S30. Development of Chemoprevention Clinical Trials: Recent Findings in the Colon

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Many candidate chemopreventive agents are now being studied in clinical trials to inhibit neoplasia. In an earlier period it was very difficult to analyze chemopreventive agent effects in humans, because large numbers of subjects had to be studied for long durations measuring tumor occurrence as an endpoint. However, the introduction of early and late-stage biomarkers into human clinical trials made it possible to study chemopreventive agents in several stages; this has expanded human studies in the chemoprevention field enabling investigators to analyze mechanisms and antitumor effects of numerous chemopreventive compounds in many organ sites.

With this multistage approach, the first candidate chemopreventive agent to be studied for colon cancer prevention was supplemental dietary calcium. In short-term studies, increasing dietary calcium demonstrated decreased hyperproliferation of colonic epithelial cells in most human studies, increased cell differentiation, and decreased fecal water cytotoxicity. Because of early positive results the late-stage biomarker of adenoma-recurrence was then studied in larger randomized clinical trials of longer duration; this recently demonstrated both a significant reduction in benign adenoma recurrence in the human colon, and a trend to adenoma reduction with increased calcium intake.

With this multistage approach to human cancer chemoprevention clinical trials, it has been feasible to begin studying many other classes of chemopreventive agents in human subjects. Newer clinical trials have ranged from modified diets with increased folic acid, fiber, fruit and vegetables, to others that administer pharmaceutical compounds with antiinflammatory properties (eg sulindac, piroxicam, aspirin, selective Cox-2 inhibitors, ASA derivatives), or anti pro 1 if eratives (eg vitamin D, DFMO, ursodiol). Some beneficial results have been noted together with suggestions of long-term adverse effects of some agents, and compounds with minimal toxicity and some activity may prove to be most useful when used over long durations in human populations.

References

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