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Original Article

Histological Changes of Aripiprazole on the Seminiferous Tubules of Prepubertal Albino Rats

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ABSTRACT

Background: Many people nowadays are suffering from mental or behavioral disorders. The Egyptian community is complaining from an increase in the appearance of mental disorders with a lot of treatment options. Increasing prevalence of psychiatric disorders is not limited to adults, but also appears in children and adolescents. The treatment of psychiatric disorders as schizophrenia, depression, bipolar disorder and autism usually involve the long-term taking of antipsychotic drugs. Therefore, the uses of antipsychotics have increased. Two main drugs are used quetiapine and aripiprazole. Aripiprazole has been used with satisfactory results. It is known to-act on the dopaminergic receptors which have been detected in the germinal cells.

Aim of work: To detect the histological changes induced by aripiprazole on the structure of the seminiferous tubules of albino rats and the possible recovery of the tubules after drug withdrawal.

Material and Methods: Twenty four prepubertal male albino rats were used in this study aged two weeks and weighed forty grams. The rats were divided into the following groups: Group (I): Control group: included twelve rats. Six rats were left without any medication throughout the experiment (group IA). The other six rats received 0.2 ml of 0.9% NaCl via oral gavage daily for 45 days (group IB). Group (II): Aripiprazole group: included twelve rats which received aripiprazole at a dose of 2 mg/kg B.W/day dissolved in 5 ml of 0.9% NaCl taken via oral gavage for 45 days. After this period (immediately after stoppage of drug administration), six of the rats in the group were sacrificed (group IIA). The other six were sacrificed after another 45 days (they were left without taking any drugs and considered group IIB i.e. a withdrawal period). After scarification, dissection of the testes was done. Specimens from both testes of all groups were taken and processed for light microscopic study.

Results: The testes of all groups showed that the seminiferous tubules lost their normal architecture pattern. Multiple vacuolations replaced the cellular elements. Focal depletions or generalized cellular loss occurred. The lumen was empty in most of the tubules. Irregularity of the basement membrane of the tubules was a common finding as well as congestion of the blood vessels and exudation in between the tubules. The withdrawal group of aripiprazole still showed damage of the seminiferous tubules.

Conclusion: The adverse effect of aripiprazole on the seminiferous tubules was evident and there was no significant improvement after withdrawal of the drug.

Key Words: Antipsychotic drugs, aripiprazole, germinal epithelium, rats, testis.

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INTRODUCTION

Many people nowadays suffer from mental or behavioral disorders (WHO International Consortium in Psychiatric Epidemiology, 2000). Prevalence of psychiatric diseases is not limited to adults but recently is observed among children and adolescents. Mostly, children suffer from autistic and attention deficit hyperactivity disorders (Amr *et al*., 2012).

In Egypt, schizophrenia is the most common chronic psychosis encountered. However, other problems have high incidence as well like: mood disorders 6.43%, anxiety disorders 22.6%, and depression 19.7% (Okasha, 2004). Mental disorders are known to have a greater negative effect on health than many serious chronic physical illnesses (Kessler and Frank, 1997).

In accordance to the previous statements, the use of antipsychotic drugs has increased nowadays (Taylor, 2003). Many studies show that the treatment options of depression and schizophrenia are accompanied with impairment of sexual function and satisfaction (Baldwin and

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Mayers, 2003). Affection of spermatogenesis can occur by different mechanisms such as inhibition of gonadotrophin secretions, inhibition of enzymes involved in androgen biosynthesis, direct effect of antipsychotics on germinal epithelium or on Sertoli cells and damage of the blood testes barrier (Kikuchi *et al*., 1995).

Aripiprazole belongs to atypical antipsychotic family. It is primarily used in the treatment of schizophrenia and bipolar disorder. Other uses include treatment of major depressive diseases, and irritability associated with autism (Taylor, 2003). In addition it is used to treat children 6 to 17 years of age with autistic disorder (a developmental problem that causes difficulty in communication and interacting with others). Short-term treatment (8 weeks) shows reduced autistic symptoms as irritability, hyperactivity, and stereotypy (Ching and pringsheim 2012). This drug exerts its effect by being a partial dopamine agonist (Burris *et al*., 2002). This means that aripiprazole binds to the D2 receptors with the same affinity as dopamine, but has a lower intrinsic efficacy, therefore the response it triggers is lower than dopamine but higher than the antagonist. Accordingly this drug is preferred more than other antipsychotics (Brunton *et al*., 2010).

In spite of aripiprazole is known to-act on the dopaminergic receptor and this receptor has been detected in the germinal cells (De Siqueira Bringle *et al*., 2011), only few studies reported their adverse histological effects on the structure of the seminiferous tubules of the testes.

Thus, it became the aim of the present work to investigate the histological changes induced by aripiprazole on the structure of the seminiferous tubules of albino rats and the possible recovery after its withdrawal.

MATERIAL AND METHODS

Animals:

Twenty four male albino rats aged two weeks were used in the present study weighed 40g. They were obtained from the Medical Research Centre, Faculty of Medicine, Ain-Shams University. Rats were housed in a separate plastic cage (3-4 rats/cage) at room temperature (20-24°C). Rats were adapted for 10 days to controlled environment of temperature and illumination. Rats were allowed free access to commercial rat chow. All rats were kept under the same circumstances throughout the experiment. All experiments were carried out in accordance with the guide of the Committee of the Animal Research Ethics (CARE) - Faculty of Medicine-Ain Shams University.

