Montreal Protocol set world-wide goals in January 1996 to reduce the use of chlorofluorocarbons (CFCs) and ultimately eliminate all CFC use\(^3\). This restriction has advanced the urgent development of alternative chemicals. Recently, in a Korean electronic factory, male and female workers exposed to 2-bromopropane (2-BP), which does not seem to affect the stratospheric ozone and is therefore used as an alternative solvent in open systems instead of CFCs, had potential hematopoietic and reproductive disorders\(^2\). Several experimental studies also indicate that 2-BP exhibits reproductive and hematopoietic toxicity\(^3\), but there are very few data containing information on the teratogenicity of 2-BP, although Lim \textit{et al.}\(^4\) showed a decrease in the number of rat pups born and no teratogenic effects after maternal treatment with 2-BP during pre-organogenesis, which is not a critical stage in organogenesis. Therefore, in the present study, we examined the potential teratogenicity of 2-BP in more detail by injecting it on day 10 of gestation (DG 10), at the late period of organogenesis of fetuses, and observing them at nearterm. This study is the first to examine whether 2-BP has teratogenic effects on rodent fetuses after maternal treatment late in organogenesis of fetuses.

Materials and Methods

Virgin female mice of the randombred Jcl: ICR strain (CLEA Japan Co.), 10 to 14 wk old, weighing at least 30 g, were maintained on a 12-h light/dark cycle at 20–24°C and 60–70% relative humidity. The mice were fed a standard granulated breeding diet, and water was supplied \textit{ad libitum}. Animal care was done in accordance with the Guidelines for Animal Experiments of Mie University School of Medicine, Japan.

Key words: 2-Bromopropane, Teratogenicity, Intrapertioneal, Mid-gestation

Short Communication

Analysis of Teratogenic Effects of Maternal Treatment with 2-Bromopropane in Mice

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Key words: 2-Bromopropane, Teratogenicity, Intrapertioneal, Mid-gestation

Results

Table 1 compares the pregnancy outcomes in control and 2-BP treated groups. The number of corpora lutea, implantation sites, the incidence of dead fetuses and resorptions and the mean fetal body weight did not differ among the groups. Table 1 also summarizes the results of the teratological analysis. The incidence of malformations was slightly higher in the 600 mg/kg, 900 mg/kg, and 1,800 mg/kg treated groups than in the control group, but no significant difference was detected among the groups. Table 1 also summarizes the results of the teratological analysis. The incidence of malformations was slightly higher in the 600 mg/kg, 900 mg/kg, and 1,800 mg/kg treated groups than in the control group, but no significant difference was detected among the groups. Table 1 also summarizes the results of the teratological analysis. The incidence of malformations was slightly higher in the 600 mg/kg, 900 mg/kg, and 1,800 mg/kg treated groups than in the control group, but no significant difference was detected between the groups (p=0.49 by one-way ANOVA). Skeletal analysis of the fetuses revealed no malformations in any group. The incidence of malformations was slightly higher in the 600 mg/kg, 900 mg/kg, and 1,800 mg/kg treated groups than in the control group, but no significant difference was detected between the groups (p=0.49 by one-way ANOVA).

Discussion

The present study is the first to examine whether there are teratogenic effects of 2-BP after maternal treatment in the period of organogenesis in mice. Previously, Lim \textit{et al.}\(^4\) showed that 2-BP induced a decrease in the number of rat pups born and had no teratogenic effects after maternal treatment from 14 d before mating to 7 d after mating. Unlike their method, we used a single injection
in the period of organogenesis of mouse fetuses with similar 2-BP doses to theirs.

The epidemiological study by the Korea Industry Safety Corporation did not refer to any toxic effects of 2-BP on embryos in female workers who might have been exposed to a cleaning solvent containing 2-BP during gestation\(^2\). Although it was reported that one pregnant woman who had been exposed to 2-BP had delivered a normal full-term baby, it was not known whether the woman had been exposed to 2-BP before conception or during gestation\(^9\). Although it is difficult to ensure the teratogenicity of 2-BP in humans from these series of studies, Khattak \textit{et al.}\(^10\) showed that in their prospective controlled study occupational exposure to organic solvents during pregnancy is strongly associated with an increased risk of fetal malformations in humans. And in the present study, several fetuses with cleft palate were observed in the treated groups. And the incidence of this type of malformation was highest among all malformations. It may be related to 2-BP treatment in the critical period for cleft palate. Some human epidemiological studies reveal a significant association between oral clefts and maternal exposure to organic solvents\(^11\). The monitoring of 2-BP in occupational settings and more extensive surveys of this chemical’s teratogenesis should be carried out.

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\textbf{References}

4) CH Lim, SH Maeng, JY Lee, YH Chung, TG Kim, JH Park, YH Moon and IJ Yu: Effects of 2-bromopropane on the female reproductive function in Sprague-Dawley

\begin{table}[h]
\centering
\caption{Reproductive effects, external malformations and skeletal variations produced by 2-BP}
\begin{tabular}{|l|c|c|c|c|c|}
\hline
Group & control & 300 mg/kg & 600 mg/kg & 900 mg/kg & 1,800 mg/kg \\
\hline
No. of pregnant dams & 14 & 15 & 15 & 16 & 18 \\
No. of dead dams & 0 & 0 & 0 & 0 & 1 \\
No. of corpora lutea & 15.5 ± 0.56 & 16.3 ± 0.50 & 15.5 ± 0.56 & 15.1 ± 0.55 & 16.0 ± 0.38 \\
No. of implantation sites & 14.4 ± 0.65 & 15.9 ± 0.55 & 14.6 ± 0.52 & 13.6 ± 0.75 & 15.4 ± 0.45 \\
% of dead fetuses & 0.48 & 0.81 & 0 & 0.42 & 0.45 \\
% of resorbed fetuses & 8.79 & 5.01 & 4.95 & 10.18 & 11.42 \\
Fetal weight (g) & \\
Male & 1.20 ± 0.03 & 1.16 ± 0.03 & 1.14 ± 0.03 & 1.19 ± 0.03 & 1.18 ± 0.02 \\
Female & 1.15 ± 0.03 & 1.10 ± 0.02 & 1.09 ± 0.03 & 1.12 ± 0.03 & 1.12 ± 0.03 \\
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