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VARIABILITY ON THE PHARMACOKINETICS OF ALCOHOL; GENDER DIFFERENCES AND INFLUENCE OF DISSOLVED OXYGEN CONCENTRATION IN ALCOHOL
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Ethanol oxidation by the microsomal ethanol oxidizing system requires oxygen for alcohol metabolism, and a higher oxygen uptake increases the rate of ethanol oxidation. We investigated the effect of dissolved oxygen on the pharmacokinetics of alcohol in healthy humans (n = 49). Furthermore, the gender differences in pharmacokinetics and pharmacodynamics were analyzed. The concentrations of dissolved oxygen were 8, 20, and 25 ppm in alcoholic drinks of 240 and 360 ml (19.5% v/v) for investigation of oxygen effect. Blood alcohol concentrations (BACs) were determined by converting breath alcohol concentrations. The high dissolved oxygen groups (20, 25 ppm) reached 0.000% and 0.050% BAC faster than the normal dissolved oxygen groups (8 ppm; p < 0.05). In analyzing pharmacokinetic parameters, AUC inf and K el of the high oxygen groups were lower than in the normal oxygen group, while C max and T max were not significantly affected. After an alcohol 240ml intake, C max and AUC last in women group were presented significantly higher values than those in men group, and volume of distribution in women group was presented significantly lower values than those in man group (p<0.05). In pharmacodynamic study, the decrease of systolic blood pressure inhibition % in women group was presented significantly lower value than that in men group (p<0.05). In conclusion, elevated dissolved oxygen concentrations in alcoholic drinks accelerates the metabolism and elimination of alcohol. Also, the clearance and the pharmacodynamics on blood pressure of alcohol showed significant gender differences.

Key words: alcohol; dissolved oxygen concentration; gender differences; pharmacokinetics; pharmacodynamics.

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CHANGES IN STRUCTURE AND FUNCTION OF TIGHT JUNCTION BY INTESTINAL ISCHEMIA/REPERFUSION
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[Purpose] The structural polarity and function of epithelial tight junctions (TJ) are regulated by apical components of intercellular junctional complexes. Since intestinal ischemia/reperfusion (I/R) leads to changes in structure of TJ, it is important to examine changes in intestinal drug absorption for the appropriate drug therapy during I/R in detail. In the present study, we examined the changes in intestinal mucosal structure, protein expression of claudin family, ZO group, and MPDP, and permeation of paracellular marker.

[Methods] The superior mesenteric vein and artery in rat were occluded by hanging themselves using surgical-sutures connected with the spring balance for 60 min, followed by reperfusion. The intestinal mucosa-to-blood permeability of fluorescein isothiocyanate dextran 4000 (FD-4) was obtained by in situ closed loop method. The mRNA and protein levels of claudin family, ZO group, and MPDP were determined by RT-PCR and Western blot, respectively.

[Results and Discussion] Absorption of FD-4 from ileum was increased at 1 hr and ameliorated at 24 hr after starting reperfusion. All protein levels of TJ components decreased in early phase of reperfusion, and recovered until 24 hour after reperfusion. Especially, a significant correlation was obtained between AUC of plasma FD-4 concentration and expression level of claudin-4. These results indicate that the displacement of TJ proteins such as claudin-4 and MPDP from membrane is induced by reperfusion and this displacement is involved with the increase in absorption of FD-4.