The rats were divided into the following groups:

Group (I): Control group: included twelve rats

Six rats were left without any medication throughout the experiment (**Group IA**).

Six rats received 0.2 ml of 0.9% NaCl via oral gavage daily for 45 days (**Group IB**).

Group (II): Aripiprazole group: the drug was purchased from Chemipharm pharmaceutical company in a powder form. This group included twelve rats which received aripiprazole at a dose of 2 mg/kg B.W/day dissolved in 5 ml of 0.9% NaCl taken via oral gavage daily for 45 days (Zhang *et al*., 2002). It was further subdivided into:

-Group II (A) included six rats sacrificed after 45 days.

-Group II (B) included six rats sacrificed 45 days from stoppage of medication.

The dose of aripiprazole was calculated according to the drug calculation formula and the average weight of the rats (Reagan-Show et al., 2007).

After 45 days, rats of group I and group IIA were sacrificed. Those of group IIB were sacrificed after further 45 days (a withdrawal period; the rats were left without taking any drug). The rats were anesthetized by ether inhalation and testes were dissected. Specimens from both testes of all groups were taken and processed for light microscopic study:

A- Half of the specimens was fixed in 10 % neutral formalin for one week then they were dehydrated in a graded ethanol series, cleared in xylene and embedded in paraffin wax. Five µm thick sections were subsequently cut and stained with haematoxylin and eosin and subsequently

examined by the light microscope (Drury and Wallington, 1980).

B- The other half of specimens was embedded immediately in 2.5% phosphate-buffered glutaraldehyde (pH 7.3) at 4°C and specimens were cut into 1 mm cubes. Postfixation in 1% buffered osmium tetroxide for 1 to 2 hours was followed by dehydration in ascending grades of ethyl alcohol, then clearance in propylene oxide, and finally embedding in fresh epoxy resin. Semithin sections 1 µm in thickness were cut with a glass knife and stained with 1% toluidine blue, and examined under light microscope (Bancroft and Gamble, 2002).

RESULTS

Group I (control group):

Light microscopic examination of the stained sections of the testes of the rats of group IA and IB showed similar results. Examination of the haematoxylin and eosin stained sections of the testes revealed the presence of numerous seminiferous tubules with regular outlines. The tubules were oval or rounded in shape (fig. 1). They were lined by multiple layers of germinal epithelium at different stages of spermatogenesis. The flagella of mature spermatids, which had whorly appearance, were seen filling the lumina of the seminiferous tubules (figs. 1&2). The seminiferous tubules appeared surrounded by a well-defined basement membrane (figs. 1, 2 & 3). In the semithin sections, the lining epithelium consisted of Sertoli cells and spermatogenic cells. Sertoli cells appeared pyramidal in shape and resting on the basement membrane. They were identified by their large triangular and vesicular nuclei and were distributed at intervals between the spermatogenic cells (figs. 4&5). The basal layer of spermatogenic cells consisted of spermatogonia, which were oval in shape with darkly stained rounded nuclei. They were arranged in one layer on the basement membrane (figs. 4&5). The next layer was formed by the primary spermatocytes, which were observed larger in size compared to the spermatogonia, with large spherical nuclei having darkly stained chromatin. The rapidly dividing secondary spermatocytes were infrequently seen (figs. 4&5). Inner to the secondary spermatocytes, the rounded or early spermatids could be identified in some cross tubular sections. They possessed a central rounded nucleus and were arranged in two or three layers (figs. 4 &5). Further observations revealed the presence of mature or late spermatids. The later were elongated cells with relatively deeply stained nuclei. Such cells appeared scattered between the layers of the early spermatids. Mature spermatids could be seen also adjacent to the lumen (fig. 5).

Group IIA (aripiprazole group):

Light microscopic examination of the haematoxylin and eosin stained sections of the testes of the rats of group IIA showed loss of architecture. Many of the seminiferous tubules were irregular, shrunken and distorted (figs. 6, 7&8). Some regions of the sections showed widely separated seminiferous tubules (figs. 6&7). Many tubules showed festooned basement membrane (fig. 6&8). Other tubules showed disruption of their basement membrane (fig. 6). Diffuse vacuolation of the seminiferous tubules was observed. There was exfoliation of spermatogonia and primary spermatocytes from the basement membrane into the lumen of some tubule leaving focal empty spaces (figs. 9&10). Other tubules exhibited areas with focal depletions of germinal cells (figs. 10&11). In some tubules there was fusion between cells with appearance of giant cells (fig. 10). Other tubules showed thinned-out walls with depleted germinal epithelium and possessed only spermatogonia. Dilated lumina of tubules were free of spermatids (fig. 8). Some tubules were degenerated with loss of the germinal epithelium leaving a foamy appearance (fig. 10). The seminiferous tubules appeared detached from the tunica albuginea coat (fig. 11). Eosinophilic cellular debris in the lumina of some tubules was observed (fig.12). Eosinophilic exudate could be seen in the interstitial tissue in between the tubules (fig. 13). Early and late spermatids were not apparent in many seminiferous tubules (figs. 7, 8&9).

