Pathological and Immunological changes induced in male rats treated with therapeutic doses of sustanon

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Abstract

This study was designed by using twenty male rates (Rattus Rattus) and divided equally into two groups each one (10 animels). First group treated with mixing of Sustanon and sesam oil (5 mg/kg.b.wt) by injection i/m for 60 days, Second group treated with 1ml of sesam oil only i/m. Both groups vaccinated with BCG vaccine. At 30^{th}, 60^{th} day animals respectively were sacrificed and lungs, liver, spleen, kidney and testes were taken for histopathology. mild lesions were seen in these organs during these periods in the sustanon treated group only. Good Immune response (humoral and cell mediated immunity) were found in both groups of rats at the end of first month and second months. Conclusion, mild pathological lesions together with good immune response in the sustanon treated group and in control- BCG group.

Key words: sustanon therapy, pathological and immunological effect, male rats.
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التغيرات المرضية والمناعية المستحدثة في ذكور الجرذان المعاملة بالجرعة العلاجية للسستانون

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الخلاصة

في دراسة صممت على 20 جرذاً من الذكور، قسمت إلى مجموعتين الأولى 10 جرذاً حقنت بالعضلة بمزيج الأندروجين النباتي (السستانون) مع زيت السمسم كمذيب بجرعة والمجموعة الثانية 10 جرذاً حقنت بالعضلة بزيت السمسم 1 مل (5mg/kg.b.wt). بجرعة 0.1 مل داخل الجلد BCG منعت المجموعتين باللقاح. بعد (30 و60) يوماً من الحقن قتلت الحيوانات واخذت الاعضاء الكبد، الرئتين، الطحال، الكليتين، والخصيتين. لغرض الدراسة المرضية حيث لحضت افات طفيفه في كل الاعضاء في المجموعة المحقونة بالسستانون في تلك الفترات واستجابة مناعية خلوية وخلطية كذلك. نستنتج من الدراسة وجود تغيرات مرضيه طفيفة في أعضاء الفئران المحقونة بالساستانون مع استجابة مناعية خلوية وخلطية.

الكلمات المفتاحية: التجريع بالسستانون، التأثيرات المرضية والمناعية، ذكور الجرذان.

Introduction

Anabolic-androgenic steroids (AAss) are the subordinates of the male sex hormone testosterone that are been made by the living body (1). Actually these (AAs) medication for example sustanon, metandienone, stanozole and deca- Durabolin are exceedingly useful meds which act various clinical helpful uses like treatment of hypogonadism. (2) delay puberty (3), micropenis (4) and other diseases. To study the immunopathological effect of therapeutic doses of testosterone derivatives anabolic androgenic steroid (sustanon) on body organs liver, lungs, kidneys, spleen and testes.

Materials and Methods

Therapeutic group of rats (20) were injected 1/M with 5 mg/kg.b.wt of sustanon. Sesam oil suspension weekly for 60 days. Other group control were injected with sesam oil 1ml/i/m weekly for 60 days. At day 0, the animals in two groups were immunized with 0.1 ml BCG vaccine 1/dermally. At 14th day booster BCG vaccine in all animals had been given. At 27th day, delayed type hypersensitivity skin test were done for half of animal groups and at 30th day, passive haemagglutination test were done for the same half of sacrificed animal groups (5) and body organs were taken liver, lungs, spleen, kidneys and testis for histopathology study(6). Other half of two groups remaining were given BCG booster doses at 30th and 44th day. At 57th day delayed type hypersensitivity skin test were done and at 60th days passive haemagglutination test were done for all the animal sacrificed and body organs liver kidney, lungs, spleen and testis we taken for histopathological study.

