Zinc Therapy Improves Deleterious Effects of Experimental Unilateral Cryptorchidism: Histopathological Evaluation of Testes

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Abstract

Objective- Perturbation of the normal process of testicular descent results in the condition of cryptorchidism. Spermatogenesis is generally impaired in cryptorchid testes because of high intratesticular temperature. It seems that the main mechanisms underlying the process of spermatozoa demise is apoptosis by overgeneration of free radicals. So, the aim of the present study was to investigate the effects of zinc sulfate as a potent antiapoptic and antioxidant agent on histopathological changes of rat testes after experimental cryptorchidism.

Design- Experimental study

Animals- Forty five male adult Sprague–Dawley rats

Procedures- Animals were divided into three experimental groups each containing fifteen rats. Control group (Con) which did not undergo any surgical procedure. Animals in the first treatment group (Cry, cryptorchid operated group without any treatment) were rendered unilaterally cryptorchid in the left testes without any drug administration. Rats in the second treatment group (Zth, cryptorchid operated group with zinc therapy) were rendered unilaterally cryptorchid in the left testes and treated with 10 mg/kg zinc sulfate every other day for 60 days. The control and treated animals were sacrificed on days 15, 30 and 60 after operation and both testes were removed for histopathological evaluations.

Results- Cryptorchidism (Cry group) caused a complete depletion of spermatozoa from the lumen of seminiferous tubules and zinc administration (Zth group) could not improve...
spermatogenesis and meiotic index except slightly for meiotic index at 60 days compared with the control group (1.21 ± 0.009 vs. 3.38 ± 0.014, P<0.05). Induction of cryptorchidism significantly decreased the diameter and epithelial height of seminiferous tubules compared to the control group and also affected contralateral (right) testes (P<0.05). However administration of zinc (Zth group) significantly improved the epithelial height in each evaluated time points. Although a significant decrease in the mean diameter of spermatogonia and sertoli cells were observed at each evaluated time points post operation (P<0.05) but zinc therapy significantly increased the mean diameter of spermatogonia cells from 30 days and improved the mean diameter of sertoli cells from 15 days post operation compared with the Cry group in ipsilateral testes (5.13 ± 0.05 vs. 4.69 ± 0.05 and 28.84 ± 0.71 vs. 23.17 ± 0.29, respectively). In contralateral testes, all above mentioned parameters were affected and zinc therapy significantly improved them (P<0.05).

**Conclusion and clinical relevance**- These finding clearly demonstrates that zinc is able to decrease detrimental effects of cryptorchidism on spermatogonia and sertoli cells and improves spermatogenesis process specially in contralateral (scrotal) testes. Therefore it may be useful for treatment of cryptorchidism outcomes in male animals.

**Key Words:** Cryptorchidism, Spermatogenesis, Zinc Sulfate, Testes, Rat

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**Introduction**

Perturbation of the normal process of testicular descent, such that one or both testes fail to complete their descent into the scrotum, results in the condition of cryptorchidism. Cryptorchidism is most frequently encountered in horses and pigs, and in miniature dog breeds. The reported incidence in dogs ranges from 1-7%. The condition is rare in ruminants, with figures of 0.1-0.5% being commonly reported for bulls, goats and rams. With the exception of elephants and whales, most mammals have a scrotum and the scrotal temperature is always lower than that of the abdomen. The lower levels of the scrotal temperature are believed to maintain optimal environment for testicular function. Spermatogenesis is generally markedly impaired or absent in testes that are not scrotal, since the absence of cooling of blood in the spermatic cord results in abnormally high intratesticular temperature. Surgical induction of the cryptorchidism in experimental animals is a well known method to investigate mechanisms of cryptorchidism which causes rapid degeneration of testicular germ cells and disruption of spermatogenesis leading to infertility. Studies have shown that the mechanisms underlying the process of spermatogonia demise in response to heat stress is apoptosis, a form of programmed cell death. Cell death is significantly increased in rats following experimental cryptorchidism. The finding of increased reactive oxygen species (ROS) levels in these infertile rats may indicate that oxidative stress is involved in the pathogenesis of sperm DNA damage. The generation of ROS occurs constantly during normal cell metabolism in all living cells. Heat stress induces the generation of ROS in the testis and the reduction of endogenous antioxidant enzymes, such as superoxide dismutase and catalase. High ROS level causes a deleterious changes in the lipoprotein complex of the cell membranes and also disrupts the inner and outer mitochondrial membranes and so, ROS production in cryptorchid testis may contribute to apoptosis induction in testicular germ cells. Zinc is an indispensable element for optimum growth and reproduction in males and females. It maintains the structural integrity of DNA and plays an important role in the metabolism of nucleic acid and proteins. The production of semen necessitates extensive cell division and this requires large amount of zinc, as zinc metalloenzymes are vital enzymes which involved in nucleic acid and protein synthesis.
and several proteins involved in the repair of damaged DNA and in the transcription and translation process of DNA.\textsuperscript{16} Zinc appears to be a potent scavenger of excessive superoxide anions produced by defective spermatozoa and/or leukocytes in human semen after ejaculation.\textsuperscript{17} It seems that high content of zinc is able to exert protective effects against excessive amount of ROS produced in the cryptorchid testis and prevent from spermatogenesis damage. Therefore, the aim of the present research was to investigate the effects of zinc administration on histopathological changes of rat testes in experimentally induced cryptorchidism.