Light microscopic examination of the semithin sections stained with toluidine blue showed variable irregularity in the basement membrane of seminiferous tubules (fig.14). The usual pattern of arrangement of the layers of the germinal epithelium was lost and the primary spermatocytes were seen in between the rounded spermatids near the lumina of the tubules (fig.14). Other tubules showed atrophy

of the germinal epithelium, with only scarce spermatogenic cells (fig.15). Early and late spermatids were either absent or very few in some tubules (figs.14 & 15).

Group II B (withdrawal group):

Light microscopic examination of the haematoxylin and eosin stained sections of the testis of the rats of group IIB showed that almost all the tubules appeared irregular and shrunken. The interstitial tissue in between the seminiferous tubules was full of exudates (figs. 16& 17). The basement membrane showed irregular contour (fig. 18). The blood vessels appeared congested in the interstitial tissue (figs. 17 & 19). There were complete atrophy and loss of the normal architecture of the germinal epithelium of most of the tubules, (figs. 18 & 19).

Light microscopic examination of the semithin sections stained with toluidine blue showed also atrophy of the germinal epithelium in most of the tubules and no cells could be detected. The lumen was free of spermatids (fig. 20).

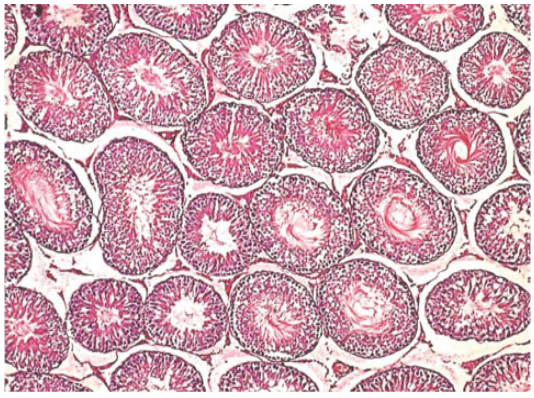

Fig. 1: A photomicrograph of a paraffin section of a rat testis from the control group showing oval and rounded seminiferous tubules, with multiple layers of the germinal epithelium. Note the whorly appearance of the spermatids. Hx & E X100.

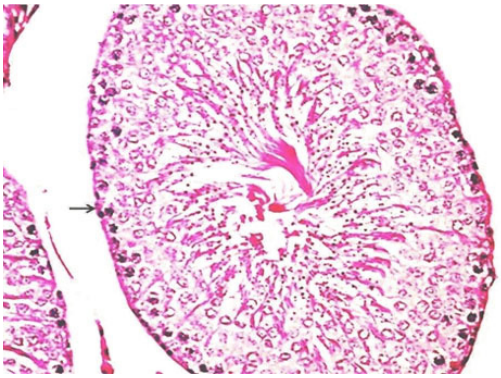

Fig. 2: A photomicrograph of a paraffin section of a rat testis from the control group showing a seminiferous tubule with different layers of spermatogenic cells surrounded by well-defined basement membrane (↑). Hx & E X400.

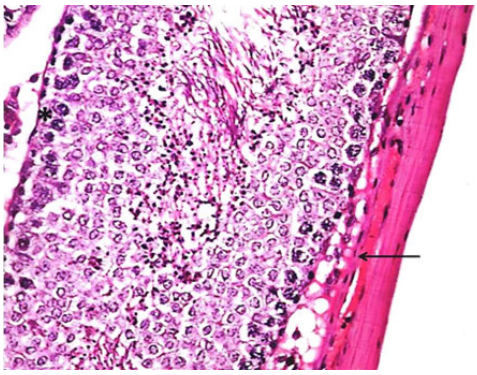

Fig. 3: A photomicrograph of a paraffin section of a rat testis from the control group showing the seminiferous tubule adherent to the tunica albuginea (↑). Hx & E X400.

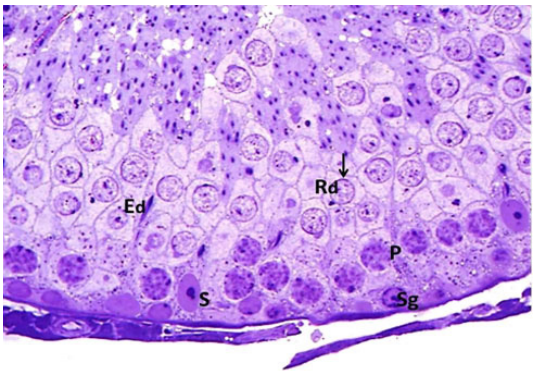

Fig. 4: A photomicrograph of a semithin section of a rat testis from the control group showing all stages of spermatogenic cells; spermatogonia (Sg), primary spermatocytes (P), rounded spermatid (Rd) with acrosomal cap (↑) and elongated spermatids (Ed). Sertoli cells (S) are seen perpendicular to the basement membrane. Toluidine blue X1000.

