positive ECG abnormalities n. (%)			10 (10.0%)	0 (0.0%)	P< 0.05

S = Significant. NS = Non-significant. Significant at P< 0.05. Non-significant difference at P>0.05.

Table (3): Investigation finding in the studies groups, (n = 120).

Groups / Tests		Study group (n=100)		Control group (n=20)		P value
		M	± SD	M	± SD	
Fasting blood sugar (mg/dL)		60.22	10.21	73.77	6.36	0.801 (NS)
Serum electrolytes	Sodium (mmol/L)	130.2	3.99	135.95	8.81	<0.001(S)
	Potassium (mmol/L)	3.5.1	3.01	3.5	2.2	>0.05(NS)
	Chloride (mmol/L).	105.5	5.4	100.5	4.1	< 0.001(S)
	Bicarbonate (mmol/L)	21.4	1.01	18.4	4.01	< 0.001(S)
Hb levels (mg/dl)		9.2	1.01	10.1	3.01	>0.05(NS)
Liver enzymes (mg/dL)	AST(U/L) (mg/dL)	54.3	10.8	21.1	6.5	>0.05(NS)
	ALT(U/L) (mg/dL)	54.7	8.28	21.77	6.27	
CPK (mcg/L)		120.9	20.89	10.11	16.89	< 0.002(S)

Tests \ Groups		Study group (n=100)		Control group (n=20)		P value
		M	± SD	M	± SD	
Renal function tests	Serum creatinine (mg/dL)	1.16	0.31	1.03	0.10	0.068 (±S)
	(BUN) (mg/dL)	4.10	1.07	4.01	1.82	
Lipid profile	Serum triglyceride (mg/dL)	168.77	70.03	140.10	55.89	< 0.001(S)
	Serum cholesterol (mg/dL)	180.19	58.58	160.11	35.07	
	High density lipoprotein (mg/dL)	34.06	9.11	39.77	10.07	
	Low density lipoprotein (mg/dL)	100.07	39.27	96.12	21.16	
Thyroid hormones	T3 (nmol/l)	1.12	0.42	1.45	0.77	< 0.002(S)
	T4 (µg/dl)	1.94	2.51	2.33	0.63	
	TSH (mIU/l)	12.64	2.51	7.33	0.83	
Plasma tramadol level ng/ml		900.10	89.9	100.01	100.1	0.001(S)

S = Significant. NS = Non-significant. Significant at P< 0.05. Non-significant difference at P>0.05

Table (4): Results of semen analysis in the study groups (n = 120).

Tests \ Groups		Study group (n=100)	Control group (n=20)	P value
Volume (ml): n. (%)	Normal	50 (50.0%)	18 (90.0%)	0. 011(NS)
	Increased	1 (1.0%)	1 (5.0%)	
	Decreased	49 (49.0%)	1 (5.0%)	
Viscosity n. (%)	Normal	11 (10.0%)	19 (95.0%)	< 0.05 (S)
	Increased	70 (2.0%)	0 (0.0%)	
	Decreased	19 (88.0%)	1 (5.0%)	
Abnormal Morphology n. (%)		70 (70.0%)	5 (25.0%)	0.420 (NS)
pH (mean±SD) (%)		(7.10±10%)	(7.5.05±4%)	0.420 (NS)
Spermatic count	Normal	11 (11.0%)	20 (100.0%)	< 0.05 (S)
	Increased	1 (1.0%)	0 (0.0%)	
	Decreased	88 (88.0%)	0 (0.0%)	
Abnormal spermatic motility		77 (77.0%)	10 (50.0%)	0.038 (S)
Abnormal spermatic progression		77 (77.0%)	10 (50.0%)	0.038 (S)
Semen white blood cells (mean±SD) (%)		(8.10±10%)	(6.5.05±4%)	0.820 (NS)

S = Significant. NS = Non-significant. Significant at P< 0.05. Non-significant difference at P>0.05

DISCUSSION

The objective of this work is to detect the possible correlation between chronic tramadol administration and the disturbances in testicular activity and fertility in male. This result was generally in accordance with Leppert et., al [18] who stated that In a prospective, non-randomized, uncontrolled study, a group of men with an early eleven years pain duration used intrathecal morphine for twelve weeks. Most of these patients showed decreased libido and difficult erection with decrease in testosterone levels significantly at the end of study period (twelve weeks)