Result

- **Histopathological findings:** Control group showed normal histological features in liver, kidney, lungs, spleen and testis. The therapeutic group showed mild degenerative changes and inflammatory cells infiltration. Liver: Showed dilation and congestion of central vein and sinusoids with vacuolar degeneration of hepatocytes and proliferation of kupffer cells at 30th and 60th days of sustanon treatment (Fig.1). Lungs: Showed mild interstitial thickening of alveolar wall giving feature of focal pneumonitis and emphysema, together with peribronchial lymphoid tissue hyperplasia with hypertrophy of pulmonary artery with narrowing their lumen due to vacuolation of their endothelial lining (Fig. 2) at 30th and 60th day of sustanon treatment. Kidneys: Showed mild cloudy swelling and mild renal casts in renal tubules and vacuolation of their epithelial lining at 30th and 60th day of sustanon treatment (Fig.3). Spleen: Showed hyperplasia of white pulp and reticuloendothelial cell lining Red pulp at 30th and 60th days of sustanon treatment (Fig.4). Testes: Showed mild loss of spermatogenesis, mild edema in the interstitial tissue and mild depletion of leydig cells and mild vacuolar degeneration in the seminefrous tubules at 30th and 60th days of sustonon treatment (Fig.5).

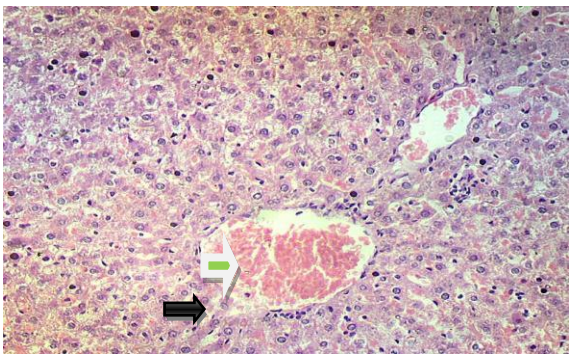

Fig. (1) Liver of male rat treated with sustanon 5 mg\ kg B.W. B.W.intramuscularly weekly alone (Tirty day period), shows dilitation and congestion of central vein (black arrow) and sinosoidal dilitation (blue arrow), together with vacuolar degeneration of hepatocytes (geeen arrow); with proliferation of kupffer's cells (thin arrows), H&E stain. X20.

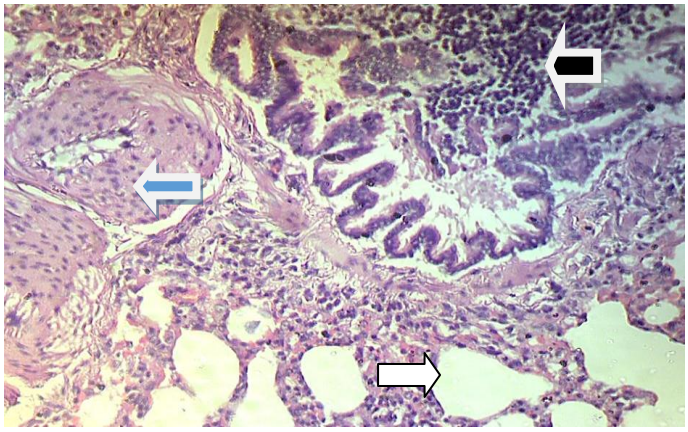

Fig. (2) lung of male rat treated with sustanon 5mg\ kg B.W. intramuscularly weeklyalone (sixty day period), shows emphysema with a mild interstitial thickening of alveolar tissue(white arrow), and peribronchial lymphoid tissue hyperplasia (black arrow) with hypertrophy of pulmonary arteries and narrowing of their lumina due to vacuolation of their endothelial lining cells (blue arrow), H&E stain X20.