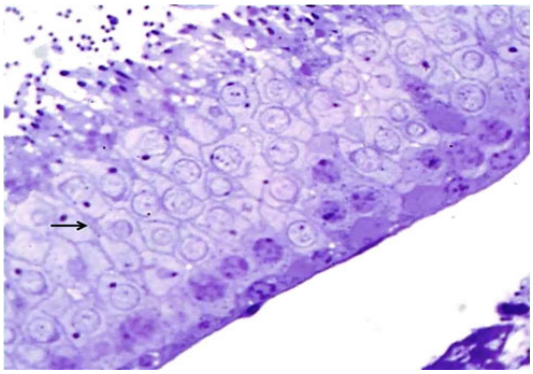

Fig. 5: A photomicrograph of a semithin section of a rat testis from the control group showing all stages of spermatogenic cells. Note the intercellular bridges in between the spermatogenic cells (↑). Toluidine blue X1000.

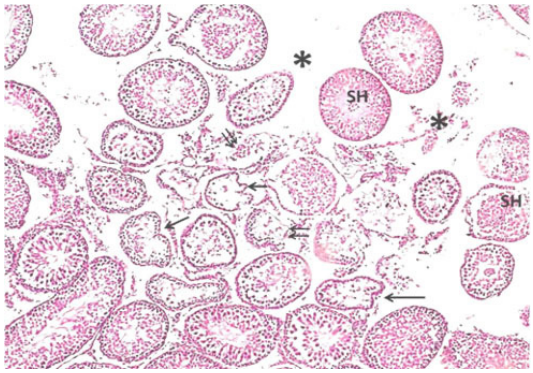

Fig. 6: A photomicrograph of a paraffin section of a rat testis from group IIA showing many irregular and distorted seminiferous tubules (↑). Notice some tubules with disruption of their basement membrane (↑↑). The tubules are widely separated (*).Other tubules show shedding of spermatogenic cells in the lumen (SH). Hx & E X100.

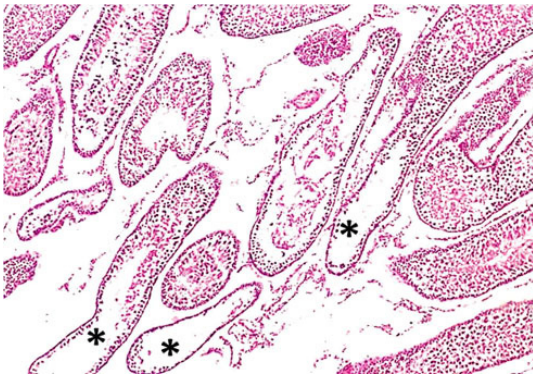

Fig. 7: A photomicrograph of a paraffin section of a rat testis from group IIA showing some tubules are totally or partially devoid of germinal epithelium (*). Hx & E X100.

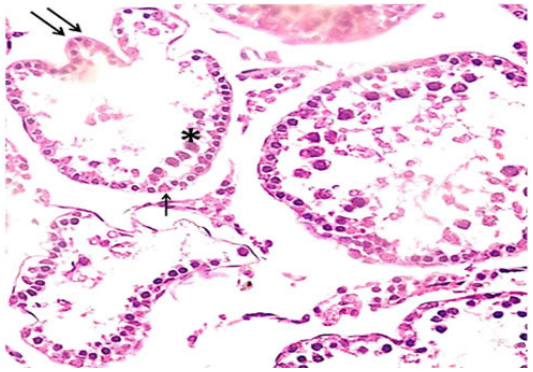

Fig. 8: A photomicrograph of a paraffin section of a rat testis from group IIA showing irregular (festooned) basement membrane (↑↑) of the seminiferous tubules. Some tubules show depletion of most of the germinal epithelium. Notice the spermatogonia and few spermatocytes (*) and the Sertoli cells (↑). Hx & E X400.

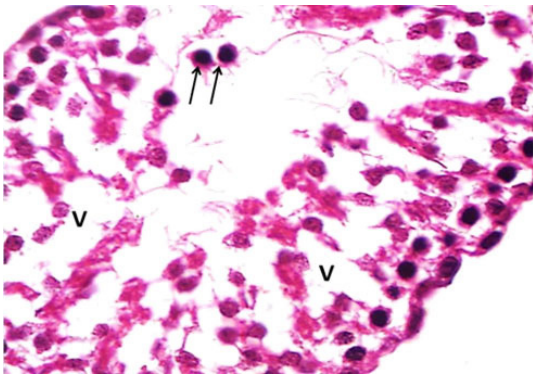

Fig. 9: A photomicrograph of a paraffin section of a rat testis from group IIA showing a tubule with loss of the normal pattern of the germinal epithelium with shedded spermatogenic cells (↑) in the lumen. Notice the evident vacuolation (V). Hx & E X1000.

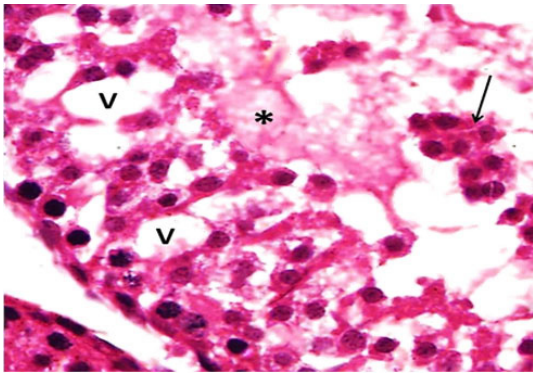

Fig. 10: A photomicrograph of a paraffin section of a rat testis from group IIA showing a tubule with vacuolations in between the spermatogenic cells (V) with loss of the germinal epithelium leaving a foamy appearance (*). Note the fusion of detached cells in the lumen together (↑). Hx & E X1000.

