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Research Article

EFFECT ON BODY WEIGHT AND FEED CONSUMPTION OF BISPHENOL - A INDUCED SUBACUTE TOXICITY IN RATS

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ABSTRACT: A subacute toxicity study of Bisphenol-A was conducted to investigate its toxic potential and as well as impact on mammals using wistar rat. The doses chosen were 50, 200 and 600 mg/kg body weight for group III, IV and V respectively and group II served as vehicle control and group I was negative control. Relative weights of different organs differed significantly ($P \leq 0.05$). Feed consumption and body weight were significantly ($P \leq 0.05$) reduced in the rats of group III, IV and V in dose dependant manner. It has toxic potential to induce anorexia.

Key words: Bisphenol-A, Body weight, Feed consumption, Wistar rat.

INTRODUCTION

India is widely developing country and its life style is largely on a change. In this scenario plastic is sufficiently being used in all spheres of life. Naturally, it affects the life cycle of animals, wildlife species and humans. Plastic has lasting use and it has proved in various known applications. It has wide public acceptance and since then its commercial popularity has increased gradually by time. Presently, Bisphenol-A (BPA) is being used in the manufacturing of several types of plastics including polycarbonates, epoxy resins and polyvinyl chloride (Staples *et al.*,1998). BPA is one of the highest volume chemicals produced worldwide; global BPA capacity in 2003 was 2,214,000 metric tons (> 6.4 billion lb), with 6-10% growth in demand expected per year (Burridge 2003). India consumes around 5 million tonnes of plastic products (The Hindu 2006).

The concern about potential exposure of BPA is based on reports indicating leaching of BPA from plastics (Yamamoto and Yasuhara 1999; Mountfort *et al.*,1997; Krishnan *et al.,* 1993), food cans lined with epoxy resins (Brotons *et al.,* 1995) and also through drinking water, dental sealants, dermal exposure and inhalation (Vandenberg 2007; Calafat *et al.,* 2005., Olea *et al.*,1996). Current limitations in understanding the global consequences of BPA exposures include incomplete understanding on the primary toxicopathological effect *i.e.* on body weight and feed consumption. In this

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context, the present study was taken up to investigate the effect of exposure of BPA on feed consumption and body weight in healthy wistar rats.

MATERIALS AND METHODS

Animals

The present study was conducted on 6 weeks old healthy Wistar rats. The rats were procured and housed in cages at Animal House, College of Veterinary Science and Animal Husbandry (Indira Gandhi Krishi Vishwavidyalaya), Anjora, Durg, Chhattisgarh, India. Animals were acclamatized to experimental room for 7 days before start of the experiment. Experimental protocol was approved by institutional animal ethics committee (IAEC, CVS & AH) before starting the experiment.

Husbandry

The animals were housed in polypropylene cages under control temperature and hygienic conditions in the animal house using sterilised husk as bedding materials. 12 hr of light and dark cycle were maintained through out the experimental period. Animals were provided standard feed (Nutri Lab, rodent feed, Vetcare Pvt. Ltd, Bangalore) and allowed water *ad libitum* (water purification was done by reverse osmosis followed by ultraviolet [UV] treatment).

Chemicals

Bisphenol-A was procured from the Department of Veterinary Pharmacology and Toxicology, Indira Gandhi Krishi Vishwavidyalaya, Raipur, India.

Formulation

Bisphenol-A was formulated using propylene glycol as a vehicle. Bisphenol-A solution was administered directly in stomach by oral gavages with dose volume of 10 ml/kg. Body weights were recorded before administration of BPA. The daily oral administration was continued for 28 days.

Experimental Design

Experimental groups consist of five groups having 6 rats. Rats of group I was kept as negative control and was given only distilled water orally. Rats of group II served as vehicle control and were given propylene glycol. Rats of group III, IV and V were administered BPA, formulated in propylene glycol, at the dose concentration of 5 mg/ml, 20mg/ml and 60mg/ml respectively. Dose rate for group III, group IV and group V were 50, 200 and 600 mg/kg body weight respectively for 28 days.

Body weight

Body weight of all rats were taken on day 0 and at weekly intervals for four weeks (0, 7^{th} 14^{th}, 21^{st} and 28^{th}) on precision weighing balance (Sartorius Quintix 3102-1s Lab Balance, Germany)

Feed Consumption

Feed Consumption of all rats were taken on at weekly intervals for four weeks (7^{th} 14^{th}, 21^{st} and 28^{th}) on precision weighing balance (Sartorius Quintix 3102-1s Lab Balance, Germany)

Organ weight

At the end of the study different organs *viz.* heart, lungs, liver, kidneys, brain, spleen, testes and epididymis were removed carefully and after trimming off fat, organs were weighed over electronic digital balance and then relative

organ weights per Kg were calculated as per following formula.

