A sucrose-rich diet induces mutations in the rat colon

A sucrose-rich diet has repeatedly been observed to have cocarcinogenic actions in the colon and liver of rats and to increase the number of aberrant crypt foci in rat colon. To investigate whether sucrose-rich diets might directly increase the genotoxic response in the rat colon or liver, we have added sucrose to the diet of Big Blue rats, a strain of Fischer rats carrying 40 copies of the lambda-phage on chromosome 4. Dietary sucrose was provided to the rats for 3 weeks at four dose levels including the background level in the purified diet [3.4% (control), 6.9%, 13.8%, or 34.5%] without affecting the overall energy and carbohydrate intake. We observed a dose-dependent increase in the mutation frequency at the cII site in the colonic mucosa with increased sucrose levels, reaching a 129% increase at the highest dose level. This would indicate a direct or indirect genotoxic effect of a sucrose-rich diet. No significant increase in mutations was observed in the liver. To seek an explanation for this finding, a variety of parameters were examined representing different mechanisms, including increased oxidative stress, changes in oxidative defense, effects on DNA repair, or changes in the background levels of DNA adducts.Sucrose did not increase the number of DNA strand breaks or oxidized bases assessed as endonuclease III-sensitive sites or 8-oxodeoxyguanosine in colon or liver. DNA repair capacity as determined by expression of the rERCC1 or rOGG1 genes was not increased in colon or liver, but the background level of DNA adducts (1-compounds) as determined by P-32 postlabeling was significantly decreased in colon. This decrease in colon 1-compounds correlated inversely with both mutation frequency and ERCC1 DNA repair gene expression. Dietary sucrose did not change liver apoptosis or cell turnover as determined by the terminal deoxynucleotidyl transferase-mediated biotinylated deoxyuridine triphosphate nick end labeling assay and proliferating cell nuclear antigen. An increase in liver ascorbate was also observed, whereas oxidative damage was not observed in proteins or lipids in liver cytosol or in blood plasma. We conclude that a sucrose-rich diet directly or indirectly increases the mutation frequency in rat colon in a dose-dependent manner and concomitantly decreases the level of background DNA adducts, without a direct effect on the expression of major DNA repair enzyme systems. We also conclude that an oxidative mechanism for this effect of sucrose is unlikely. This is the first demonstration of a genotoxic action of increased dietary sucrose in vivo. Both sucrose intake and colon cancer rates are high in the Western world, and our present results call for an examination of a possible direct relationship between the two.

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