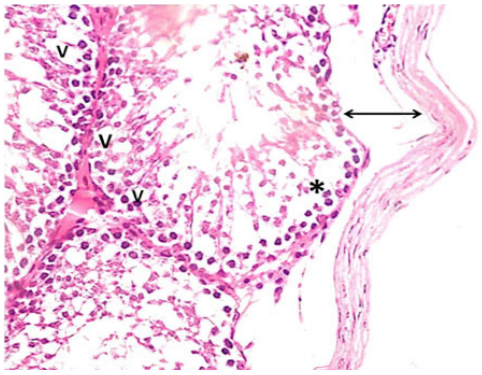

Fig. 11: A photomicrograph of a paraffin section of a rat testis from group IIA showing detachment of the seminiferous tubules from the tunica albuginea (↔). Note vacuolations in between the spermatogenic cells (V). Hx & E X400.

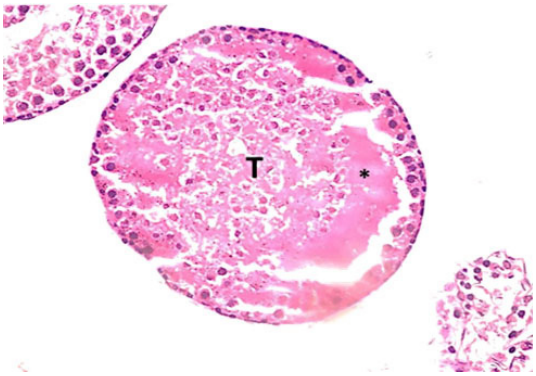

Fig. 12: A photomicrograph of a paraffin section of a rat testis from group IIA showing a degenerated tubule (T) with loss of the normal architecture. The germinal cells are shedded inside the lumen with the presence of eosinophilic cellular debris (*). Hx & E X400.

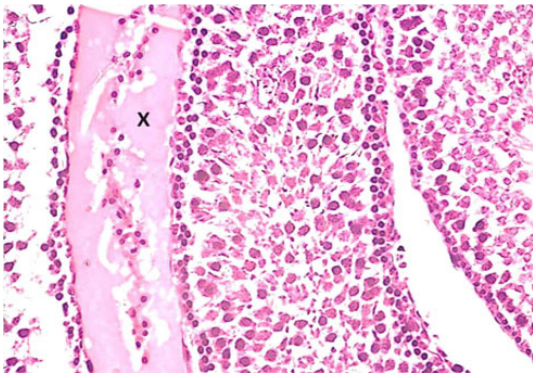

Fig. 13: A photomicrograph of a paraffin section of a rat testis from group IIA showing eosinophilic exudates in the interstitial tissue (X). Hx & E X400.

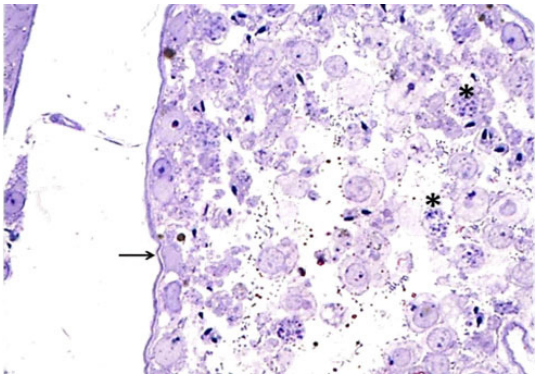

Fig. 14: A photomicrograph of a semithin section of a rat testis from group IIA showing loss of normal architecture of the germinal epithelium resting on irregular basement membrane (↑). Note that the spermatocytes (*) are present near the lumen in between the rounded spermatids. Toluidine blue X1000.

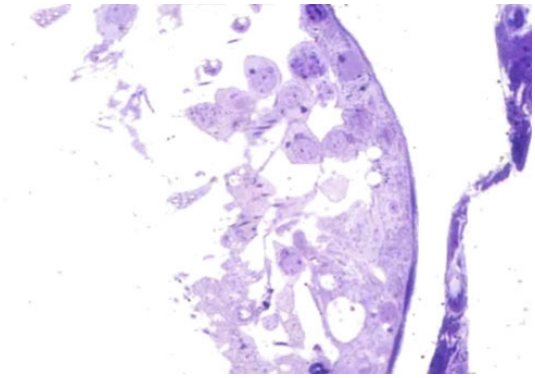

Fig.15: A photomicrograph of a semithin section of rat testes from group IIA showing a seminiferous tubule that has scarce spermatogenic cells. No further steps of the maturation cascade could be detected in this section. Toluidine blue X1000.

