Histological Changes in Albino Rat Testis After Cimetidine Therapy

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Ninety six adult male rats were divided into four groups. They were treated with Cimetidine 5.7mg/Kg body weight twice daily for 3,6 & 9 weeks intramuscularly. The testis were studied, showed decrease in spermatogenesis.
Key words: Testis, Cimetidine Therapy

Millions of patients have been treated with Cimetidine and list of adverse reactions reported is a long one. Thiel[1], Peden[2] and Fuentes[3] studied the various comparative parameters of semen analysis in patients on Cimetidine therapy. They reported a decrease in sperm count of variable degree. Contradictory reports have been made by other workers regarding the results on sperm count.

The present work was undertaken to study the histological features of testis in albino rats after giving Cimetidine for different time periods.

Material & methods

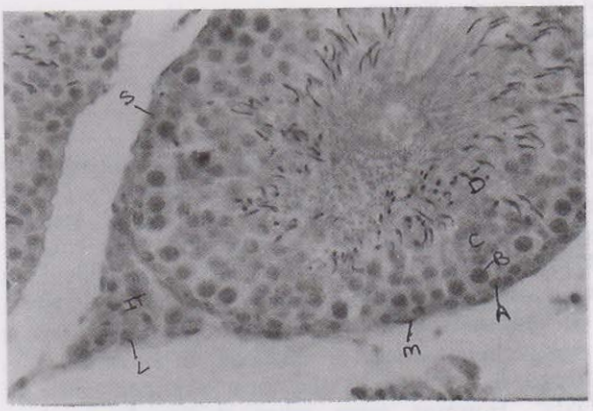
Ninety six adult albino rats of 110gram body weight were selected for the study and divided into four groups I, II, III and IV. Group I was treated as control groups and contained 24 animals, other groups comprised of twenty four rats in each were kept as experimental animals. The animals of II, III and IV groups were given Cimetidine i/m 5.7mg/kg body weight daily for three, six and nine weeks respectively. Afterwards testis of experimental group animals were removed.

The testis of all the groups were cut into small pieces fixed in Zenker- Formaline for 24 hours. Processed, sectioned and stained by haemotoxylin stain. A qualitative microscopic assessment of the germinal epithelium was made on the basis of an arbitrarily chosen spermatogenic index. The diameter of seminiferous tubules were measured by an ocular micrometer. The tubules cut at right angles to the Zxix of the seminiferous tubules were measured and observations were recorded at random from two different sections in each slide.

Results

The Group I (control) showed normal gross and histological appearances (Fig1,2).

Group II & III - size of testis was unchanged, soft in consistency and some decrease in weight of paired testis. Average tissue ratio was decreased with normal tubular diameter in group II and slight decrease in group III rats. Seminiferous tubules were full of spermatogenic series, with normal nuclear and cytological appearance. Unchanged basement membrane sertoli cells and myoid cells were seen(Fig.3,4,5).



(Fig.1; Photomicrograph of normal testis showing S: Sertoil cell, M: Myoid cells, L: Leydig cells, A: Spermatogonia, B: Spermatocytes, C: Spermatids, D: Spermatozoa, IT: Interstitial tissue. H&E Stain.

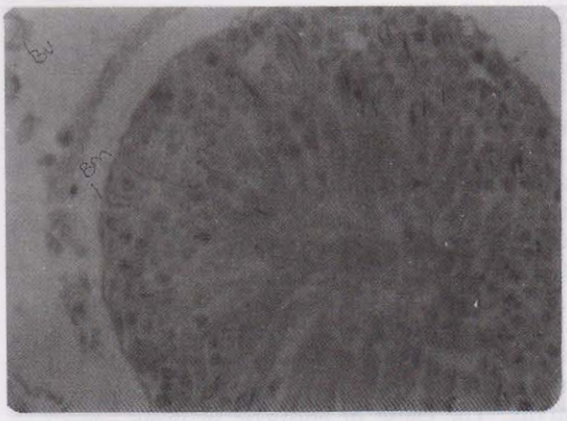


Fig.2: Photomicrograph of normal testis showing BM: Regular basement membrane, BV: Patent blood vessel.
PAS-H Stain Group I Mag:1400x

