

EFFECT OF *m*-XYLOHYDROQUINONE ON THE GENITAL ORGANS AND FERTILITY OF MALE RATS

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Summary. *m*-Xylohydroquinone had no effect on the genital organs of male rats. Fertility was unaffected even after persistent administration of the drug.

INTRODUCTION

It has been reported that *m*-xylohydroquinone (MXHQ) caused acute interruption of spermatogenesis and eventual degeneration of the seminiferous epithelium in rats, and that the fertility was impaired (Sanyal, 1958). The effect on spermatogenesis appeared in mild form as early as 2 days after administration of the drug (5 mg by the parenteral route) and by 4 days complete aspermia was observed. The Leydig cells, however, were unaffected. The anti-spermatogenic effect was imputed to the production of a state of avitaminosis of vitamin E as well as inhibition of pituitary gonadotrophic activity (Sanyal, 1958). The drug has also been tried in men and it has been claimed that it causes 50% reduction in fertility (Sanyal & Rana, 1959). A transient fall in sperm count (50%) was believed to be responsible for such reduction in fertility (Sanyal, 1960). There was no adverse effect on libido. However, Batra & Hakim (1956) could not observe any effect of MXHQ on the genital organs of male rats and mice.

In view of the above, it was considered worthwhile to re-investigate the effect of MXHQ on the genital organs and fertility of male rats and to substantiate, if possible, Sanyal's (1958) findings. Cognate data on pituitary and adrenal glands are also included in this communication.

MATERIALS AND METHODS

Colony bred young adult (80 to 90 g) and adult rats (180 to 200 g) of this Institute were used in this investigation. The animals were maintained under uniform laboratory conditions throughout the experimental period.

m-Xylohydroquinone (5 mg/rat in 0.5 ml distilled water) was administered daily by the subcutaneous route for 30 days. The control animals received distilled water alone in a similar manner. Before administration on each day, it was first ensured that the drug (General Drugs and Antiseptics Ltd, Calcutta), conformed to the physicochemical tests of purity prescribed by Sanyal & Guha Sarkar (1958) and Sanyal (1960).

The animals were killed 2, 4 and 30 days after administration of MXHQ. A batch of animals was killed 15 days after cessation of treatment in order to examine the reversibility of the anti-testicular effect, if any. The testis, seminal vesicles and the ventral prostate were dissected out and weighed to the nearest 0.1 mg in a Roller-Smith balance. The testes were fixed in Bouin's fluid, and serial paraffin sections were stained with Ehrlich's haematoxylin and eosinol. The fructose concentration of the coagulating glands was estimated by the method employed previously (Kar, Dasgupta & Das, 1961).

For a fertility performance test, proven adult male and female rats (200 to 220 g) were used. The males were put to mating after 20 days of MXHQ treatment (5 mg daily/rat, subcutaneous injection). The drug was continued for another 20 days (during the cohabitation period) in a similar manner. The rest of the procedural detail was the same as in a previous study (Kar & Dasgupta, 1961).

RESULTS

EFFECT OF MXHQ ON THE GENITAL ORGANS OF YOUNG ADULT RATS

Except for the 2-days group, the testis weight was significantly greater than that of the (initial) controls ($0.02 > P > 0.001$, Table 1). This progressive increase in testis weight was, to be expected, however, because the animals were growing young adults. This was further indicated by the similar range of weight of the organ in 45-days-MXHQ pretreated and terminal control groups ($P < 0.3$).

In the initial control animals the histological picture of the testis was typical of a young adult rat. Spermatogenesis had yet to attain the adult tempo but the interstitium presented virtually adult features. The testis of terminal control animals, however, showed full spermatogenesis. The seminiferous epithelium exhibited successive stages of transformation into mature spermatozoa. The interstitium contained numerous active Leydig cells. The histological features of 2- and 4-days-MXHQ groups were similar to those of the initial controls but those of the 30- and 45-days groups were typical of normal adult rats.

The seminal vesicle weight showed a similar pattern. Thus, there was no significant difference between the initial control and 2- or 4-days groups. But the seminal vesicle weight of the rest of the groups was significantly higher than that of the initial controls ($P < 0.001$, Table 1). There was, however, no significant difference between the terminal controls and the 45-days pretreated animals in this respect. The situation was somewhat different with ventral prostate weight. In 2- and 4-days groups, the average weight of this organ was significantly less than that of the initial controls ($P < 0.001$); but that of animals treated with MXHQ for 30 days was significantly greater ($P < 0.001$, Table 1). The terminal controls had significantly larger ventral prostates than the 45-days pretreated group ($P < 0.001$).

m-Xylohydroquinone had no significant effect on adrenal weight (Table 1). The pituitary weight of the 30-days group was significantly lower than that of the initial controls ($P < 0.02$); but the pituitary weight of animals treated for 2 and 4 days was virtually similar to that of the initial controls. The terminal controls had significantly lower average pituitary weight than the 45-days group ($P < 0.01$).

