Ethanol Consumption Disrupts Mitochondrial Redox Balance in Wistar Rats and Alters Mitochondrial Permeability Transition

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The rates of alcoholism have increased steadily over the last century. Along with this, the cost of treating the associated pathologies has also increased, such that this is now considered a public health concern. Still, the molecular events leading to several of these conditions are yet not clearly understood. Hepatic tissue is the most affected by alcohol, and mitochondria have been suggested to be a crucial target in alcohol-induced liver toxicity. Thus, the aim of our study was to further investigate how ethanol consumption affects redox metabolism and mitochondrial functional integrity in liver. Young and old male adults Wistar rats were given a 25% ethanol solution as the only source of drinking water. Control groups received water only. Liver mitochondria were isolated using standard techniques. Mitochondria from alcohol-drinking rats were more resistant to induction of permeability transition (MPT) by calcium when compared to mitochondria from animals drinking water. This effect was abrogated in presence of agents that oxidize pyridine nucleotides (oxaloacetate and diamide), suggesting that mitochondria from the alcohol group had higher levels of reduced pyridine nucleotides. Similarly, calcium uptake by isolated mitochondria, which is also related to intramitochondrial redox state, was higher in the alcohol group. Reactive oxygen species production, monitored spectrofluorimetrically using AmplexRed® and H2DCF-DA, showed no differences between the control and alcohol groups. Our results suggest that liver mitochondria from acute and chronic alcohol-drinking rats have a more reduced pyridine nucleotide pool, likely reflecting an adaptative mechanism which may involve upregulation of antioxidant systems. Experiments to test this hypothesis are underway.

Key words: Alcohol, Mitochondria, Mitochondrial Permeability Transition, Oxidative Stress, Redox Metabolism.