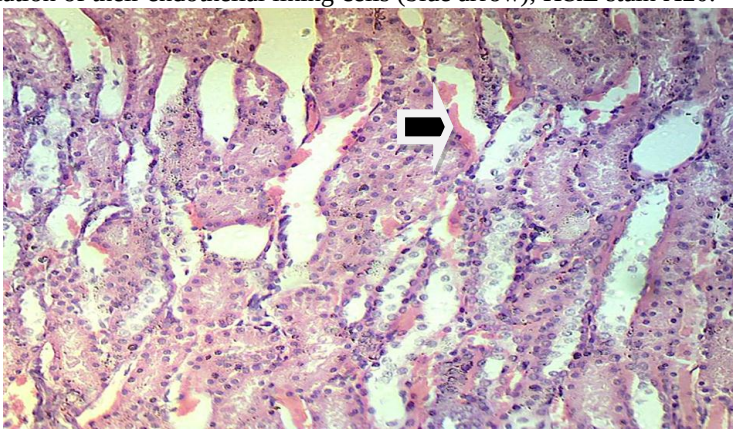

Fig. (3) kidney of male rat treated with sustanon 5 mg\ kg B.W. intramuscularly weekly alone (sixty day period), shows cloudy swelling and vacuolation together with mild renal casts and dilatation of renal tubules (black arrow). H&E stain X20.

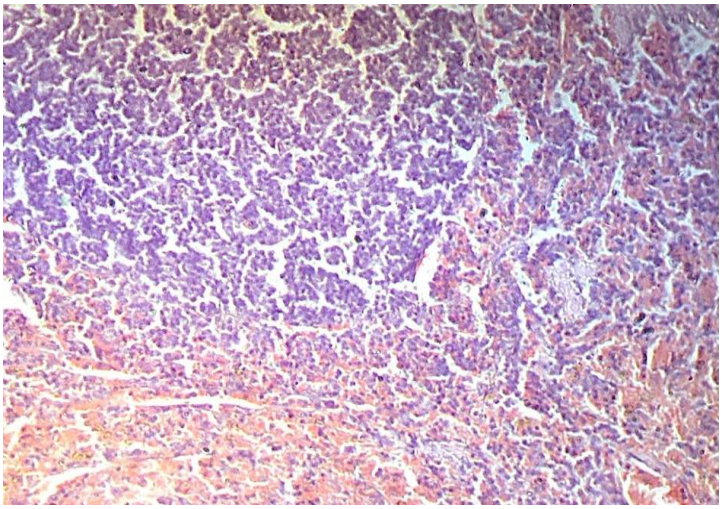

Fig. (4) spleen of male rat treated with sustanon 5 mg\ kg B.W.intramuscularly weekly alone (sixty day period), shows marked hyperplasia of lymphoid tissue of white pulp and reticuloindothelial lining red pulp. H&E stain X20.

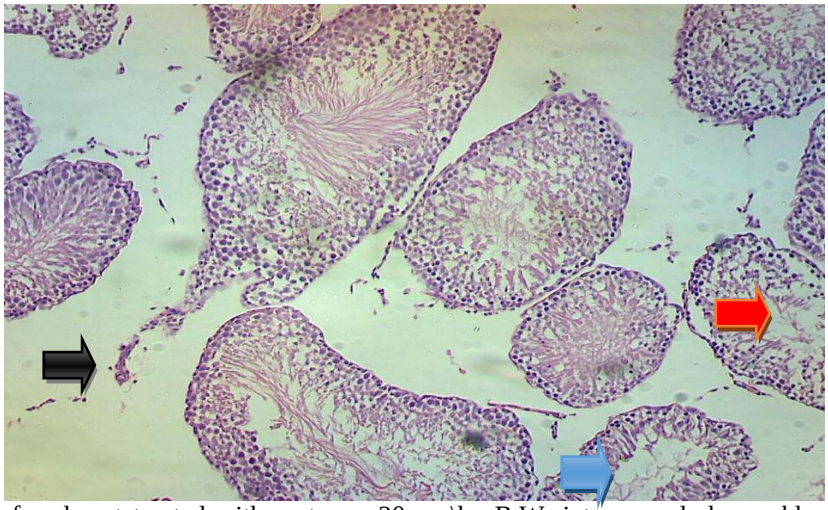

Fig. (5) testis of male rat treated with sustanon 20 mg\kg B.W. intramuscularly weekly alone (sixty day period), shows a mild loss of spermatogenesis (red arrow), vacuolar degeneration (blue arrow), with extensive interstitial edema and depletion of Leydig cells (black arrow) H&E stain X10.