TABLE 1
EFFECT OF MXHQ ON THE GENITAL ORGANS OF YOUNG ADULT MALE RATS

Days after MXHQ administration	Mean testis weight (mg) with s.e.	Mean seminal vesicle weight (mg) with s.e.	Mean ventral prostate weight (mg) with s.e.	Mean adrenal weight (mg) with s.e.	Mean pituitary weight (mg) with s.e.
Controls (initial)	557.5 ± 28.28 (8)†	30.8 ± 3.25 (8)	29.6 ± 1.41 (7)	10.7 ± 0.42 (6)	4.4 ± 0.31 (7)
2	624.4 ± 54.51 (8)	28.3 ± 2.88 (6)	15.3 ± 1.93 (8)	10.1 ± 0.40 (7)	3.7 ± 0.17 (7)
4	671.7 ± 40.38 (10)	29.0 ± 3.43 (6)	16.4 ± 0.80 (8)	10.0 ± 0.77 (6)	4.7 ± 0.42 (7)
30	884.3 ± 34.79 (11)	30.4 ± 3.11 (8)	45.4 ± 4.23 (7)	10.6 ± 1.33 (6)	3.1 ± 0.35 (8)
45†	964.0 ± 23.22 (8)	154.0 ± 8.75 (6)	95.2 ± 8.00 (6)	9.3 ± 0.33 (6)	4.8 ± 0.24 (8)
Controls (terminal)*	996.8 ± 11.53 (13)	169.0 ± 9.46 (6)	116.0 ± 12.31 (8)	9.3 ± 0.42 (6)	4.0 ± 0.00 (8)

* Killed at 45 days

† No. animals.

‡ MXHQ stopped after 30 days administration.

TABLE 2
EFFECT OF MXHQ ON THE GENITAL ORGANS OF ADULT MALE RATS

Days after MXHQ administration	Mean testis weight (mg) with s.e.	Mean seminal vesicle weight (mg) with s.e.	Mean ventral prostate weight (mg) with s.e.	Mean fructose concentration of the coagulating glands (mg/g) with s.e.	Mean adrenal weight (mg) with s.e.	Mean pituitary weight (mg) with s.e.
Controls	1273.6 ± 86.34 (6)*	174.7 ± 10.40 (6)	249.0 ± 33.32 (6)	0.19 ± 0.02 (6)	18.1 ± 0.75 (6)	12.0 ± 0.72 (6)
2	1132.5 ± 50.77 (6)	215.0 ± 17.08 (6)	256.3 ± 29.16 (6)	0.15 ± 0.04 (3)	17.0 ± 0.38 (7)	8.3 ± 0.33 (6)
4	1131.3 ± 68.88 (7)	209.3 ± 19.15 (6)	219.7 ± 23.04 (7)	0.15 ± 0.09 (4)	17.3 ± 0.64 (7)	8.0 ± 0.32 (6)
30	1290.2 ± 62.00 (8)	226.5 ± 18.49 (6)	233.1 ± 20.06 (6)	0.32 ± 0.04 (5)	18.6 ± 1.13 (7)	9.5 ± 0.71 (6)
45†	1195.0 ± 56.56 (6)	207.0 ± 24.94 (6)	209.8 ± 35.43 (6)	0.19 ± 0.01 (6)	14.0 ± 1.21 (6)	5.3 ± 0.61 (6)

* No. animals.

† MXHQ stopped after 30 days administration.

EFFECT OF MXHQ ON THE GENITAL ORGANS OF ADULT RATS

It will be evident from Table 2 that MXHQ treatment caused a reduction in testis weight in 2- and 4-days groups but the difference from controls was not statistically significant ($P < 0.2$). The weight of the testis in 30-days-treatment or 45-days-pretreatment groups did not differ significantly from that of the controls.

The histological features of the testis of MXHQ treated animals were normal. The tubules were at the height of spermatogenic activity and the interstitium contained numerous active Leydig cells. The vascularity of the testis was also normal.

m-Xylohydroquinone administration did not evoke any significant change in seminal vesicle and ventral prostate weight (Table 2). This was also the case with the coagulating gland fructose concentration in the 2-, 4- and 45-days groups. There was, however, a significant increase in coagulating gland fructose in 30-days MXHQ-treated animals (versus controls = $P < 0.05$).

The adrenal weight did not undergo any significant change after MXHQ treatment. However, the weight of this organ in the 45-days group was significantly lower than that of the controls ($P < 0.02$). The pituitary weight of MXHQ-treated groups was consistently lower than that of the controls ($0.02 > P > 0.001$, Table 2).

EFFECT OF MXHQ ON FERTILITY

m-Xylohydroquinone had no effect on the fertility of adult proven male rats. The percentage of males proved fertile in mating tests was virtually the same in control and MXHQ groups (Table 3). There was no difference in the number of young born per litter.

TABLE 3

EFFECT OF MXHQ ON FERTILITY OF ADULT MALE RATS

Treatment	No. males mated	No. females mated	No. and % males fertile	Mean No. young per litter (with S.E.)
Controls	6	12	4 (80%)*	6.5 ± 0.50
MXHQ (5 mg daily/40 days)	12	24	10 (83.3%)*	6.0 ± 0.60

* Percentage of males fertile out of the total number.

DISCUSSION

The results of the present study show that MXHQ has no effect on the genital organs of adult rats. Fertility remains unimpaired, even after 40 days of persistent treatment. There is no effect on adrenal weight but the pituitary weight shows a consistent reduction. The physiological significance of this is, however, difficult to assess. It cannot imply a suppression of pituitary gonadotrophin production because the genital organs continue to be normal at every stage of the MXHQ regimen.

Studies with young adult rats show that m-xHQ does not interfere with the attainment of the typical adult spermatogenesis pattern. All the genital organs gain weight progressively, the spermatogenic process assumes normal adult tempo in spite of continued m-xHQ treatment, and there is no noteworthy change in adrenal or pituitary weight.

The data obtained in the present study, therefore, do not substantiate Sanyal's (1958) claims for an antifertility effect of m-xHQ in male rats.

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