## Intraperitoneal injection of thimerosal and aluminum hydroxide causes histological alterations in *Danio rerio*

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Introduction: Thimerosal is a mercury-based compound used in pharmaceutical formulations. Aluminum hydroxide is used as an adjuvant in vaccines. These compounds are used together in vaccine formulations, which makes the study of their toxicity together extremely important. Aim: This study aimed to evaluate the histopathological effects of exposure to thimerosal and aluminum hydroxide (alone or in mixture) on D. rerio. Methods: Fish were divided into four groups (n=30/group) and exposed to the compounds intraperitoneally. The groups were: control (saline), thimerosal (TMS - 7.5 mg/kg), aluminum hydroxide (Al - 175.0 mg/kg), and mixture (TMS+Al - 7.5 mg/kg of TMS + 175.0 mg/kg of Al). Liver, kidney, brain, and muscle were removed 24h, 96h, and 21 days after the exposure for histopathological analysis. Results: Kruskal-Wallis' test revealed a statistically significant increase in the injury index in TMS+Al group in the liver 96h [H(3)=15.16; p<0.0001] and 21 days after the exposure [H(4)=23.33;p<0.0001]. The alterations observed were necrosis and steatosis, respectively. In the kidney, was observed a statistically significant increase in the injury index [H(3)=10.95; p=0.0120] in TMS+Al group 24h after the exposure. Ninety-six hours after exposure revealed an effect of Al (Al and TMS+Al groups) exposure [H (3)=17.63; p=0.0005]. The same was observed after 21 days in the Al (Al and TMS+Al group) [H(4)=28.72; p<0.0001]. Hemorrhage was the main alteration observed in both periods. In muscle a statistically significant increase was observed at 96h [H(3)=16.81; p=0.0008] and 21 days [H(4)=35.19; p<0.0001] after the exposure to TMS (TMS and TMS+Al groups). The main alteration was the increase in intramyofibril space. In the brain, the Kruskal-Wallis' test revealed a statistically significant increase in the injury index 24h [H(3)=8.362; p = 0.0391] and 96h [H(3)=12.08; p = 0.0071] after the exposure in TMS+Al group. The test revealed a statistically significant increase in the injury index after 21 days [H(4)=26.89; p < 0.0001] to both metals (TMS, Al, and TMS + Al group). The main alterations observed in the zebrafish brain were necrosis, leukocyte infiltration, and neuropil disorganization. Conclusion: Exposure to thimerosal and aluminum hydroxide causes histopathological changes in zebrafish organs. Further studies with these compounds together are necessary to better elucidate their mechanisms of action and toxicity.