As regarding demographic data of the studied cases, all studied groups are males. This explained also by Afshari et.,al [1] as most of tramadol administration are male as it is effective in delaying premature ejaculation and beside it is using in acute and chronic pain. The majority of male cases is due to the fact that male are more likely to report the use of psychoactive substance and still be accepted in the society Lotaet et., al [19]. The mean ages of the studied groups were (15.10±11%) in study group and (20.05±03%)in control group. These finding signify an alarming trend in the prevalence of tramadol ingestion in such age. These results are in agreement with Lozano et., al[20], in which tramadol indicated for relief of moderate to severe pain in adults and children. As regarding residence distribution in the study group, urban were (55.0%) and rural (45.0%). These results explained that, oral administration of tramadol are nearly equally in rural and urban area. As regarding the smoker index in the study group; The number of non-smokers (4.0%), mild (20.0%), moderate (32.0%) and heavy smokers (44.0%). This observation was recorded by Martyn et., al [21] who, stated smoking tramadol allows the drug to quickly enter the blood stream through the nasal tissues. However, tramadol hydrochloride isn't the only thing you're inhaling when you smoke tramadol. Tramadol pills contain binders and fillers which aren't absorbed by the body, which can cause irritation of the eyes and respiratory system. The prevalence of alcohol administration, were 4 cases (4.0%) in the study group, these explained by deceased number of alcohol consumption due to religious practices. These results are not agreement with Miller et., al [22] and stated that alcohol increase the risk for tramadol induced respiratory depression.

As regarding the clinical data, there is no significant difference between cases and controls as regard systolic and diastolic blood pressure, temperature, respiratory and heart rates (P>0.05). As regarding CNS manifestations; depression (40.0%), seizures (20.0%), confusion (10.0%), trouble in concentrating (50.0%) and irritability (30.0%). These results are in agreement with Moghaddam et.,al[23] who reported that most common noticed symptoms in the hospitals ranging from mild central nervous system depression to deep coma. In contrast, agitation and seizures are also reported. Also Perdreau et., al [23] who reported that within the

first year of tramadol marketing, the FDA had received 83 reports of tramadol induced seizures and more than 200 reports in the second year. There was significant increase in Glasgow Coma Scale in study group in comparison to control group and these results are in agreement with Robinson et., al [24], who reported that the majority of included cases in their study were mild according to Glasgow Coma Scale. As regarding GIT manifestations, anorexia and nausea were 85 cases (85.0% each), vomiting was 65 case (65.0%) while anorexia was positive in 2 cases (10.0%), these results are in agreement with (23) who mention that nausea and vomiting was also reported and they have an incidence varying between 14 to 76%. ECG abnormalities were positive in 10 cases (10.0%) and it is statistically significant as compared with control groups ($p<0.05$). These results are in agreement with Elkalioubie et., al [11], who reported that changes in ECG after overdoses of tramadol may include QRS prolongation, non-specific T-wave and ST-segment changes, first-degree atrioventricular block, prolonged corrected QT intervals, atrial fibrillation and ventricular dysrhythmias. There is no significant difference between cases and controls groups as regard; fasting blood sugar, serum electrolytes (potassium), Hb levels, liver enzymes (AST and ALT) and renal function tests.

The results of fasting blood sugar are in agreement with Rothmann et.,al[25], who reported that hypoglycemia is an uncommon presentation of tramadol toxicity. The suggested mechanism is that intravenous tramadol injection activate μ opioid receptors in the CNS directly, resulting in an increase of glucose utilization or a reduction of hepatic gluconeogenesis (or both) in streptozocin induced diabetic rats. Another suggested mechanism is that tramadol increase 5-HT level in the nerve endings which increases insulin concentration in mice.

Also Tokdemir et., al [26], who reported a significant difference in blood urea nitrogen (BUN) and creatine kinase (CK) biochemistry parameters was detected between the control group and all other groups indicating toxicity induced by tramadol administration was detected. There was no significant difference detected between all studied groups as regard serum creatinine (SC), total protein (TP), glucose level, hematocrit %, and platelet count.

There is a significant difference between cases and controls groups as regard; electrolytes (sodium, chloride and bicarbonate), CPK, lipid profile (serum triglyceride, serum cholesterol, high density lipoprotein and low density lipoprotein), thyroid hormones (T3 , T4 & TSH) and plasma. Hyponatremia was reported also by Verebey et., al[27], who stated that tramadol stimulate opioid receptors affecting renal excretion of water and sodium producing anti-diuretic effect and increase 5-HT concentration stimulating antidiuretic hormone (ADH) release. Therefore, both opioid and 5-HT pathways may act in synergy producing profound dilutional hyponatremia. Also Lozano et., al[20] was reported that there is a dramatic increases in CPK especially with seizure and may be associated with acute renal failure. However, independent CPK rise from seizures was also

reported. The results of decrease in lipid profile are agreement with Victor et., al[28], who reported that the recreational use of tramadol alter serum lipid profile, with poor reversibility following their withdrawal. Considering the serum cholesterol depleting effects of tramadol it is important to tame their abuse, as this could affect processes that depend largely on serum lipids for their proper functioning (example; synthesis of steroid hormones). On the other hand, in view of the serum lipid lowering effects of tramadol, it will be worthwhile to assess the possibility of treating hyperlipidemia with these drugs using hyperlipidaemic rat models.

