Brief Report

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Toxic effects of low doses of methyl-tertiary butyl ether on hematological indices in the male rats

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Abstract

Methyl-tertiary butyl ether (MTBE), as a fuel additive is added to reformulated gasoline to enhance octane number and air quality. The aim of this study was to investigate the effect(s) of low doses of MTBE on some hematological indices in the male rats. In this study, two separate experiments (A and B) were conducted. In experiment A, the rats were randomly divided into 2 equal (n=5) groups that received 0 and 10 mg MTBE/kg/day in tap water by gavage for 28 consecutive days. In experiment B, animals were assigned into two equal groups (n=5) that received 0 and 1 mg MTBE/kg/day for 10 consecutive days. At the end of the exposure period, the white blood cell count (WBC), red blood cell (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and platelet count (PLT) were determined. Statistical analysis revealed that, there was a significant alteration in MCHC between control and treatment groups ($P<0.05$) in experiment A. No changes were observed for the other blood parameters. Also, in experiment B, the means of WBC, MCH and MCHC showed significant differences between groups ($P<0.05$).In conclusion, the present study showed that exposure to low and very low levels of MTBE can alter some hematological indices in the male rats.

Keywords: Hematological indices, Methyl tertiary butyl ether (MTBE), Rat.

1. Introduction

Methyl-tertiary butyl ether (MTBE), as a fuel additive is added to reformulated gasoline to enhance octane number and air quality by decreasing vehicle tailpipe exhaust emissions. According to the physicochemical properties' of MTBE, it can penetrate faster to the groundwater resources than other gasoline components (1). So, the possible adverse effects of MTBE is a public concern. Due to the human risk potential of MTBE in contaminated water resources and air, its use was banned in the USA in 2005. However it is still used in some Middle East countries such as Iran. Several animal studies (2-4) have shown the carcinogenicity of MTBE and the American Conference of Governmental Industrial Hygienists, has listed MTBE as a "Confirmed animal carcinogen with unknown relevance to human" (5).

MTBE is absorbed immediately into the bloodstream upon entering the body, then it is metabolized in the liver by cytochrome P-450 isoenzymes (6, 7). Existing studies mainly have been conducted to investigate the effect(s) of high levels of MTBE on liver function (7-9), reproductive system (10, 11), activity and expression of genes involved detoxification (12-14). There is a little information about the effect of high levels of MTBE on blood parameters (9, 15, 16). It should be noted that the results of these studies are inconsistent.

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In public places, people are usually exposed to low or very low concentrations of MTBE (1). Based on our knowledge, there is no publication investigating the effect(s) of low levels of MTBE on hematological indices. Therefore, the current study was carried out.

2. Materials and methods

2.1. Animals and experimental design

Male Wistar rats, weighing 180-200 g, 9 weeks old, were purchased from the animal house of Shiraz University of Medical Sciences. MTBE (CAS No. 1634- 04-4, 98.8% of purity) was obtained from Shiraz Oil Refinery (Iran). Animals were housed in plastic cages under standard animal room conditions with a 12 hr light/dark cycle at temperature of 25±2 °C, received standard pellet food, and tap water was available ad libitum. In this study, two separate experiments (A and B) were conducted. In experiment A, rats were randomly divided into 2 equal (n=5) groups that received 0 and 10 mg MTBE/kg/day in tap water by gavage for 28 consecutive days. In experiment B, animals were assigned into two equal groups (n=5) that received 0 and 1 mg MTBE/kg/day for 10 consecutive days. All experimental animals were adapted for 10 days. Body weights and food consumption were measured every two days. None of the animals died during experiment period. This research was approved by Ethics committee of Shiraz University. This study is carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving animal experiments.

2.2. Measurements

At the end of the exposure period, experimental animals were sacrificed under ether anesthesia and blood samples were collected from heart. The white blood cell count (WBC), red blood cell (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and platelet count (PLT) were determined with the aid of an automatic hematology analyzer (Mindray Hematology analyzer, BC-2300

2.3. Statistical Analysis

Data were presented as the mean ± standard error (SE). Effects of MTBE on the mean of hematological indices were investigated using Analysis of Variance (ANOVA) followed by Duncan post hoc. Statistical analysis was performed using SPSS statistical software package (version 11.5) for windows (SPSS Inc., Chicago, IL, USA). In all cases, $P<0.05$ was considered significant.

3. Results

Table 1 shows results of low doses of MTBE on hematological indices after 28 and 10 days exposure. Statistical analysis revealed that in experiment A, there was significant alteration in MCHC between control and treatment groups ($P<0.05$). No changes were observed for the other blood parameters. In experiment B, the means of WBC and MCHC were significantly lower in experimental group compared to control ($P<0.05$).

Table 1. Effect of MTBE on some hematological indices in the male rats

Parameters	Control	MTBE concentration	
		10 mg/kg/day (28 day)	1 mg/kg/day (10 day)
WBC (10^6/L)	15000±2284	11480±1529	6560±559*
RBC (10^{12}/L)	8.62 ±0.24	8.74±0.19	8.51±0.32
HGB (g/dL)	16.0±0.32	16.02±0.28	16.4±0.45
HCT (%)	50.7±1.11	52.8±1.10	53.7±1.08
MCV(fL)	58.8±0.71	60.5±0.90	63.2±1.18*
MCH (Pg)	18.6±0.31	18.3±0.25	19.3±0.39
MCHC (%)	31.6±0.22	30.4±0.30*	30.5±0.29*
PLT (10^9L)	955±40.0	899±42.0	991±38

On the other hand, the means of MCV was significantly increased in treatment vs control (P<0.05).

4. Discussion

Few data with inconsistent results are available which has investigated the association of high levels of MTBE and hematological indicators. For example in one study (9), elevation of HGB was reported after exposure to oral MTBE. On the other hand, in another study (16) reduction of HGB was reported following MTBE administration. In the previous study, we did not observe any significant alteration for hematological indices after high doses (400, 800 and 1600 mg/kg) of MTBE exposure by gavage during 30 days (8). Very interestingly, here we observed that in low and very low concentrations of MTBE (10 and 1 mg/kg/day), some blood parameters (WBC, MCV, MCHC) were significantly changed in treatment group compared to the control (P<0.05). This finding is largely consistent with the results of the gene expression in our previous publication (18). It should be mentioned that some other chemicals such as lead, radon, airborne particles, asbestos, tobacco, and benzene are proportionately more toxic at the lowest levels of exposure (19, 20).

5. Conclusion

According to the results of the present study combined with our other publications (18), we found that exposure to low and very low levels of MTBE could significantly alter GSTs expression and some hematological indices. Since the most people are usually exposed to low and very low amounts of MTBE, further studies are needed to clarify this finding and plan for public health programs.

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Conflict of Interest

None declared.

6. References

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