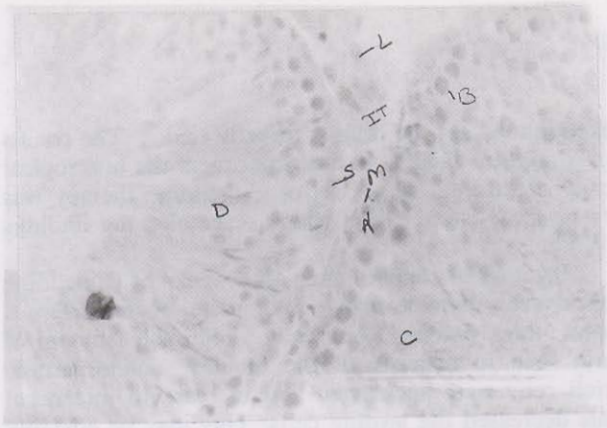


Fig.3. Photomicrograph of testis showing S: Sertoli cell, M: Myoid cells, L: Leyding cells, A: Spermatogonia, B: Spermatocytes, C: Spermatids, D: Spermatozoa occupying the lumen, IT: Interstitial tissue.
H&E Stain Group II Mag:1400x

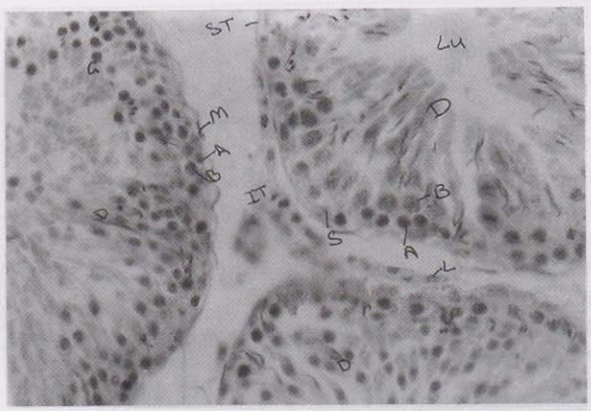


Fig. 4. Photomicrograph of testis showing ST: Seminiferous tubules, Lu: Lumen, S: Sertoli cells, M: Myoid cells, L: Leyding cells dispersed between lightly increased interstitial tissue (IT), A: Spermatogonia B: Dividing, non-dividing Spermatocytes, G: Few spermatids lining the lumen of the tubules, D: Mature spermatozoa advancing towards the lumen.
H&E Stain Group III

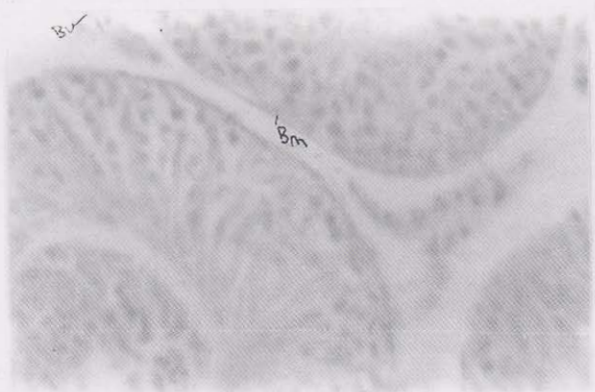


Fig. 5: Photomicrograph of testis showing BM: Near normal basement membrane, BV: Slightly thick walled blood vessel with patent lumen.
PAS-H: Stain: Group III

In Group IV testis were small in size, firm in consistency, markedly decreased in weight, average tissue ratio was also markedly decreased, tubular diameter was much reduced, the spermatogonia were few, with small Spermatocytes, spermatids and very few small sized sperms seen. Basement membrane thickened, with prominent myoid cells and decrease in sertoli cells (Fig.6,7).

