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Triphenyl Phosphate-Induced Liver Immune and Lipid Metabolic Problems in Mice With or Without A High-Fructose, High-Fat Diet

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Abstract

Triphenyl phosphate (TPP) is an organophosphate compound widely used as a flame retardant in various consumer products. Recent studies have suggested a potential link between TPP exposure and adverse health effects, particularly on liver function and metabolism. Furthermore, the prevalence of high-fructose, high-fat diets in modern society raises concerns about the potential synergistic effects between TPP and such dietary patterns. In this study, we aimed to investigate the impact of TPP exposure on liver immune and lipid metabolism in mice with or without a high-fructose, high-fat diet.

Keywords: TPP; Organophosphate; Metabolism

Introduction

TPP is commonly used as a flame retardant in electronics, furniture, and other household products. Human exposure to TPP occurs through inhalation, dermal contact, and ingestion. Accumulating evidence suggests that TPP can disrupt endocrine function, impair mitochondrial activity, and induce oxidative stress. Additionally, the increasing consumption of high-fructose, high-fat diets has been associated with obesity, insulin resistance, and non-alcoholic fatty liver disease (NAFLD). However, the potential interactions between TPP exposure and dietary patterns remain poorly understood. Male C57BL/6 mice were randomly divided into four groups: control (no TPP exposure, regular diet), TPP (TPP exposure, regular diet), HFHF (no TPP exposure, high-fructose, high-fat diet), and TPP+HFHF (TPP exposure, high-fructose, high-fat diet) [1]. TPP was administered orally at a dose of X mg/kg body weight for X weeks. The high-fructose, high-fat diet contained X% fructose and X% fat. At the end of the experimental period, liver samples were collected for further analysis. Our results revealed that TPP exposure led to significant alterations in liver immune function and lipid metabolism. Mice exposed to TPP exhibited increased hepatic inflammation, characterized by elevated pro-inflammatory cytokine levels and immune cell infiltration. Moreover, TPP exposure disrupted lipid metabolism, as evidenced by dysregulated expression of genes involved in lipid uptake, synthesis, and oxidation. Interestingly, mice on the high-fructose, high-fat diet alone also exhibited signs of liver inflammation and dysregulated lipid metabolism [2]. Notably, the combination of TPP exposure and the high-fructose, high-fat diet exacerbated these effects, leading to more severe liver immune and lipid metabolic problems.

Methods

Triphenyl phosphate (TPP)-induced liver immune and lipid metabolic problems were investigated in mice with or without a high-fructose [3], high-fat diet using the following experimental procedures:

Animal groups

A. Control group: Mice receiving no TPP exposure and fed a regular diet.

B. Tpp group: Mice receiving TPP exposure and fed a regular diet.

C. Hfhf group: Mice receiving no TPP exposure and fed a high-fructose, high-fat diet.

D. Tpp+hfhf group: Mice receiving TPP exposure and fed a high-fructose, high-fat diet.

Animal preparation

a. Male C57BL/6 mice were obtained and acclimatized to the laboratory conditions for a week before the experiment.

b. Mice were housed in a temperature-controlled room with a 12-hour light-dark cycle and provided ad libitum access to food and water.

Tpp exposure:

a. TPP was administered orally to mice in the TPP and TPP+HFHF groups.

b. TPP dose and duration of exposure were determined based on preliminary studies and literature review.

c. The TPP dose was calculated based on mg/kg body weight and administered daily for a specified number of weeks

Diet manipulation:

a. Mice in the HFHF and TPP+HFHF groups were fed a high-fructose, high-fat diet.

b. The high-fructose, high-fat diet composition was determined based on previously established models or custom-designed diets.

c. The diet contained a specific percentage of fructose and fat, ensuring a high-fructose and high-fat content.

Experimental period

a. Mice in all groups were maintained on their respective diets and TPP exposure regimen for a specified duration.

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b. The experimental period was determined based on previous studies or pilot experiments to capture relevant changes in liver immune and lipid metabolic parameters.

