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Protective effect of royal jelly on the sperm parameters in adult mice treated with lithium carbonate

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Abstract
In the current study, was assessed the protective effects of royal jelly on sperm parameters, adult mice treated with lithium carbonate. Adult male albino mice with a mean weight of 25±2 g were divided into two experimental groups and one control group, each with ten mice. The first experimental group was treated with 75 mg/kg doses of lithium carbonate lithium which was taken by injection intraperitoneal for a 20 day of spermatogenesis process. In each gavage, 0.5 mL of lithium carbonate was given to the mice. The second experimental group was treated with 75 mg/kg doses of lithium carbonate lithium which was taken by injection pm and Royal Jelly (RJ) received dose of 250 mg/kg daily for 20 days orally. The result shows that lithium carbonate caused significant changes at level (P≤ 0.05) in total sperm count as compared to control. However, lithium carbonate plus RJ treatment were insignificant in total sperm count as compared to control. In group treated with lithium carbonate the study was showed that the decrease in sperm motility (%), viability, life sperm % and sperm abnormal %were significant at the level of (P≤ 0.05). The motility (%), viability and life sperm % were significant increase at the level of (P≤ 0.05).

Keywords: protective, royal jelly, sperm parameters, adult mice, lithium carbonate

Introduction
Infertility is one of the most common health problems worldwide, and affecting around 15% of couples. About 50% of infertility is associated with male factor, although it can be present in both sexes. Decreased sperm count, motility and deformity of sperm are the most important factors associated with male infertility (Karamzade A, *et al.*, 2013) [16].
Several studies reported increasing prevalence of infertility; stating that it can be due to factors, which can affect the reproductive system and reduce fertility (Csupor-Loffler B, *et al*., 2009) [5]. Plasma membrane of sperm is susceptible to oxidative damage due to large amounts of unsaturated fatty acids that leads to decreased motility and viability of sperm. Antioxidant compounds increase sperm function and can improve fertility (Hamza AA and Amin A., 2007) [11]. Royal Jelly (RJ) is produced by hypo pharyngeal and submandibular glands of young worker bees of the genus Apismeliphera (Nakajima *et al*., 2009) [18]. It is an essential nutrient for young larvae bees and queens and has an important role in queen's feeding. It has also been shown that royal jelly has different types of biological activity in various cells and tissues of animal models (Hashimoto *et al*., 2005) [12]. RJ is mainly made of proteins, sugars, lipids including sterols and fatty acids, and small amounts of mineral salts and vitamins (Hattori *et al*., 2007) [13] RJ have medical uses it has been used commercially in pharmaceutical products, foods, and cosmetics (Kanbur, 2009) [15]. Lithium belongs to alkali group of metals, having atomic no.3 and atomic weight of 6.93. It is water soluble, non-protein bound and is distributed in all body fluids (Sharif N, *et al*., 2011) [22] it may require 6-8 days to reach steady blood concentration and desired therapeutic responses. Distribution of lithium in the human organs is almost uniform; it is concentrated in tissues like brain, kidney, thyroid, bone, liver, and muscle cells against concentration gradient (Groleau G. 1994) [10]. The lithium ion is the effective drug used for treating manic depression, it is often used as carbonate and chloride salts (Zarnescu O and Zamfirescu G, 2006) [25]. Lithium is a medication commonly used to treat schizophrenia, eating disorders, impulse control disorders, and certain mental illnesses in kids and have many side effects in various organs including the reproductive system (Shima Toghyani *et al.*, 2012) [23]. The lithium ion (+Li) is among the factors that affecting sperm parameters negatively and reducing male fertility (Zarnescu O and Zamfirescu G, 2006) [25].

Material and method
Study subject and course of treatment
Thirty adult male albino mice (mean weight of 25 ±2 g) were housed at temperature of 23-25°C and a humidity of 60-75% for 20 days under 12h/12h light/dark cycles. The mice were divided in three groups: Group (A) (control group) of 10 mice were fed with routine diet and water, Group (B) (lithium carbonate group): this group of 10 mice was fed with routine diet, water and was injected intraperitoneal (IP) with 75 mg/kg doses of Lithium Carbonate for 20 days of spermatogenesis process and group (C) (lithium carbonate + RJ group) was injected intraperitoneal (IP) with 75 mg/kg doses of lithium carbonate for 20 days and at the same time received 250 mg/kg doses of RJ for 20 days orally. The animals of three groups were kept in different cages labeled (A), (B) and (C).

