CHEMOPREVENTIVE EFFECT OF GRAPE JUICE ON NF-KAPPA B, INOS AND TNFα IN WISTAR RATS AFTER COLON CARCINOGENESIS INDUCED BY AZOXIMETHANE

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Background: Introduction: Colorectal cancer is the third cause of cancer in the world. The intake of foods with chemopreventive properties may decrease the incidence and the risk of recurrence. Aim: to evaluate the effects of grape juice in colon carcinogenesis induced by azoximethane, in Wistar rats by counting the number of aberrant crypt and the RNA expression of NF-kappa B (NF-kB), iNOS and TNFα.

Methods: 40 male Wistar rats aged 8 and 9 weeks were distributed in 7 groups; G1 (n = 6): control; G2 (n = 5): received 15mg/kg AOM; G3 (n = 6): grape juice intake 1% two weeks before the AOM; G4 (n = 6): 2% grape juice intake two weeks before the AOM; G5 (n = 6): grape juice 1% intake four weeks after AOM; G6 (n = 6): intake grape juice 2% four weeks after AOM; G7 (n = 5): intake 2% grape juice without AOM. In experimental surgery the colon was removed to analysis of aberrant crypt foci (ACF’s). The RNA expression of NF-kappa B, TNF-α and iNOS was evaluated by RT-PCR and qPCR.

Results: FCAs were not found in G1 and G7. G2 had an increase number of crypts per focus compared to G4 (p = 0.004). G4 showed a smaller number of crypts per focus compared to G5 (p = 0.009) and G6 (p = 0.026). Regarding the crypts of smaller size (1-3), G4 showed a higher amount of crypts in relation to G2, G5 and G6 (p = 0.009, p = 0.009 and p = 0.041, respectively). The RNA expression of iNOS and TNFα were not different between the groups. The RNA expression of NF-Kb were decreased in animals of the groups G3 and G4 compared to group G2 (p = 0.004 and p = 0.002, respectively). A positive correlation has been found between the gene expression of TNF-α and NF-Kb (p = 0.002).

Conclusion: The administration of 2% grape juice before the induction of carcinogenesis with AOM did not interfere in the formation of FCAs, but reduced its multiplicity, exerting a decrease effect on carcinogenesis. A reduced expression of NF-kappa B occurred in animals that were exposed longer to grape juice, regardless of its concentration, 1% or 2%. Decreased signaling pathway of NF-kappa B can be one approach to the study chemopreventive and chemotherapeutic agents such as grape juice concentrate. Study supported by Sao Paulo Research Foundation n 11/07317-4.