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TESTING EFFICACY OF HERBAL DRUG "FORTEGE" IN TREATMENT OF METAL INDUCED INFERTILITY IN MALE MICE

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ABSTRACT: Fertility was tested in 0.5 mM/kg b. wt. (*i.p*) Lanthanum chloride exposed mice. Beneficial effects of "Fortege" an ayurvedic medicine (Alarsin co. Bombay) were also tested. Lanthanum chloride affected sperm count and motility. Lanthanum chloride could have affected Sertoli cells adversely and that have reduced sperm's ability of uptake of fructose and as a result of it sperms became unable to reach ovum and thus antifertility was shown. Maximum effects of Lanthanum chloride were on the weight of seminal vesicles and their fructose content. When such mice were exposed to "fortege" for 21 days and the efficacy obtained, was 87.5%. Only way to overcome Lanthanum toxicity is to remove Lanthanum from the tissues. For the removal of Lanthanum from the body tissues, the chelating activity of some alkaloids of these plants can be considered as the one of the main reason and it is supplemented by improvement in testosterone and LH level.

INTRODUCTION: Industrialization, that is the need of development, is also cause of increased chemical hazards. Toxic chemicals are released into lithosphere and hydrosphere from chemical industries. Bhopal gas tragedy of 1984 is one such recent examples that has caused a heavy toll and people of that area are still bearing aftereffects. Some rare earth metals have been reported to have mild toxic effects on the testes [1, 2, 3] of rodents.

Lanthanum is used profoundly in research, industry and medicine [4, 5], it is found desirable to study the effects of Lanthanum chloride exposure on the fertility of male mice.

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Drug "Fortege" is made from *Withania somnifera, Mucuna pruriens, Argyreia speciosa, Leptadenia reticulata* and *Anacyclus pyrethrum* is used for curing common male sexual disorders[6]. This drug has been tested to treat male sterility against Lanthanum induced infertility.

MATERIAL AND METHOD: Healthy male mice weighing ±30gm were under uniform animal husbandry conditions. These experimental animals were randomly divided into three major groups.

Each group was divided into three subgroups each having 8 animals. Ist subgroup was taken as control while IInd subgroup received Lanthanum chloride at a dose of 0.5mM/kg b. wt. (*i.p.*) for 7, 14 and 21 days respectively for each group. Subgroup IIIrd of all major groups received Lanthanum chloride as in subgroup IInd and "Fortege" medicine 60mg/kg b. wt. (*p.o.*). Autopsy was performed after 24 hrs of the last treatment. Mating behavior and fertility of control and treated mice was studied after treatment of pairing with proestrous female (1:1).

The presence of sperms in vaginal smear following morning was assigned as day one of pregnancy. The female mice were laparotomized on day 10 and the implantations sites were counted. The percentage of mice showing no implantation sites, was taken as the measure of the antifertility activity.

Weight of seminal vesicle and biochemical estimation of seminal fructose was done after 7^{th}, 14^{th}, and 21^{st} day of exposure to Lanthanum chloride. Results were analyzed statistically using student's "t" test.

RESULTS: Lanthanum chloride was found to have induced antifertility in male mice. 100% resorption sites were observed after 21 days of exposure. With the conjoint treatment of Lanthanum chloride and "Fortege", fertile mating occurred and 87.5% implantation sites were observed (**Table 1**). Administration of Lanthanum chloride decreased the weight of seminal vesicle and fructose content, sperm count and motility reduction in control mice whereas "Fortege" treated mice showed normal weight of seminal vesicle and fructose content at 21^{st} day of exposure (Table 1). Sperm count and motility recouped.