- **Immunological findings:**

- **Control group**: showed extensive variation in the skin thickness differences after 24, 48 and 72 hrs with the mean of 1.76±0.022, 2.03±0.036 and 1.91±0.031 respectively at 27th day of sustanon treatment and at 57th day of treatment skin thickness differences mean were 1.87±0.021, 2.12±0.024 and 2.00±0.025 at 24, 48 and 72 hrs respectively (Table.1). Humoral immunity, showed high level of Abs at 30th and 60th days of sustanon treatment with a mean of 83.20±9.776 and 108.80±9.776 respectively (Table. 2).
- **Therapeutic group**: Showed moderate variation in skin thickness differences after 24, 48 and 72 hrs with the mean of 1.71±0.031, 1.93±0.021 and 1.79±0.023 respectively at 27th day of sustanon treatment and at 57th day the mean of skin thickness differences were 1.74±0.030, 1.96±0.033 and 1.83±0.033 at 24, 48 and 72 hr respectively (Table.1). Humoral immunity, This group showed high variation in elevation of antibodies level at 30th and 60th day of inoculation of sustanon with the mean of 51.20±5.225 and 102.40±10.54 respectively (Table. 2).

Table (1) The mean values of the foot pad thickness of the rat (in mm) after 27 days and 57 days post the first inoculation

Group		Mean ±SE			
		0hrs	24hrs	48hrs	72hrs
1st group (control)	27 days period	1.44 ± 0.016A	1.76 ± 0.022C	2.03 ± 0.036D	1.91 ± 0.031A
	57 days period	1.55± 0.016A	1.87± 0.021C	2.12± 0.024D	2.00± 0.025D
2nd group	27 days period	1.46 ± 0.016A	1.71± 0.031C	1.93± 0.021C	1.79± 0.023A
	57 days period	1.55± 0.016A	1.74± 0.030B	1.96± 0.033C	1.83± 0.033C

The different letters in the vertical refer to significant differences while the similar letters refer to non-significant differences at (p≤0.05).

Table (2) Mean values of antibodies titers in different groups immunized with BCG vaccine at day 30 and day 60 after first inoculation

Mean±SE	1st Group (control)	2nd Group
30 days period	83.20±9.776B	51.20±5.225B
60 days period	108.80±9.776B	102.40±10.541B

The different letters refer to significant differences at (p≤0.05).

Discussion

The study revealed that high doses of sustanon caused significant lesions in the different organs while lower doses induced mild and simple lesions, this belonged to their oxidative stress (7) subsequently the targeted molecule becomes a free radical itself and initiates a cascade of events that ultimately lead to cellular damage in different organs like lungs, kidneys, liver, spleen and testes. A similar study (8) showed mild effect under low doses of sustanon caused mild degenerative changes in the liver due to toxic hypoxia and reflected injury to liver cells. A similar mild lesions were induced in testes such as edema at interstitial tissue and depletion of leydig cells together with vacuolation of seminefrous tubular epithelia were reported by (9) due to toxic hypoxia caused by suscanon therapy. Mild lesions were seen in kidneys such as vacuolar degeneration of renal tubules and renal casts which similarly reported by (10) due to toxic hypoxia and injury to the renal tubular epithelia. Lungs and spleen showed mild pathological lesions such as emphysema, mild pneumonitis and hyperplasia of white pulp and reticuloendothelial cells of red pulp of the spleen these lesions occurred as a result of oxidative stress inuced by sustanon treatment (11). Regarding immunological finding good immune response were seen in therapeutic dose group of sustanon comparable to control group, indicated that the therapeutic doses of sustanon induced good immune response (12). Comparable to the control group which received BCG vaccine only and the elevation of immune response detected by delayed hypersensitivity skin test in BCG control group and therapeutic group, a similar finding reported by (13) that the BCG a good immunostimulator enhanced the cellular immunity and (14) showed therapeutic sustanon doses induced immune response which is evident in this study a high level of antibodies detected in control (BCG) group alone comparable to therapeutic group with sustanon. A similar finding reported by (15) whom showed that the BCG induced good immune response comparable to therapeutic doses of sustanon which induced good level of immune response detected in this study, a similar observation were reported by (14).

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