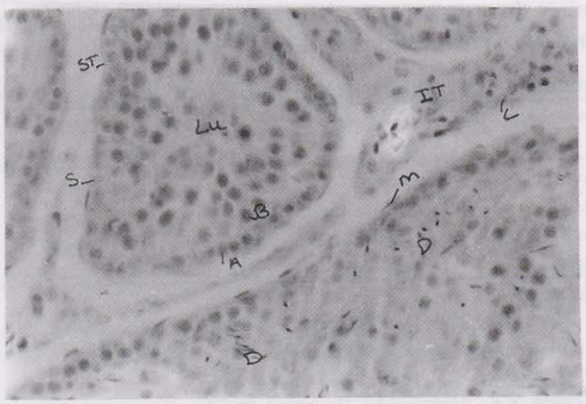


Fig. 6. Photomicrograph of testis showing ST: Small size seminiferous tubules, LU: Lumen occupied by few spermatids ©: M: Prominent myoid cells, S: Decrease in number of Sertoli cells. A: Spermatogonia small sized, B: Undividing Spermatocytes, D: very few spermatozoa in between the spermatogenic cells, IT: Increased interstitial tissue, L: Very few scattered Leyding cells.
H&E Stain Group IV

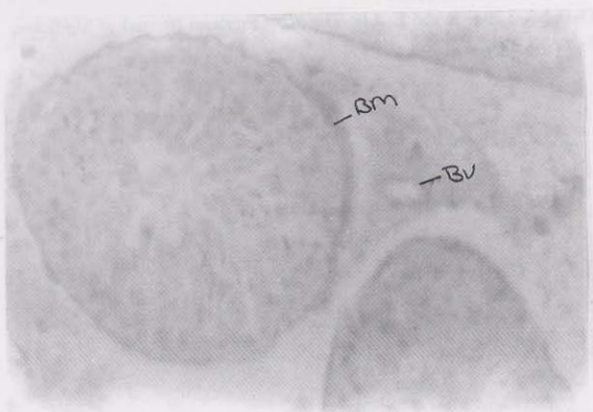


Fig. 7. Photomicrograph of testis showing BM: Thickening of basement membrane, BV: Blood vessels with patent lumen but with thick walls.
PAS Stain Group IV

Discussion

The competition for survival has put man under lot of stress. Hypersecretion of gastric acid and peptic ulceration account for much illness. A search for the drug to combat

this illness led to the discovery of Cimetidine. Although there are adverse reactions of the drug but popular use of the drug explains that the incidence of adverse reactions is low.

Thiel[1,4] found a 43% reduction in sperm count by treatment of Cimetidine for 9 weeks. Not much is known regarding the mechanism responsible for the sperm count reduction. Several potential mechanisms exists beside a direct toxic effect on spermatogonia[9,10,11].

White[11,12] did not agree with Thiel, he was of the opinion that spermatogenesis takes 10-13 weeks, sperm counts after nine weeks are unlikely to reflect any effect of Cimetidine unless the drug is directly toxic[2,7]. The results were similar to Theil[12]. In our experiment the histological picture of three to six weeks of Cimetidine therapy was very near the control level which resembled the findings of White.

Histological changes after nine weeks of Cimetidine showed a considerable change in diameter of semineferous tubules, thick basement membrane negligible amount of sperm seen in majority of the tubules - oligospermia. Sertoli cells were unchanged and increase in interstitial tissue decreased the leyding cells. This may be effecting the spermatogenic cycle [8].

Table No 1: The comparison f histological parameter between various treatment groups

Duration of therapy group	Size of tubules	Mean tubular diameter (% change)	Basement membrane	Spermatonia	Spermatocytes	Spermatids	Spermatozoa	Sertoli cells	Leyding cells
Control I	Normal	207.5	Normal	+++	+++	+++	+++	+++	++
3 weeks II	Normal	208.1	Normal	+++	+++	+++	+++	+++	++
o weeks II	Normal	201.9	Normal	+++	+++	+++	+++	+++	++
9 weeks IV	Decreased	148.1	Thick (+++)	++	++	++	+	+	+

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