Statistical analysis

Data were expressed as mean± SE. The results were analysed by one way ANOVA followed by Dunnett's t test.

$$\text{Organ Weight} = \frac{\text{Organ weight}}{\text{Whole body weight}} \times 1000$$

RESULTS AND DISCUSSION

Table 1 illustrates the effect of exposure of rats to BPA on feed consumption. Feed consumption was significantly ($P = 0.01$) reduced in the rats of group III, IV and V from day 7 onwards. The average weekly body weights (g) of rats recorded in different groups have been summarized and presented in Table 2. A dose dependent significant ($P = 0.05$) decrease in body weights were found from day 14 in rats fed BPA.

On 0 day post treatment, body weights (g) of rats of experimental animals were recorded separately. However, at this stage, no significant differences ($P \leq 0.05$) were observed in the body weights of rats in any of the groups. The increase in live body weights were noticed in all the rats of control group. While, all the BPA treated rats in this experiment *viz.*, group III, IV and V showed decreased body weight gain compared to control animal, significantly ($P \leq 0.05$). Highly significant ($P \leq 0.01$) dose dependant reduction in body weights in rats at 21 and 28 days post treatment was observed in group IV and V. Al-Hiyasat *et al.* (2002) also observed decrease in body weight gain when BPA was fed by gavage to male mice for 30 days at doses of 5, 25 and 100 μg/kg/day. Higashihara *et al.* (2007) too recorded dose related reduction in body weight when bisphenol F was administered orally in young adult rats at doses 0, 20, 100 and 500 mg/kg per day for at least 28 days.

Furukawa *et al*. (1994) also reported suppression of body weight gain in both males and females of the high dose groups in a 13 week subchronic toxicity of BPA in male and female B6C3F1 mice. Nunez *et al*. (2001) also conducted an experiment on adult female Sprague Dawley rats by administering BPA at doses 1, 4 or 5 mg/day for 15 days and observed that food consumption was not affected, but body weight gain was reduced at 4 or 5 mg/day. Honma *et al.* (2002) observed lower body weight relative to controls when BPA was injected into pregnant ICR mice at doses of 2 and 20 μg/kg/day.

The effect of subacute exposure of BPA in different doses on liver, lungs, heart, kidneys, brain, spleen, ovary and testes have been shown in Table 3. Subacute toxicity of BPA caused significant ($P < 0.01$) increase in the weights of liver and lungs of rats of group IV and V and significant ($P < 0.05$) increase in liver of group III as compared to the rats of control groups (group I and II). Significant ($P < 0.01$) decrease in the weights of brain, kidneys and spleen of rats of group IV and V and significant ($P < 0.05$) decrease in kidneys and brain of group III as compared to the rats of control groups (group I and II).

The present findings are in agreements with the findings of Woo *et al*. (2007). They conducted a 28 day repeated oral dose toxicity study of nonylphenol in Sprague-Dawley rats and observed hepatic and renal toxicity in both sexes with increase of relative liver and kidney weight. Increased relative weights of lungs might have occured due to severe haemorrhage and congestion in BPA treated rats.

Table 1. Effect of daily oral administration of bisphenol-A on feed consumption (g/day) in rats (n = 6).

Groups	Mean Feed Consumption (g/day/rat) ± SE			
	7 day	**14 day**	**21 day**	**28 day**
Gr I	9.03 ± 0.04	12.03 ± 0.07	17 ± 0.04	19.42 ± 0.07
Gr II	9.29 ± 0.05	12.28 ± 0.04	17.14 ± 0.07	19.46 ± 0.06
Gr III	8.78 ± 0.03	11.25 ± 0.04	13.23 ± 0.06*	15.12 ± 0.04*
Gr IV	7.95 ± 0.04	8.82 ± 0.04*	9.6 ± .04**	10.48 ± 0.03**
Gr V	6.66 ± 0.04	7.14 ± 0.03*	7.5 ± 0.05**	7.72 ± 0.05**

Superscripts may read column wise for comparison of means. (*P=0.05) and (**P=0.01).

Table 2. Effect of daily oral administration of bisphenol-A on body wt. (g) in rats (n = 6).