Epididymis sperm count, viability and motility
Sperms from the cauda epididymis released by cutting into 2 ml of medium containing 0.5% bovine serum albumin, After

5 min incubation at 37°C (with 5% CO_2), the cauda epididymis sperm concentration determined using the standard hemocytometric method and sperm viability using eosin stain and sperm motility analyzed with microscope (Nikon ECLIPSE E100) at 10 field and reported as mean of motile sperm.

Statistical analysis

Statistical comparisons were made using the ANOVA test for comparison of data in the control group and the experimental groups. The results expressed as mean ± S.E.M (standard error of means). Significant difference is written in parentheses.

Results

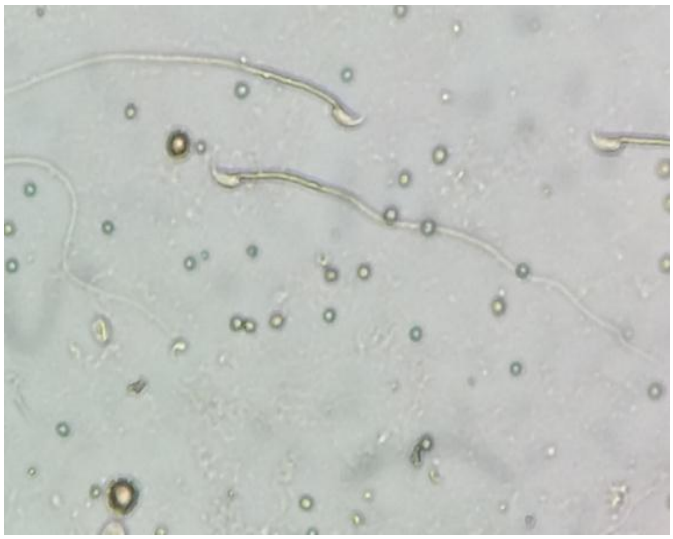
In the study; lithium carbonate treatment caused significant decrease in total sperm count in group (B), whereas lithium carbonate +RJ treatment showed in significant decrease in total sperm count in group (C) compared to control group (A). In group (B), which was treated with lithium carbonate, showed significant decrease in sperm motility (%) and showed significant increase in group (C), which was treated with lithium carbonate +RJ, compared to control group (A). The study showed markedly significant decrease in viability in group (B), and slight increase in group (C), compared to control group (A). Group (B) showed significant decrease in life sperm, and showed significant increase in group (C), compared to control group (A). Sperm abnormality showed slight increase in group (B), and no significant difference in group (C) compared to control group (A), ($P \leq 0.05$) Table 1.

Table 1: Effect of Lithium Carbonate and Lithium Carbonate+ RJ on the sperm parameters in adult mice

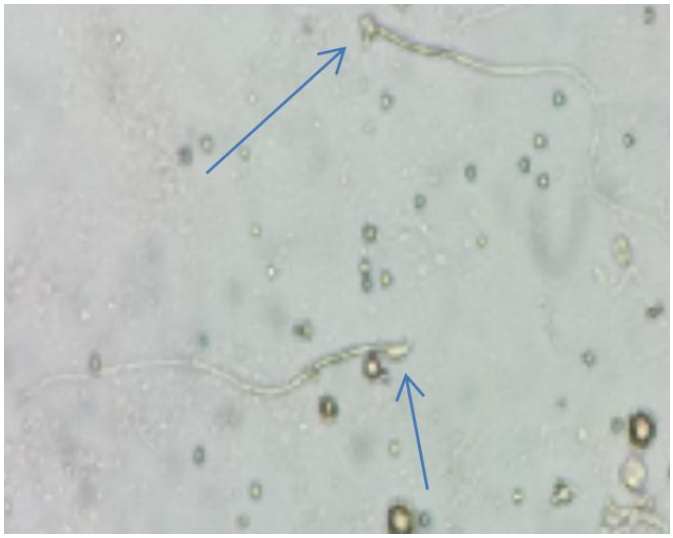
Treatment	Control	Lithium	Lithium Carbonate
		Carbonate + Royal jelly	
Total count (No of sperm/mice 10^6)	65±0.83	32±1.43*	58±0.44
Motility %	57±0.32	23±0.45*	59±0.38*
Viability %	49±0.13	12±2.53*	44±0.57*
Life sperm %	67±0.89	29±0.65*	71±0.22*
Abnormal %	12±0.56	14±0.78*	12.5±0.93