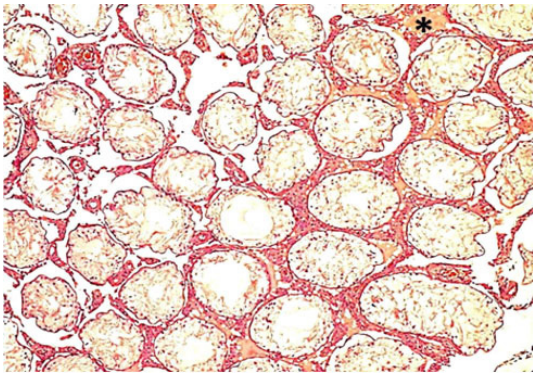

Fig. 16: A photomicrograph of a paraffin section of a rat testis from group IIB showing distorted and shrunken seminiferous tubules. Notice the interstitial exudate in between the tubules (*). H & Ex X100.

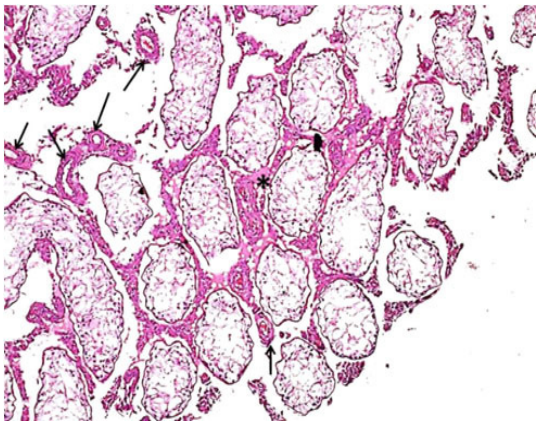

Fig. 17: A photomicrograph of a paraffin section of a rat testis from group IIB showing almost all the tubules are distorted and irregular with loss of the normal architecture of the germinal epithelium. Notice the eosinophilic exudates in the interstitial space (*) and the presence of multiple congested blood vessels (↑). H & Ex X100.

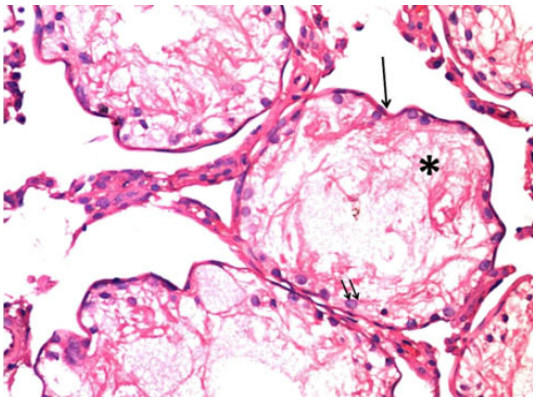

Fig. 18: A photomicrograph of a paraffin section of a rat testis from group IIB showing irregular basement membrane of the tubules (↑). There is massive destruction of all spermatogenic cells (*), only few cells could be detected (↑↑). H & Ex X400.

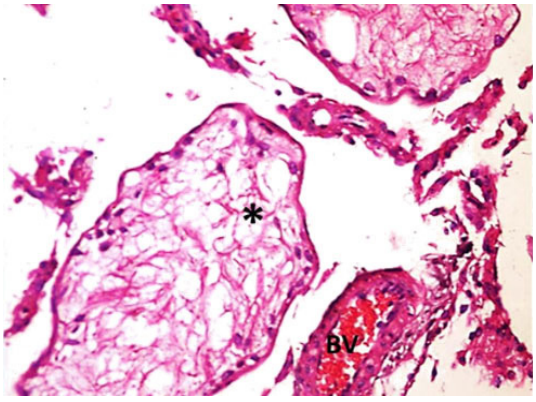

Fig. 19: A photomicrograph of a paraffin section of a rat testis from group IIB showing a tubule with atrophy of the germinal epithelium (*). Notice the congested blood vessel (BV). H & Ex X400.

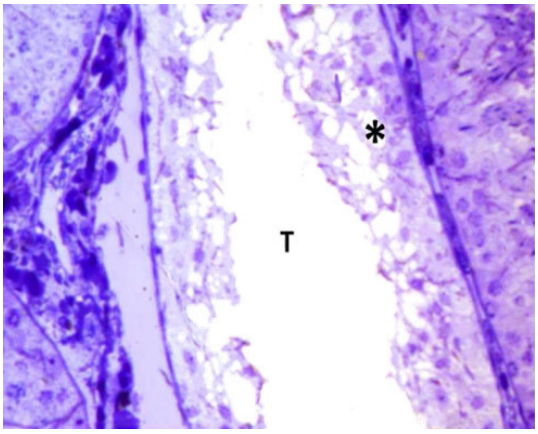

Fig. 20: A photomicrograph of a semithin section of a rat testis from group IIB showing a tubule (T) with atrophy of the germinal epithelium (*), no cells could be identified. Toluidine blue X1000.

DISCUSSION

The prevalence of psychotic diseases is increasing nowadays in the Egyptian community (Ghanem, *et al*., 2009), especially depression, anxiety disorders, schizophrenia, and acute manic episodes of bipolar disorders. Atypical antipsychotic drugs, such as aripiprazole, have been used in treating these disorders with satisfactory results (Taylor, 2003). Sexual dysfunction and infertility are symptoms which have been rarely studied in patients treated with antipsychotic drugs for long period especially from the histopathological point of view. Therefore, the present work was designed to detect any adverse histological effects of aripiprazole on the structure of seminiferous tubules of the testis in albino rats. Also, the work was concerned whether the effect of such drug on the function of the testis is reversible or not.