Groups	Mean Body Weight (g) ± SE				
	0 day	**7 day**	**14 day**	**21 day**	**28 day**
Gr I	67.11 ± 2.83	76.16 ± 2.86	84.38 ± 2.87	92.77 ± 2.28	101.5 ± 2.81
Gr II	66.5 ± 2.86	75 ± 2.90	82.33 ± 2.87	90.38 ± 2.83	98.66 ± 2.86
Gr III	72.11 ± 1.67	77.11 ± 1.61	83.72 ± 1.65	89.55 ± 1.67	95.38 ± 1.61*
Gr IV	69.83 ± 1.17	73.44 ± 1.14	77.66 ±1.14*	82.5 ± 1.13**	87.55 ± 1.14**
Gr V	72.5 ± 1.42	74.61 ± 1.46	77.27 ± 1.51*	80.27 ± 1.5**	83.5 ± 1.53**

Superscripts may read column wise for comparison of means. (*P=0.05) and (**P=0.01)

Table 3. Effect of daily oral administration of bisphenol A on relative organ weights.

Organ Weight	GROUPS				
	Group I	**Group II**	**Group III**	**Group IV**	**Group V**
Liver	35.25 ± 0.53	35.45 ± 0.61	38.25 ±0.57*	39.3 ± 0.5**	40.47 ±0.95**
Brain	12.8 ± 0.48	12.68 ± 0.57	11.08 ± 0.33*	10.13 ± 0.16**	9.7 ± 0.14**
Heart	3.9 ± 0.08	3.91 ± 0.09	4.03 ± 0.17	3.85 ± 0.12	3.77 ± 0.10
Kidney	7.25 ± 0.23	7.15 ± 0.23	6.9 ± 0.19*	6.5 ± 0.08**	6.01 ± 0.09**
Lungs	6.67 ± 0.12	6.65 ± 0.16	6.92 ± 0.12	7.45 ± 0.10**	7.97 ± 0.11**
Spleen	3.008 ± 0.07	2.97 ± 0.09	2.81 ± 0.08	2.52 ± 0.11**	2.18 ± 0.08**
Testes	18.07 ± 0.33	18.13 ± 0.38	17.96 ± 0.40	17.05 ± 0.50	15.84 ± 0.51**
Epididymis	5.34 ± 0.22	5.35 ± 0.28	5.14 ± 0.17	4.88 ± 0.12	4.14 ± 0.08**

Superscripts may read row wise for comparison of means. (*P=0.05) and (**P=0.01).

Kabuto *et al.* (2004) too observed decrease weight in brain, kidney liver and testis when mice were exposed to BPA throughout embryonic/fetal life and during lactation by feeding their pregnant/lactating mothers with BPA at 5 or 10 µg per milliliter of drinking water (approximately 2.5-5 ìg/kg/day).

The increased relative weight in liver was probably due to functional hypertrophy of the smooth endoplasmic reticulum and increased drug metabolizing multi-enzyme complex as suggested by Krishnappa (2001). Al-Hiyasat *et al.* (2002) also reported that if BPA is fed by gavage to male mice for 30 days at doses of 5, 25 and 100 µg/kg/day, it resulted in a decrease in body weight and all organ weights. Weight loss in spleen of this group possibly could be the effect of direct toxicity in the organ that leads to severe depopulation of lymphocyte in periarteriolar sheath and also from the Malpighian corpuscle. Decrease in spleenic weight was reported in cypermethrin intoxication in rats (Varshneya *et al.*, 1992). NTP-CERHR, 2006 too agreed with decreased absolute kidney weight and increased relative lung weights when treated with BPA in rats.

Seki *et al.* (1987) reported significant increase in weights of liver and kidney in d.d-prallethrin toxicity in rats. However, Parker *et al.* (1984) observed increased organ body weight ratio of brain, spleen, heart and testes with liver and kidney in fenvalerate toxicity in rats. Kabuto *et al.* (2004) recorded exposure to bisphenol-A during embryonic/fetal life leading to underdevelopment of the brain and testis in mice.

No significant changes were recorded in the weights of heart of rats in any of the treatment groups.

Significant ($P < 0.01$) decrease was found in the weight of testes and epididymis of rats belonging to group V as compared to rats of control groups. Chitra *et al.* (2003) also observed a significant decrease in the weight of the testis and epididymis in rats treated with BPA as compared to the corresponding group of control animals. Takahashi and Oishi (2003) too observed significantly decreased weights of testes, epididymis, prostate and seminal vesicle in subcutaneous administration of BPA in rats @ 200 mg/kg/day for 4 weeks. Mani *et al.*(2001) also found significant reduction in the weight of testes in fenpropathrin toxicity in rats. The changes observed in organ weight factors in the present study may be due to a direct effect of BPA on organ weights and decreased body weight gain of BPA treated rats.

CONCLUSION

In the present study, as because bisphenol-A was given by oral gavage, it causes anorexia which lead to decreased feed consumption and so on to decreased body weight gain.

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