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Effects of ozone exposure on the oxidative capacity for drug biotransformation in Wistar rats

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The aim of the present study was to determine if ozone (O_3) exposure modifies theoxidative capacity of cytochrome P450 (CYP450) using pharmacokinetic analysis of metronidazole. A total of 84 male Wistar rats were placed in two groups. Group I was subdivided into two subgroups of 30 and 12 rats. The metronidazole pharmacokinetic study was performed on the group of 30 rats, which was in turn divided into two subgroups of 15 rats each, one exposed to 0.15 ppm O_3, the other not exposed (control group). The group of 12 rats was subdivided into two subgroups of 6 rats each; one was exposed to O_3 (0.15 ppm), the other was not exposed (control). Liver microsomes were obtained from these two subgroups for immunodetection of CYP450 families. The same procedure was applied to group II, except for an O_3 concentration of 0.45 ppm. Plasma metronidazole was determined by high performance liquid chromatography. The maximum plasma concentration (Cpmax), area under the curve (AUCo!1), volume of distribution (Vd), and clearance (CL) showed a significant increase in the group exposed to 0.15 ppm O_3 compared to the group exposed to 0.45 ppm. Further, data were significantly increased compared to control. The elimination half-life time ($t_{1/2}$el) in the 0.15 ppm O_3 group was similar to the 0.45 ppm rats, however, these values were significantly decreased compared controls. No statistically significant differences were found among rats in the electrophoretic band pattern for any of the CYP450 families evaluated, 1A, 3A, 2B and 2E. The expression of these subfamilies in hepatic and renal tissue is in agreement with other reports.

Keywords: exposure; ozone; biotransformation; metronidazole; pharmacokinetics