TABLE 1: EFFECT OF LANTHANUM CHLORIDE AND "FORTEGE"ON WEIGHT OF SEMINAL VESICLES AND THEIR FRUCTOSE CONTENT OF MALE MICE (All the values are mean ± SE)

Groups	Sub-groups	Dose administered 0.5 mM/Kg. b. wt.	Day of autopsy after exposure	No. of treated males	No. of females with implantation sites	Number of female without implantation sites	Percentage of mice showing antifertility	Weight of seminal vesicles (in mg)	Fructose content in vesicle (in µg/100mg)
1	I	Control	7	8	8	0	0	162.1± 0.61	233.5± 6.11
	II	Lanthanum chloride	7	8	0	8	100	161.4 ± 0.65^{+}	168.1 ± 5.95^{+}
	III	Lanthanum chloride + Fortege	7	8	2	6	75	162 ± 0.30	159 ± 4.93^{+}
2	I	Control	14	8	8	0	0	163.6 ± 0.65	232.2 ± 5.95
	II	Lanthanum chloride	14	8	0	8	100	157.9 ± 0.51^{+}	135.5 ± 6.05^{+}
	III	Lanthanum chloride + Fortege	14	8	3	5	62.5	164.6 ± 0.45^{+}	201.5 ± 5.31^{+}
3	I	Control	21	8	8	0	0	164.8 ± 0.30	229 ± 5.95
	II	Lanthanum chloride	21	8	0	8	0	158.1 ± 0.38^{+}	110.5 ± 1.73^{+}
	III	Lanthanum chloride + Fortege	21	8	7	1	12.5	159.8 ± 0.33^{+}	231 ± 4.95^{+}

Level of significance = + < 0.05

DISCUSSION: Many chemical agents exert antifertility effect on the recipient by affecting testicular tissue. Many of the salts cause aspermia and athenospermia by acting at various levels. Such as disintegrating sperms in ductus deferens by separating head and tail and by inhibiting utilization of fructose as energy source for movement.

Fertility in male rats has been reported to be lost [7] in response to cadmium chloride. In the present study similar findings were observed. Regarding the failure of fertilization, the author supports view of Hoey [8] that salts of Silver, Tin, Nickel, Copper and Cobalt are taken up rapidly by spermatozoa in the lumen of seminiferous tubules. He attributed that effect of metal administration produces irreparable damage to the Sertoli cells.

Fructose is attributed to be [9] essential for the activity of spermatozoa. Duration for which spermatozoa are in epididymis, remain immotile due to absence of oxygen needed to mobilize fructose [10]. Studies made on Gossypol [11] also suggest suppression in motility with reduced fructose content.

The present study confirms the above reports as fructose level is reduced after Lanthanum chloride treatment. Metallic salts exert toxic effects not only on spermatozoa but also on other reproductive organs. Reduced weight of seminal vesicles lends support to this view. Since Sertoli cells are said to be responsible for passing nutrition to maturating spermatozoa, it is possible that the abnormal spermatozoa which were deposited in the vagina were unable to reach the ovum, due to absence of

adequate supply of fructose. High doses of Lanthanum chloride inhibit the activity of alkaline phosphatase, reduce the sperm quantity and quality. Medium dose of Lanthanum chloride could boost the activity of nitric oxide synthetase, reduce the sperm count, and damage the sperm quality [12].

Exposure of cells to $LaCl_3$ at the concentration of 0.1 μM suppressed the β-glycerophosphate-induced alkaline phosphatase activity and calcium deposition [13]. Lanthanum is reported to block Ca channels and thus inhibits Ca influx and acrosome exocytosis [14]. It might be the main reason behind inability of sperms to fertilize ovum in addition to decrease in sperm count and motility.

Tetrahydroisoquinoline alkaloids of *Mucuna pruriens* are found to show chelating activity for iron [15, 16]. The Ayurvedic drug "Fortege" recouped the fructose content of the seminal vesicles to control value by day 21. Fertility testing also showed gradual improvement and by day 21 "Fortege" recouped fertility efficacy to 87.5%. It might be because of chelating activity of alkaloids of the constituent plants of "fortege" that removed Lanthanum form the body tissues.

Testosterone analogous effects of the aqueous extract of the *Anacyclus pyrethrum* [17] and *Leptadenia reticulata* [18] are reported, in which increase in seminal fructose and motility of sperms are major effects. Increase in level of testosterone and LH [19] and decrease in number of deformed spermatozoa [20] has been reported by administration of *Withania somnifera*.

To summarize the discussion it could be assumed that removal of Lanthanum from tissues by the alkaloids together with improvement of hormonal level would have helped in recouping fertility of males. After the thorough human trial this drug can be used to treat metal induced antifertility in industrial workers.

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