The results of hypothyroidism are not in agreement with Tokdemir et.,al [26], who reported that there is no thyroid significant changes histopathologically was follicular hypertrophy and hyperplasia with crowding of follicular epithelium nuclei and minimal protrusion into the follicular lumen in addition to mild.

The decreased volume of semen analysis in the study group is (49.0%) and increase in (1.0%). The depletion of the spermatogenic cells coincide with the results of Cooper et.,al [8] who has found the same results at the end of one month of daily administration of tramadol but she did not have a withdrawal group. Also she did not compare the effect of doubling the dose of the reproductive organs. The increased viscosity of semen in the study group is (70.0%) and decrease in (19.0%). Abnormal spermatic motility and abnormal spermatic progression were detected in (77.0% each). Abnormal morphology was positive in (70.0. The results of sperm quality analysis are in agreement with [(4,6)] who, detected a significant increase in viscosity with decreased in sperm concentration, motility and morphology and vitality that indicate the possibility of adverse effects of long term administration of tramadol on sperm.

In the study group, the decreased number of spermatic count is (88.0%) and increase in one case (1.0%) and it is statistically significant. This result are in agreement with Cooper et.,al [8], who recorded that ingestion of tramadol affects many of the seminiferous tubules in rats of test groups lacked sperms, spermatids and secondary spermatocytes. Furthermore, Azari et.,al [6] stated that the affected seminiferous tubules in rats of test groups showed necrotic spermatocytes with nuclear changes such as karyolysis and karyorrhexis and also showed absence of spermatids and spermatozoa. There was a non-significant difference in the mean white blood cells in semen in the studied group. It reported by Zhang et., al [29] that white blood cells in semen is not an problem, unless there is the presence of more than 1 million white blood cells per milliliter of semen.

CONCLUSION

The results of the present study revealed a significant correlation between tramadol administration and impaired sperm quality parameters in adult males especially on long and the doctors must not prescribed tramadol until its highly indicated due to it is hazards effects.

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RECOMMENDATION

Any males with delayed fertility and under long term treatment with tramadol should undergo regular screening for their fertility, more researches to study the effects of tramadol on female genital especially on female with no obvious causes of infertility and all husband who taken a tramadol for a long period especially for premature ejaculation must know about effects of tramadol on fertility and opposite is the true on a long run.

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العلاقة بين إمكانية التعرض المزمن لعقار الترامادول وحدوث اعتلال في النشاط التناسلي والإنجابي لدى الذكور

الملخص: هدف هذا البحث إلى دراسة العلاقة بين إمكانية التعرض المزمن لعقار الترامادول وحدوث اعتلال في النشاط التناسلي والإنجابي لدى الذكور، وقد شملت هذه الدراسة مائه حالة من وحده السموم بمستشفى الأزهر بدمياط الجديدة، كما تم اختيار عشرون حالة كمجموعة ضابطة، تم أخذ موافقتهم على إجراء البحث، وتم الكشف عن نواتج عقار الترامادول، مستخدمين في ذلك "جهاز الفصل الكروماتوجرافى السائلي عالي الجودة" وتم عمل بعض التحاليل الروتينية في الدم، كما تم فحص السائل المنوي ميكروسكوبيا لكل الحالات، كما تم الفحص الإكلينيكي لهم، مع الأخذ في الاعتبار اعتلال الجهاز (العصبي، الهضمي، رسم القلب وأشعة تليفزيونية (دوبلر) لاستبعاد وجود دوالي بالخصية. وأسفرت نتائج الدراسة عموما عن وجود علاقة قوية ذات دلالة إحصائية بين التعرض المزمن لعقار الترامادول وحدوث اعتلال في نتائج ومكونات السائل المنوي لدى الذكور البالغين، حيث زادت نسبة اللزوجة بنسبة (70%) والنقص في (كمية، وعدد، وحركة والتقدم للسائل المنوي) حيث كانت (49%)(88%)(77%) و(77%) على التوالي وذلك بالمقارنة بالمجموعة الضابطة. لذا بناءً على ما سبق نوصى بأنه: يجب على الأزواج المتعاطين لعقار الترامادول لفترات طويلة مثلاً لتأخير سرعة القذف أن يدركوا تأثيره السيئ والسلبي على الصحة الإنجابية وأن ما يحدث عكس ما يعتقدون وذلك على المدى الطويل.

الكلمات المفتاحية: الترامادول، السائل المنوي، الجهاز التناسلي جهاز الفصل الكروماتوجرافي السائلي عالي الجودة.