In the present study the groups of rats that received aripiprazole showed many shrunken seminiferous tubules with irregularities in the basement membrane. The tubules were detached from the tunica albuginea and widely separated from each other. There was evident decrease in the epithelial height and loss of the usual spermatogenic pattern. This can be attributed to the increased levels of prolactin, which can induce hypogonadism leading to inhibition of gonadotropin releasing hormone (GnRH), follicle stimulating hormone (FSH), luteinizing hormone (LH) and testosterone resulting in dysfunction in the reproductive-endocrine axis

(Wieck and Haddad, 2004 and Konarzewska *et al*., 2009). Such alteration leads to a delay in spermatogenesis as well as morphological changes in the testis (De Rosa *et al*., 2003).

Kelly and Conley (2004) supported the previous idea by reporting that reduced levels of testosterone can occur as a result of increased levels of prolactin, an adverse effect previously described during the treatment of schizophrenia by atypical antipsychotics. Kane *et al*., (2007) stated that aripiprazole causes less hyperprolactinemia than other antipsychotics, so considering this drug better than other medications.

In the present study, some sections showed disorganization of the cellular contents of the seminiferous tubules with dispersion of the spermatocytes and spermatids. Many tubules were shrunken and showed areas of focal or complete depletion of the spermatogenic cells with only apparent Sertoli cells. Also, it was evident the increase in the spacing between the spermatogenic cells and Sertoli cells. Maran and Aruldhas, (2002) noticed similar adverse effect of neonatal hypothyroidism on spermatogenesis in wister rats. The authors stated that the cause of the depletion of the germinal epithelium could be attributed to arrest in differentiation and proliferation of germinal cells. Marked reduction in plasma testosterone, estradiol and sex hormone binding globulins, are common associated factors.

In the present study cellular elements were sometimes replaced by cellular debris as well as shedding of spermatogenic cells in the lumen of the tubules. Similar findings were generally described due to degenerative testicular effect from different treatments (Hess and Nakai, 2000; Sasso and Cerri, 2008). Sloughing of germinal cells was explained by authors on the basis of organization of the germinal cells that are kept in place by a close association between their plasmalemmas and specialized junctions of cell membranes of the Sertoli cells. Early effects of cellular degeneration of the germinal cells might lead to disturbance of the structure of their plasmalemmas causing their shedding into the lumina of seminiferous tubules. Simorangkir *et al*., (1997); Hess and Nakai, (2000) stated also that the presence of the germinal cells in the adluminal compartment could interfere with the germinal cell development. Sloughing or exofoliation observed in the present study might be due to a disturbance of the Sertoli cell function resulting in breakdown of Sertoli cell spermatid connection. Also, Ge *et al*., (2008) explained that the decreased intratesticular testosterone resulted in apoptosis of the germinal cells. Kim *et al*., (2001) added that down regulation of the cell adhesion proteins such as cadherin in the Sertoli cells increase sloughing of the seminiferous epithelial cells, which lead to tubular atrophy.

In the present study vacuolations in the germinal epithelium was a common finding. Vacuolated seminiferous epithelium was previously reported by Wistuba *et al*., (2007) and was attributed to arrest in the process of spermatogenesis and resulting in disorganization of cells.

Giant cells were seen in the testes sections. Giant cells appeared to be one of the vital signs of testicular atrophy (Khattab, 2007). It resulted from fusion of the spermatogenic cells due to changes in their intercellular bridges (Singh and Abe, 1987), failure of cytokinesis (Goldsworthy *et al*., 1996; Abdu, 2008) or due to an increase in the phagocytic capacity of apoptotic spermatogenic cells (Wang *et al*., 2006; Gouda and Selim, 2013). Loss of germ cell attachment, with the appearance of germ cells in the tubular lumen, is a common response to many testicular toxicants (Ahbab *et al*., 2015).

The current study revealed irregular (festooned) basement membrane of the seminiferous tubules of the treated rats. Richardson *et al*., (1998) stated that the basement membrane played an important role in transportation of substances between the interstitial tissue and the spermatogenic cells. It also had an important role in keeping the structural and functional integrity of the tissues. Moreover, Zheng *et al*., (2008) reported that the disturbance in the basement membrane of the seminiferous tubules affected the oxygen, nutrition and hormone transport. Similar results were observed in irradiated rats (Sawada and Esaki, 2003). It was explained by either contraction of myoid cells or reduction of tubular diameter. Testosterone and many substances such as prostaglandins, oxytocin, TGF-ß have been suggested to affect the contraction of myoid cells. Changes of testosterone level or damaging of the epithelium promotes secretion of some

factors such as oxytocin or prostaglandins causing myoid cells contraction (Maekawa *et al*., 1996).

Regarding the mechanism of action of the antipsychotic drugs, it was reported that aripiprazole exerts its effect by one of two mechanisms either by increasing the prolactin level, or acting directly on the dopamine receptors present in all types of germ cells. Dopamine is a recognized modulator in the central nervous system (CNS) and peripheral organ functions (Missale *et al*., 1998). De Sequeria bringle *et al* (2011) stated that germ cells have dopamine receptors. These receptors are present in all types of spermatogenic cells and spermatozoa. The presence of peripheral dopamine receptors outside the CNS has suggested the presence of an interaction between the nervous system and other functional systems, such as the reproductive system. Several studies have clarified the importance of testosterone and follicle stimulating hormone to the qualitative and quantitative maintenance of spermatogenesis (Walker and Cheng, 2005).

