The Estrogenicity and Reproductive Toxicity by Combined Treatment of Bisphenol A and Benzyl butyl phthalate during Gestation, Lactation Period in Rats

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Abstract

The co-administration of BPA and BBP induced slow weight gain compared with single administration in dams. Also, such mixture induced low neonatal body weights in next generation. The dams treated with BPA and BBP showed significant organ weight changes in liver, spleen exposed during lactational periods. But the dams exposed during lactational periods showed significant organ weight changes not only in liver, spleen but also in kidney, uterus and ovary. The F1 female rats exposed during lactation periods showed significant organ weight changes in liver, spleen, ovary. The F1 male rats showed significant organ weight changes in liver, kidney, epididymis, vesicular glands, prostate. However no clear synergistic effects of BPA and BBP could be found.

Estrogen receptor α expression by BPA and BBP in the uterus(dam, F1 female) and testis(F1 male) were studied. There was no significant different ERα expression pattern between control and treated groups. But ERα expression were increased in F1 male testis and female uterus. F1 male showed distinct ERα expression, especially in the group of lactational combined exposure. Synergistic ERα expression was found by combined treatment of BPA and BBP.

Introduction

Environmental estrogens (xenoestrogens) are a diverse group of chemicals that mimic estrogenic actions. Bisphenol A (BPA), a monomer of plastics used in many consumer products, has estrogenic activity in vitro. Benzyl butyl phthalate (BBP) has been used extensively as a plasticizer in floor tiles, adhesives, synthetic leather and hairspray. BBP is reported to be developmentally toxic in mice and rats. This

study has been focused on both developmental and estrogenic activity of BPA and BBP to the second generation of Sprague-Dawley rats ingested on gestaional or lactational periods.

Materials and Methods

Rats were given BPA and BBP on gestational and lactation periods. Maternal body weight and neonatal body weight were recorded. The rats were killed on day 21 of birth. Reproductive organs of dam and neonate were used by receptor binding assay. The plasma concentrations of BPA and MBeP, one of the major metabolites of BBP were analyzed by HPLC.

Results and Discussion

There was no or a little effects to the maternal body weights treated on gestational and /or lactational periods. However, such treatment increased neonatal body weights slightly. administration during lactation period also induced increase of F1 male body weights. There were no significant changes in maternal organ weight except in relative liver weights of administered on gestational periods. There were significant changes in liver, spleen weights in F1 female rats treated with BPA on gestational periods. In the F1 female rats treated with BPA on lactational periods, there were significant changes in liver, kidney, uteral weights. In F1 male rats, there were significant changes not only in liver, spleen, kidney but also in testis, epididymis, vesicular glands. The prostate was smaller than the control's. BPA 200 ㎍/㎏ induced early recovery of estrus in delivered rats.
There was no significant body weight changes of dams treated BBP 5, 10, 100㎎/㎏ during gestational periods, but significant low body weights were shown in high treated groups during gestational day after 12. Neonatal body weights were decreased significantly in the group of 100㎎/㎏. Lactational exposure of BBP caused significant low neonatal body weights. The kidney weight and liver weight of treated dams showed significant changes compared with control group. The F1 female rats showed significant organ weight changes in liver, spleen, ovary, uterus exposed on lactational periods. The F1 male rats showed significant organ weight changes in testis, epididymis, vesicular glands, prostate exposed on gestational periods. BBP 5㎎/㎏ or 10㎎/㎏ induced early recovery of estrus in fostering dams.

Conclusion

There was no effects on the body weights changes of dams and neonates treated with low dose of BPA and/ or BBP. But, medium and high dose of treatment showed body weight gain retardation. The lactation exposure induced significant changes on relative organ weight. BPA and /or BBP induced early recovery of estrus cycle in fostering dams. This study could not find any evidences of synergistic effects on BPA and/or BBP combined administration on dams and their fetuses, except in ERα expression of F1 male.

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