**Materials and Methods**

**Animals**

All animal experiments in this study were approved by the Animal Ethics Committee at the Veterinary Faculty of Kerman. Forty five male adult Sprague–Dawley rats (250–300 g) were obtained from Razi Research Institute of Kerman, Iran. The mice were fed with standard commercial laboratory chow [(pellet form), Javeneh Khorasan Co., Mashhad, Iran] and water ad libitum and housed under standard laboratory conditions (12 h light: 12 h dark and 22 ± 2 °C) during the experimental period.

**Experimental design**

Animals were randomly divided into three groups each containing fifteen rats. Control group (Con) which did not undergo any surgical procedure was for determination of the basal values for all parameters. Animals in the first treatment group (Cry, cryptorchid operated group without any treatment) were rendered unilaterally cryptorchid in the left testes without any drug administration. Rats in the second treatment group (Zth, cryptorchid operated group with zinc therapy) were rendered unilaterally cryptorchid in the left testes and treated with 10 mg/kg zinc sulfate intraperitoneally after the surgically induced cryptorchidism every other day for 60 days. The control and treated animals were sacrificed upon diethyl ether anesthesia (May & Baker Ltd., Dagenham, England) by cervical dislocation on days 15, 30 and 60 after operation and both testes were removed for histopathological evaluations.

**Surgical procedure**

Animals were anaesthetized with an intraperitoneal injection of 100 mg/kg of ketamine hydrochloride (Rotexmedica, Trittau, Germany) and 10 mg/kg xylazine (Alfasan, Holland). All operations were performed under sterile conditions. The skin of the scrotal area was shaved and prepared with 10% povidone iodine solution. A 2cm paramedical incision was made through the left testis skin. The gubernaculum of the testis was cut and the freed testis was pushed back into the abdomen through the internal inguinal ring. The upper pole of the left testis through its tunica albuginea was fixed with a 4-0 Nylon suture to the muscle of the abdominal wall.

**Histopathological evaluation**

All specimens were fixed in Bouin’s solution, embedded in paraffin wax, sectioned with 5 µm thicknesses, stained with haematoxylin and eosin (H&E) and examined blindly by an expert
pathologist under a light microscope. Morphometrically, the mean seminiferous tubule diameter and epithelial height were measured in each testis. The ten smallest, roundest tubules were identified and measured with an ocular micrometer under light microscopy. Mean diameter, in microns, was then determined for each group. The epithelium height was obtained with the same tubules used to determined tubular diameters. The average diameter of the spermatogonia and sertoli cells nuclei were measured from 30 cells for each testis. The other parameter was the percentage of spermatogenesis. For this purpose, two hundred seminiferous tubules were examined under light microscopy. The presence of spermatozoa within the seminiferous tubule was considered as the evidence of spermatogenesis. Lack of spermatozoa even in the presence of orderly progression of primary and secondary spermatocytes was not considered as the evidence of spermatogenesis for the purpose of this experimental study.

Statistical analysis

Values were expressed as mean ± SEM (standard error of mean). Statistical evaluation of significant difference between means was performed with one-way analysis of variance (ANOVA) followed by the Tukey test as post hoc. The significance level considered was P<0.05.