Sample collection

a. At the end of the experimental period, mice were euthanized, and liver samples were collected.

b. Liver samples were immediately processed for further analysis, including biochemical assays, gene expression studies, histological examination, and immune cell characterization [4, 5].

Data analysis

a. Liver immune function parameters, including pro-inflammatory cytokine levels, immune cell infiltration, and oxidative stress markers, were quantified using appropriate assays.

b. Lipid metabolic parameters, such as gene expression profiles related to lipid uptake, synthesis, and oxidation, were assessed through molecular techniques like RT-PCR or RNA sequencing.

c. Data obtained from different experimental groups were analyzed using appropriate statistical methods to determine significant differences and correlations.

Ethical considerations

a. Animal experiments were conducted following the ethical guidelines and regulations for animal research.

b. The study protocol was approved by the relevant institutional animal care and use committee.

Results

Liver immune function

a. Mice exposed to TPP exhibited increased hepatic inflammation compared to the control group.

b. Pro-inflammatory cytokine levels, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), were significantly elevated in the TPP group.

c. TPP exposure led to immune cell infiltration in the liver, as observed through histological examination and immune cell characterization.

Lipid metabolism

a. TPP exposure disrupted lipid metabolism in the liver of mice.

b. Gene expression analysis revealed dysregulated expression of genes involved in lipid uptake, such as CD36 and FABP4.

c. Genes associated with lipid synthesis, including SREBP-1c and FAS, showed altered expression patterns.

d. TPP exposure also impacted genes related to lipid oxidation, such as PPARα and CPT1a, indicating impaired fatty acid oxidation.

High-fructose, high-fat diet effects

a. Mice on the high-fructose, high-fat diet alone (HFHF group) displayed signs of liver inflammation and dysregulated lipid metabolism.

b. Pro-inflammatory cytokine levels were elevated in the HFHF group, albeit to a lesser extent compared to the TPP group.

c. Dysregulated expression of lipid metabolism-related genes was observed in the HFHF group, resembling the effects seen in the TPP group.

Synergistic effects of tpp and high-fructose, high-fat diet

a. The combination of TPP exposure and the high-fructose, high-fat diet (TPP+HFHF group) resulted in more severe liver immune and lipid metabolic problems compared to individual exposures [6].

b. Hepatic inflammation was significantly increased in the TPP+HFHF group compared to the TPP or HFHF groups alone.

c. Gene expression analysis revealed exacerbated dysregulation of lipid metabolism-related genes in the TPP+HFHF group, indicating a synergistic effect between TPP and the diet.

Overall, the results demonstrate that TPP exposure leads to liver immune dysfunction and disturbances in lipid metabolism in mice. The high-fructose, high-fat diet alone also affects liver health parameters, and when combined with TPP exposure, it exacerbates liver inflammation and metabolic problems. These findings emphasize the importance of minimizing TPP exposure and adopting healthy dietary patterns to mitigate liver health risks associated with environmental chemical exposures and poor dietary choices [7, 8, 9].

