INFLUENCE OF GROWTH AND DEVELOPMENT ON ALDEHYDE OXIDASE ACTIVITY IN NEONATES AND INFANTS

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Aldehyde oxidase (AO) plays an important role in metabolizing antitumor drugs such as methotrexate, cyclophosphamide and ifosfamide. The information of AO activity in individual patients may be a useful parameter for dose adjustment to avoid severe toxicity. Despite the clinical advantage, it is difficult to make a direct evaluation of AO activity in human livers. We have already reported a significant correlation between AO activity and the ratio of nicotinamide and metabolites in the urine of humans and rats. However, there is little information for neonates and infants, who may show different physiological and biochemical features. In the present study, we investigated the influence of the growth and development of children on AO activity. The AO activities in rat liver cytosol were also studied in vitro. Human urine samples were eluted by pressure from ultra-absorbent types of disposable diapers from the healthy children. Rat liver cytosols were obtained from 18-day-old fetuses and young rats. Amounts of $N_1$-ynmethicotinamide (NMN) and its two oxidated metabolites, $N_1$-methyl-2-pyridone-5-carboxamide (M2) and $N_1$-methyl-4-pyridone-5-carboxamide (M4) were determined by using HPLC. The AO activity was expressed as a ratio of $(M2+M4) / (NMN+M2+M4)$. This AO activity was rapidly increased according to the subject’s age in a saturable manner. The AO activity continued to increase until about 2 years of age in children. This fact suggests that the AO activity steeply increases after birth in humans.