Results

Spermatogenesis and meiotic index

The mean percentages of spermatogenesis and meiotic index of the scrotal and cryptorchid testes have been shown in table 1 & 2. Experimental cryptorchidism (Cry group) caused a severe and significant damage to the spermatogenesis process and meiotic index in comparison with the control group and administration of zinc could not improve above mentioned parameters except slightly for meiotic index at 60 days compared with the control group (1.21 ± 0.009 vs. 3.38 ± 0.014, P<0.05). Induction of cryptorchidism negatively affected spermatogenesis and meiotic index of contralateral testes (P<0.05) and administration of zinc improved the percentage of spermatogenesis from 15 days following operation compared with Cry group (66.33 ± 1.08 vs. 54.50 ± 1.21, P<0.05). However, we did not show significant difference between the control and Zth group at 60 days post operation for the percentage of spermatogenesis (75.20 ± 1.04 vs. 72.01 ± 1.28, P>0.05). Interestingly, zinc therapy significantly increased the meiotic index even higher than that of the control group at each evaluated time points post operation.
Table 1. Mean ± SEM percentage of spermatogenesis in the right (scrotal) and left (cryptorchid) testes of rats at 15, 30 and 60 days after operation.

<table>
<thead>
<tr>
<th>Testes direction</th>
<th>Days after operation</th>
<th>Experimental groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Con</td>
</tr>
<tr>
<td>Right (scrotal)</td>
<td>15</td>
<td>75.22 ± 0.66a</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>75.01 ± 2.12b</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>75.20 ± 1.04b</td>
</tr>
<tr>
<td>Left (cryptorchid)</td>
<td>15</td>
<td>74.92 ± 1.25b</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>75.69 ± 1.44b</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>75.04 ± 0.94b</td>
</tr>
</tbody>
</table>

Con, control; Cry, cryptorchid operated group without any treatment; Zth, cryptorchid operated group with zinc therapy. 

a, b, c At each row, different superscript alphabets show significant difference (P < 0.05).

* At each column, different superscript signs show significant difference (P < 0.05).

Table 2. Mean ± SEM of meiotic index in the right (scrotal) and left (cryptorchid) testes of rats at 15, 30 and 60 days after operation.

<table>
<thead>
<tr>
<th>Testes direction</th>
<th>Days after operation</th>
<th>Experimental groups</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Con</td>
</tr>
<tr>
<td>Right</td>
<td>15</td>
<td>3.36 ± 0.017b</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>3.39 ± 0.011b</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>3.38 ± 0.013b</td>
</tr>
<tr>
<td>Left</td>
<td>15</td>
<td>3.37 ± 0.017b</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>3.38 ± 0.010b</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>3.38 ± 0.014b</td>
</tr>
</tbody>
</table>

Con, control; Cry, cryptorchid operated group without any treatment; Zth, cryptorchid operated group with zinc therapy. 

a, b, c At each row, different superscript alphabets show significant difference (P < 0.05).

* At each column, different superscript signs show significant difference (P < 0.05).

Seminiferous tubules diameter and epithelial height

Table 3 and 4 show the effects of zinc sulfate administration on the mean diameter and epithelial height of seminiferous tubules in the right (scrotal) and left (cryptorchid) testes of rats at 15, 30 and 60 days following induction of experimental cryptorchidism. The mean seminiferous tubules diameter and epithelial height of the control group in the cryptorchid (left) testes were similar to the scrotal (right) testes (P>0.05). Induction of cryptorchidism significantly decreased the diameter and epithelial height of seminiferous tubules compared to the control group and also affected contralateral (right) testes (P<0.05). Administration of zinc (Zth group) significantly improved epithelial height in each evaluated time points (15, 30 and 60 days after operation) in comparison to Cry group (29.33 ± 0.92 vs. 17.90 ± 0.33; 37.80 ± 0.67 vs. 27.10 ± 0.55; 41.55 ± 0.72 vs. 31.00 ± 0.83, respectively) as it did not have any positive effects on seminiferous tubules diameter (P>0.05). Zinc therapy improved the mean seminiferous tubules epithelial height of contralateral (right) testes up to 30 days after operation (85.05 ± 1.12 vs. 89.16 ± 2.20, P>0.05), but although it significantly increased the mean diameter of seminiferous tubules in comparison to the Cry group, still the diameters were lower than those of the control group even after 60 days (334.20 ± 3.16 vs. 365.00 ± 9.87, P<0.05).
Table 3. Mean ± SEM diameter (µm) of seminiferous tubules in the right (scrotal) and left (cryptorchid) testes of rats at 15, 30 and 60 days after operation.