*$P \leq 0.05$

Control



Lithium carbonate + Royal jelly



Lithium carbonate

Discussion

The use of lithium leads to reduction in the number of the total sperm count that is because lithium ion affects the development of sexual cells affecting maturation. Lithium ion pass through the blood-testis barrier leading to the release of spermatozoa out of seminiferous epithelium, stopping cell differentiation and growth cycle and consequently reduces the number of the total sperm count (Banerji TK, *et al*., 2001) [3]. Many studies explain side effects of treatment with high-dose of lithium intestes, in the current study, 75 mg/kg doses of lithium carbonate given to group (B), resulted in a significant difference in spermatogenic parameters in adult mice, this finding is similar to that reported by Shima Toghian *et al.*, 2012 [23] in a study on adults male wistar rats, that showed lithium carbonate, in a 48 -day period, resulted in a significant difference in the number of spermatogonia, primary spermatocytes, spermatid and spermatozoa cells when compared to the control group. The study showed decreased motility of sperms when using lithium carbonate, which was supported by Ahmadi R and Faraji N, 2015 [1], Ensieh Zahmatkesh *et al.*, 2014 [9] findings, who showed that lithium caused decreased motility of sperms, the more

concentration of lithium applied, the more decrease in sperm motility occurred. The current study demonstrated that treatment with RJ +Lithium Carbonate, produced increase in the sperm count and the viability compared to group (B) treated with lithium carbonate, and also to control group (A). The study showeda significant increase in motility and life sperm percentage and no significant difference in sperm abnormality in group (C) compared to group (B) treated with lithium carbonate, and also to control group (A), that is because RJ is used for treatment of impotence infertility, and significantly increase leutinizing hormone (LH) levels (Nutritional supplements. Com 2004) [20], LH is responsible for stimulation of testosterone secretion from interstitial cell (Schally AV *et al.*, 1972) [21]. Hunt CD *et al.*, 1992 [14], Netter A. CD *et al.*, 1981 [19] suggested that elevation of testosterone level could be to zinc found in RJ and zinc supplementation can raise testosterone level and increase fertility. Testosterone is essential for spermatogenesis from spermatogonium to spermatide (West JB. *et al.*, 1997) [24], Elnagar SA., 2010 [8] reported that RJ increased serum testosterone levels in heat-stressed male rabbits. RJ also contains vitamin C, vitamin Eand arginine (Bayer R, 1990) [4]. Vitamin E and C is a well-documented antioxidant and has been shown to inhibit free-radical induced damage to sensitive cell membranes of the testis (Ebisch IMW *et al.*, 2006) [6]. The administration of RJ plus lithium carbonate the results were supported by the finding of Al-Sanafi *et al.*, (2007) [2], El-Hanoun AM *et al.*, (2014) [7], Majeed H *et al.*, (2015) [17] who concluded that Chinese royal jelly supplementation for heat-stressed male rabbits can counteract summer infertility and improve their physiological status.

Conclusion

It was concluded from the present study that the RJ orally administration enhance strongly certain sperm function parameters of male mice. This increase in sperm parameter of experimental groups in comparison to control group could be due to the protective effect of RJ administration. RJ may be used in combination with low dose Lithium Carbonate to improve male infertility. On the basis of results, RJ is safe and effective in the treatment of male infertility.

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