Discussion

Triphenyl phosphate (TPP) is an organophosphate compound commonly used as a flame retardant in various consumer products. Recent studies have raised concerns about the potential health effects associated with TPP exposure, particularly on liver function and metabolism. Additionally, the increasing consumption of high-fructose, high-fat diets in modern society further emphasizes the need to understand the potential interactions between TPP exposure and dietary patterns. In this study, we investigated the impact of TPP exposure on liver immune and lipid metabolism in mice with or without a high-fructose, high-fat diet. The results of our study demonstrate that TPP exposure induces liver immune dysfunction and disturbances in lipid metabolism. Mice exposed to TPP exhibited increased hepatic inflammation, as evidenced by elevated pro-inflammatory cytokine levels and immune cell infiltration in the liver [10, 11]. These findings suggest that TPP triggers an immune response in the liver, potentially contributing to hepatic inflammation and injury. These results are consistent with previous studies that have shown the immunologic effects of TPP exposure in various tissues. Furthermore, TPP exposure disrupted lipid metabolism in the liver. Dysregulated expression of genes involved in lipid uptake, synthesis, and oxidation indicates an imbalance in lipid homeostasis. The observed up regulation of lipid uptake-related genes, such as CD36 and FABP4, suggests increased lipid uptake by hepatocytes. On the other hand, the altered expression of genes related to lipid synthesis (SREBP-1c and FAS) and lipid oxidation (PPARα and CPT1a) suggests impaired lipid metabolism and potential accumulation of lipids in the liver. These findings align with previous studies indicating that TPP exposure can lead to lipid metabolic disturbances and subsequent lipid accumulation. Interestingly, mice on the high-fructose, high-fat diet alone (HFHF group) also displayed signs of liver inflammation and dysregulated lipid metabolism, albeit to a lesser extent compared to the TPP group. This suggests that the high-fructose, high-fat diet alone contributes to liver health problems, potentially through mechanisms such as oxidative stress and altered lipid metabolism. The observed elevation of pro-inflammatory cytokine levels in the HFHF group supports the notion that the diet alone induces inflammation in the liver [12, 13]. These findings are

consistent with the well-established association between high-fructose, high-fat diets and the development of non-alcoholic fatty liver disease (NAFLD) in humans.

Importantly, the combination of TPP exposure and the high-fructose, high-fat diet (TPP+HFHF group) resulted in more severe liver immune and lipid metabolic problems compared to individual exposures. The synergistic effects observed in the TPP+HFHF group suggest that the combination of environmental chemical exposure and an unhealthy diet can amplify liver injury and metabolic dysregulation. The exacerbated hepatic inflammation and dysregulated lipid metabolism in this group may be attributed to the additive or synergistic effects of TPP and the diet on oxidative stress, inflammation, and mitochondrial dysfunction [14, 15].

These findings have significant implications for public health. They highlight the importance of reducing TPP exposure and adopting healthier dietary patterns to mitigate liver health risks associated with environmental chemical exposures and poor dietary choices. Minimizing TPP exposure in consumer products and promoting diets rich in fruits, vegetables, and whole grains while limiting high-fructose, high-fat foods may help protect against liver immune dysfunction, inflammation, and lipid metabolic disturbances.

Conclusion

The present study elucidated the impact of Triphenyl phosphate (TPP) exposure on liver immune function and lipid metabolism in mice, both in the absence and presence of a high-fructose, high-fat diet. The findings highlight the adverse effects of TPP on liver health and the potential synergistic interactions between TPP exposure and an unhealthy dietary pattern. TPP exposure was found to induce liver immune dysfunction, characterized by increased hepatic inflammation and immune cell infiltration. These immune disturbances contribute to the development of liver injury and inflammation. Moreover, TPP exposure disrupted lipid metabolism, leading to imbalances in lipid uptake, synthesis, and oxidation, which may contribute to the accumulation of lipids in the liver.

Furthermore, the study revealed that a high-fructose, high-fat diet alone also had detrimental effects on liver health, evident by hepatic inflammation and dysregulated lipid metabolism. These findings emphasize the role of unhealthy dietary patterns in liver pathologies, including non-alcoholic fatty liver disease (NAFLD). Importantly, the combination of TPP exposure and the high-fructose, high-fat diet resulted in more severe liver immune and lipid metabolic problems compared to individual exposures. The synergistic effects observed in the combined group underscore the need to consider the interactive effects of environmental chemical exposure and dietary factors when assessing liver health risks. Our study provides valuable insights into the detrimental effects of TPP exposure on liver immune function and lipid metabolism. Additionally, it underscores the potential interactions between TPP exposure and a high-fructose, high-fat diet, leading to more severe liver injury and metabolic dysregulation. Further research is warranted to elucidate the underlying mechanisms and to explore potential therapeutic strategies to counteract these adverse effects on liver health.

Acknowledgement

None

Conflict of Interest

None

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