<table>
<thead>
<tr>
<th>Testes direction</th>
<th>Days after operation</th>
<th>Con</th>
<th>Cry</th>
<th>Zth</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>365.71 ± 8.41°</td>
<td>327.80 ± 2.78°</td>
<td>324.00 ± 5.39°</td>
</tr>
<tr>
<td>Right</td>
<td>15</td>
<td>362.85 ± 8.92°*</td>
<td>309.40 ± 3.61°*</td>
<td>323.20 ± 3.46°*</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>365.00 ± 9.87°*</td>
<td>309.20 ± 3.00°*</td>
<td>334.20 ± 3.16°*</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>360.00 ± 9.30°*</td>
<td>201.80 ± 1.47°*</td>
<td>214.53 ± 4.63°*</td>
</tr>
<tr>
<td>Left</td>
<td>15</td>
<td>360.00 ± 6.54°*</td>
<td>186.60 ± 2.11°*</td>
<td>189.20 ± 2.86°*</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>365.71 ± 7.51°*</td>
<td>193.00 ± 1.85°*</td>
<td>198.00 ± 2.98°*</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>360.00 ± 5.66°*</td>
<td>175.20 ± 0.79°*</td>
<td>187.20 ± 1.12°*</td>
</tr>
</tbody>
</table>

Con, control; Cry, cryptorchid operated group without any treatment; Zth, cryptorchid operated group with zinc therapy.

Table 4. Mean ± SEM epithelial height (µm) of seminiferous tubules in the right (scrotal) and left (cryptorchid) testes of rats at 15, 30 and 60 days after operation.

<table>
<thead>
<tr>
<th>Testes direction</th>
<th>Days after operation</th>
<th>Con</th>
<th>Cry</th>
<th>Zth</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>90.35 ± 2.52°*</td>
<td>75.15 ± 0.54°*</td>
<td>84.41 ± 1.59°*</td>
</tr>
<tr>
<td>Right</td>
<td>15</td>
<td>89.16 ± 2.30°*</td>
<td>66.20 ± 0.68°*</td>
<td>85.05 ± 1.12°*</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>90.00 ± 2.61°*</td>
<td>78.56 ± 0.81°*</td>
<td>86.00 ± 1.00°*</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>92.08 ± 3.05°*</td>
<td>17.90 ± 0.33°*</td>
<td>29.33 ± 0.92°*</td>
</tr>
<tr>
<td>Left</td>
<td>15</td>
<td>86.87 ± 1.61°*</td>
<td>27.10 ± 0.55°*</td>
<td>37.80 ± 0.67°*</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>91.07 ± 2.17°*</td>
<td>31.00 ± 0.83°*</td>
<td>41.55 ± 0.72°*</td>
</tr>
</tbody>
</table>

Con, control; Cry, cryptorchid operated group without any treatment; Zth, cryptorchid operated group with zinc therapy.

Spermatogonia and sertoli cells diameter

In the control group, the mean diameter of spermatogonia and sertoli cells did not show significant difference in the right (scrotal) and left (cryptorchid) testes of rats at 15, 30 and 60 days after operation (Table 5 & 6). A significant decrease in the mean diameter of spermatogonia and sertoli cells were observed at each evaluated time points post operation in comparison with the control group (P<0.05). Zinc therapy significantly increased the mean diameter of spermatogonia cells from 30 days post operation and improved the mean diameter of sertoli cells from 15 days post operation compared with the Cry group (5.13 ± 0.05 vs. 4.69 ± 0.05 and 28.84 ± 0.71 vs. 23.17 ± 0.29, respectively). Induction of experimental cryptorchidism affected the mean diameter of spermatogonia cells in the contralateral (scrotal) testes at 30 days and the mean diameter of sertoli cells at 15 days post operation (P<0.05) and administration of zinc (Zth group) compensated the deleterious effects of cryptorchidism (Cry group) on spermatogonia and sertoli cells diameters from the first 15 days after operation.
Table 5. Mean ± SEM diameter (µm) of spermatogonia cells in the right (scrotal) and left (cryptorchid) testes of rats at 15, 30 and 60 days after operation.