Withdrawal of aripiprazole was done 45 days later in the present work. The seminiferous tubules of rats that were administered aripiprazole showed more damage and atrophy of their germ cells than those of the control. This might be explained by the fact stated by Gründer *et al*., (2008) that aripiprazole has high affinity to the dopamine receptors and a long elimination half-life. The authors added that aripiprazole at clinical doses occupies a high fraction of its targeted receptors everywhere. Its dissociation from those receptors is very slow, such that their receptors remain nearly saturated for as long as 1 week after the last dose. Moreover, Mauss *et al*., (1974) stated that a marked recovery of spermatogenesis did not occur before 13 weeks after testosterone restoration in human.

CONCLUSION

In conclusion, the present work demonstrated that rat testes treated with aripiprazole were subjected to damage. After withdrawal of the drug, rats' testes did not show recovery which might indicate the prolonged effect of the drug even after withdrawal. Other antipsychotic drugs with less side effects should be considered especially in children.

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التغيرات النسيجيه للاريبيبرازول على انيبيبات ناقل المنى فى الجرذ الأبيض

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ملخص البحث

المقدمة: يعانى فى الوقت الحاضر الكثير من الافراد من اضطرابات نفسيه او سلوكيه. ويشكو المجتمع المصرى من زياده فى ظهور الاضطرابات النفسيه مع وجود الكثير من خيارات العلاج. ولا تقتصر الاضطرابات النفسيه على الكبار فحسب بل ايضا تتواجد فى الاطفال والمراهقين. علاج الاضطرابات النفسية مثل الفصام والاكتئاب والاضطراب الثنائي القطب والتوحد عادة ما تنطوي على أخذ الأدوية المضادة للذهان على المدى الطويل . ولذلك زادت استخدامات مضادات الذهان فى الوقت الحاضر. يوجد نوعان من الادويه الرئيسيه: الكوتيابين و اريبيبرازول . وقد استخدم الاريبيبرازول فى علاج الاضطرابات النفسيه مع نتائج مرضيه . ومن المعروف ان اريبيبرازول يعمل على مستقبلات الدوبامين، وقد تم اكتشاف وجود هذه المستقبلات فى جميع خلايا انيبيبات ناقل المنى.

الهدف من البحث: وبالتالى اصبح الهدف فى هذه الدراسه الكشف عن التغيرات النسيجيه الناجمه عن عقار الاريبيبرازول على هيكل الانيبيبات المنويه فى الجرذان البيضاء قبل البلوغ ودراسه التحسن المحتمل للانيبيبات من تأثير سحب العقار.

المواد و الطرق المستخدمه: استخدم فى هذا البحث اربع وعشرون من الجرذان البيضاء فى عمر الاسبوعين وزنهم اربعون جراما. وتم تقسيمهم الى المجموعات التاليه: المجموعه (I) : مجموعه ضابطه، وتتكون من اثنى عشر جرذا تم تقسيمهم الى مجموعه (AI) لم تاخذ اى ادويه طوال مده التجربه. ومجموعه (BI) تم اعطاؤهم0.2 ملليترمن كلورايد الصوديوم يوميا لمده 45 يوما عن طريق الفم. المجموعه (II): تم اعطاؤهم عقار الاريبيبرازول مذاب فى 5 ملليتر كلورايد الصوديوم بجرعه 2 مليجرام لكل كيلوجرام من وزن الجسم يوميا عن طريق الفم ، ثم تم تقسيم هذه المجموعه الى: (AII) عددهم ست جرذان تم التضحيه بهم بعد 45 يوما من توقف الدواء مباشره و (BII) عددهم ست جرذان تم تركهم بدون دواء لمده 45 يوما اخرى لدراسه امكانيه تماثل الخلايا للشفاء بعد سحب الدواء. بعد اكتمال مده كل مجموعه تم تخدير الجرذان و تم تشريح الخصيتين وقد تم اخذ العينات من كل الخصيتين من جميع المجموعات وتجهيزها للفحص بالمجهر الضوئى.

النتائج: أظهرت الخصى من جميع المجموعات ان الانيبيبات المنويه فقدت تركيبها الطبيعى مع وجود تقطع فى المحيط الخلوى للغشاء المبطن لها ووجود تجاويف متعدده استبدلت العناصر الخلويه. كما ظهرت تعريجات فى الغشاء القاعدى فى معظم الانيبيبات. ولوحظت سمه مشتركه احتقان الاوعيه الدمويه وترشيح بين الانيبيبات. وهذه النتائج لم تظهر تحسنا ملحوظا بعد سحب الدواء.

الخاتمه: وقد استنتج ان اريبيبرازول له تاثير سلبى على الانيبيبات المنويه و بعد سحب الاريبيبرازول لم يحدث تحسن فى خلايا الخصيه. ووفقا لهذه النتائج نستخلص ان الضرر يلحق بخلايا الخصيه نتيجه العلاج بالاريبيبرازول ولا تعود الى هذه الخلايا الى سابق عهدها بعد سحب العقار.