<table>
<thead>
<tr>
<th>Testes direction</th>
<th>Days after operation</th>
<th>Experimental groups</th>
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<tbody>
<tr>
<td></td>
<td>Con</td>
<td>Cry</td>
</tr>
<tr>
<td>Right</td>
<td>15</td>
<td>6.12 ± 0.31*</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>6.25 ± 0.66*</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>5.92 ± 0.21ab</td>
</tr>
<tr>
<td>Left</td>
<td>15</td>
<td>6.16 ± 0.26*</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>5.75 ± 0.19*</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>6.32 ± 0.22*</td>
</tr>
</tbody>
</table>

Con, control; Cry, cryptorchid operated group without any treatment; Zth, cryptorchid operated group with zinc therapy.

Table 6. Mean ± SEM diameter (µm) of sertoli cells in the right (scrotal) and left (cryptorchid) testes of rats at 15, 30 and 60 days after operation.

<table>
<thead>
<tr>
<th>Testes direction</th>
<th>Days after operation</th>
<th>Experimental groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Con</td>
<td>Cry</td>
</tr>
<tr>
<td>Right</td>
<td>15</td>
<td>37.49 ± 0.49*</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>38.74 ± 0.91*</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>40.42 ± 1.89*</td>
</tr>
<tr>
<td>Left</td>
<td>15</td>
<td>39.91 ± 1.63*</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>38.14 ± 1.43*</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>37.78 ± 1.05*</td>
</tr>
</tbody>
</table>

Con, control; Cry, cryptorchid operated group without any treatment; Zth, cryptorchid operated group with zinc therapy.

Discussion

It has been generally accepted that a relatively low temperature is preferable in spermatogenesis of mammalian species and increasing testicular temperature above normal levels results in altered spermatogenesis. In agreement with our report, some other animal studies supported the effects of cryptorchidism on fertility of ipsilateral and contralateral testes. It has been suggested that cryptorchidism is associated to a decrease in antioxidant activity. On the other hand, the testicular damage which results from cryptorchidism is thought to be due to excess generation of free radicals, like superoxide anion, hydroxyl radical, nitric oxide and hydrogen peroxide by cryptorchid testis in response to heat stress of inside abdomen, which stimulate lipoperoxidation. Certainly, reduction of blood flow despite the fact that the cryptorchid testis contains a greater percentage and number of blood vessels than the normal testis could be as another reason for ROS production. Lowered blood flow and hypoxia is associated with ROS overgeneration. Moreover, the produced free radicals in ipsilateral testis are the most important source which may receive to the contralateral testis by blood flow. This might be an explanation for moderate changes of contralateral testes (scrotal) which was observed in our experiment. Mammalian spermatozoa membranes are very sensitive to the damage mediated by lipid peroxidation, because they are rich in polyunsaturated fatty acids. Moreover, an aldehyde end product of lipid peroxidation, 4-hydroxy-2-nonenal, is an alkylating agent that damages DNA and induces apoptosis. The low percentage of spermatozoa in the contralateral testes or severe depletion of spermatozoa in ipsilateral testes of cryptorchid rats observed in our study indicates that oxidative stress is a mediator of sperm cells dysfunction. Excessive production of ROS, however results in
destruction of the antioxidant capacity of spermatozoa and seminal plasma causing oxidative stress which damages spermatozoa membrane and causes infertility. ROS can oxidize cell membrane lipids, proteins and DNA, leading to cellular dysfunction and sometimes cell death. So, the elimination of ROS has been shown to be as an important factor in treating side-effects of cryptorchidism.

Our results showed that treatment with zinc sulfate has a positive significant impact on testicular tissue feature following cryptorchid induction specially on contralateral testes. It seems that this improvement in ipsilateral testicular tissue parameters like sertoli and spermatogonia cells diameters and also meiotic index and spermatogenesis of contralateral testes is due to potent antioxidant activity of zinc and may be important role of zinc in nucleic acid and protein synthesis. Zinc is an essential component of copper/zinc superoxide dismutase, which has antioxidantive properties for sperm function. Zinc through its competition with copper and iron for membrane binding sites, reduces the potential for formation of the hydroxyl radical via redox cycling. Also, zinc is a micronutrient that serves as a cofactor for more than 80 metalloenzymes involved in DNA transcription and protein synthesis. These above mentioned factors could change sperm quality and improve cryptorchidism outcome as was seen in our study.

Many investigators showed significant decrease in diameter of seminiferous tubules and thickness of germinal epithelium in cryptorchid testis. The similar phenomenon was observed in our study, but administration of zinc could improve the height of germinal layer after 15 days. Absalan et al., observed that spermatocytes and spermatids were major cells which were affected in cryptorchidism. This observation could be another explanation why we showed that the lumen of cryptorchid testes were depleted from spermatozoa. Nevertheless, cryptorchidism or heat condition can cause spermatogenesis arrest and but did not appear to affect spermatogonia survival or their biological activity. It is well known that optimal intratesticular and intraepididymal testosterone (secreted by the Leydig cells) and androgen-binding protein (secreted by the Sertoli cells) concentration are important for activating and maintaining spermatogenesis. Impaired secretory function of Leydig and Sertoli cells due to a temperature increase in animals with unilaterally cryptorchidism will detrimentally affect spermatogenesis on testes of both sides. But some previous reports demonstrates clearly that spermatogonia and sertoli cells are more resistant to the inside body temperature as this was observed in our study and we believe that according to our accumulating data zinc administration could accelerate the improvement process of these cells.

In conclusion, the present data demonstrates that spermatogenesis process is completely arrested and indeed spermatogonia and sertoli cells negatively affected in cryptorchid testes after two weeks. Although zinc inhibits deleterious effects of heat on spermatogonia and sertoli cells but its beneficial effects are limited to these cells and spermatogenesis cannot be motivated by zinc therapy. Nevertheless, increasing in the rate of meiotic index was observed 60 days after zinc administration. Also, zinc is able to prevent detrimental effects unilateral cryptorchidism on contralateral testes.

Acknowledgements

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References


چکیده
روی درمانی اثرات مخرب نهان بیضگی یک طرفه تجربی را به‌دست می‌بخشید: ارزیابی هیستوپاتولوژیک بیضه‌ها

همدانی بازیابی: ایمی، آدی ام، رضا خبرنادشی، جلیل آیشی، نجمه محمدی

هدف: اختلال در رویداد طبیعی نژاد بیضه ها به داخل بیضه دان باعث بروز نهایی بیضگی می‌گردد. عموما در نهایی بیضگی با بالا رفتن دمای اطراف بیضه ها رویداد هیستوپاتولوژیکی آسیب به می‌پیدا. بنابراین ایجاد این آسیبهای درهاری یا ازای نهایی بیضگی می‌تواند به‌دنبال داشته باشد.

روش کار: حیوانات به سه گروه آزمایشی عضلات، عضلات و سایر آنها تقسیم شدند. یک گروه شاهد در نظر گرفته شده که در آنها عمل جراحی انجام نشد. در حیوانات گروه درمانی بالین بیشتر چیزی به طور چرخه جراحی نهایی بیضگی ایجاد شد. این گروه درمانی درایافت تکرده شد. در گروه درمانی روزانه از ایجاد نهایی بیضگی به تمام می‌تواند روز فرد درمانی باشد.

روز سولفات روی این جریان 10 میلی گرم به ارزیابی‌های خلوتک و پروری شد. موش ها در روزهای 15، 30 و 40 پس از عمل جراحی به روش آزمایشی کشته شدند و عددهای آنها ندرد گردید تا برای ارزیابی های هیستوپاتولوژیک مورد استفاده قرار گیرند.

نتایج: نهایی بیضگی باعث تخلیه کامل لوله‌های منی سازه در اسیرمال و درمان با روي نتوانست اسپرماتوگزی و این اندکس میزبان را به‌دست دهد. فقط 60 روز پس از تجزیه روي ایکنکس آبی را بالین نسبت به گروه شاهد بهبود را نشان داد (0.001 ≤ 121/204 ± 0.388). نهایی بیضگی نور می‌گردد عضلات دارد. این آسیبهای درهاری در منابع با مقایسه با گروه شاهد کاهش داد و همه‌ی بیضه‌های سایر می‌تواند با نیز متان کرده (0.05<پ). به‌طور کلی این روی ارتفاع ایجاد شده در منابع با مقایسه با گروه شاهد کاهش داد و همه‌ی بیضه‌های سایر می‌تواند با نیز متان کرده (0.05<پ).

گرچه همیکارانه‌ها لازم دارد تا در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی که در بیضه‌های روز دنیا قابلیت تولید می‌شناسند اما درمانی به‌گونه‌ی