PEG – polietilenoglicol e câncer

Cytostatic effect of polyethylene glycol on human colonic adenocarcinoma cells.

Laboratoire des XénoBiotiques, Institut de la Recherche Agronomique, Toulouse, France.

Polyethylene glycol (PEG 8000) is a potent cancer chemopreventive agent. This osmotic laxative polymer markedly suppresses colon cancer in rats. To explain the mechanism, we have tested in the in vitro effect of PEG on four human cell lines. Two poorly differentiated adenocarcinoma lines (HT29 and COLO205), a fetal mucosa line (FHC) and a differentiated line (post-confluent Caco-2) were incubated with various PEG concentrations for 2-5 days. Results show that PEG markedly and dose-dependently inhibited HT29 and COLO205 cell growth. This cytostatic effect was associated with a blocking of the cell cycle in G0/G1 phase. In addition, PEG decreased the viability of HT29 and COLO205 adenocarcinoma cells. In contrast, post-confluent intestinal-like Caco-2 cells and normal FHC cells were, respectively, not or little affected by PEG. Moreover, the lactate concentration increased twofold in the medium of PEG-treated HT29 cells compared with untreated cells. Microscopic observations showed that PEG induced cell shrinking, membrane blebbing and the condensation of nuclear chromatin. However, because no DNA ladder and no annexin staining were detected, we presume that PEG did not induce apoptosis. PEG increased the osmotic pressure of the culture medium. Hypersmotic media with added NaCl or sorbitol also inhibited HT29 cell growth, and increased lactate release. These results suggest that PEG may be selectively cytostatic for proliferating cancer cells. This growth inhibition may be due to the high osmotic pressure induced by PEG in vitro. Because the osmotic pressure is higher in feces of PEG-fed rats, it may explain the suppression of colon carcinogenesis by PEG. Copyright 2001 Wiley-Liss, Inc.

PMID: 11279607

Polyethylene glycol induces apoptosis in HT-29 cells: potential mechanism for chemoprevention of colon cancer.

Section of Gastroenterology/Hepatology, Department of Internal Medicine, University of Nebraska Medical Center/Eppley Institute for Research into Cancer and Allied Diseases, 982000 Nebraska Medical Center, Omaha, NE 68198-2000, USA. hroy@unmc.edu

Recent experimental evidence suggests that polyethylene glycol (PEG) is a highly effective chemopreventive agent against colon cancer; however, the mechanism(s) remain largely unexplored. To further elucidate this issue, we evaluated the effect of PEG on two human colon cancer cell lines. PEG treatment resulted in a dose- and time-dependent reduction in cell number without alteration in markers of cell proliferation. However, there was a dramatic and specific, concentration-dependent induction of apoptosis, with 50 mM PEG rendering approximately half the cells apoptotic. This corresponded with a 17-fold induction in the expression of the pro-apoptotic protein, prostate apoptosis response-4. Our data suggest that induction of apoptosis may be responsible, at least in part, for the ability of PEG to prevent experimental colon cancer.

PMID: 11356199

Restoration by polyethylene glycol of characteristics of intestinal differentiation in subpopulations of the human colonic adenocarcinoma cell line HT29.

Laboratoire de Biologie et de Physiologie des Cellules Digestives (U239 I.N.S.E.R.M.), Faculté X. Bichat, Paris, France.

The human colon cancer cell line HT29 is morphologically undifferentiated in standard culture conditions. The cells were incubated for 30 s in polyethylene glycol (27%, v/v), then washed, and refed with standard medium. In these conditions of treatment, polyethylene glycol was unable to induce a significant cell multinucleation. Three wk after the treatment, circular "flat-foci" developed in the culture, which consisted of circular monolayers of polarized cells. These subpopulations were isolated, then grown as independent lines (lines 27, 28, 30, and 31) in standard culture conditions, and characterized. Two types of differentiated cells were present in these lines, namely, enterocytic cells and mucus-secreting goblet cells. These characteristics of intestinal differentiation were found to be stable during the long-term culture of these lines in standard medium. We were able to isolate from line 27 a clonal derivative (C1.27H) exhibiting 2 lineages of differentiation, as assessed by electron microscopy, immunofluorescence, and immunoblot analysis of cell membranes with anti-sucrase-isomaltase antibodies, and enzyme activities. Sucrase-isomaltase was present in two forms, namely, the high-molecular-weight precursor and the cleaved subunits. Finally, the C1.27H cells were found to be significantly less tumorigenic than the parental HT29 cells in both in vitro and in vivo tumorigenicity tests. This stably differentiated cell clone could represent the cancer derivative of the normal stem cells of the intestinal crypt. It is therefore a possible model system for the study of intestinal cell differentiation.

PMID: 3281752

Polyethylene glycol and prevalence of colorectal adenomas.

Gastroentérologie, Hôpital Trousseau, CHRU de Tours. dorval@med.univ-tours.fr <dorval@med.univ-tours.fr>

BACKGROUND AND AIM: Dietary polyethylene glycol (PEG) is extraordinarily potent in the chemoprevention of experimental colon carcinogenesis. PEG is used to treat constipation in France and in the USA. French laxatives include Forlax (PEG4000), Movicol and Transipeg (PEG3350), and Idrocol (pluronic F68). This study tests the hypothesis that use of a PEG-based laxative might reduce the prevalence of colorectal tumors. METHODS: In this population-based study, consecutive patients attending for routine total colonoscopy were enrolled during four months by the gastroenterologists of Indre-et-Loire. They were asked if they had previously taken a laxative or a NSAID. Age, gender, previous polyps, family history of colorectal cancer, constipation, digestive symptoms were also recorded. Tumors found during colonoscopy were categorized histologically. RESULTS: Records from 1165 patients fulfilled the inclusion criteria, 607 women and 498 men, mean age 58.3. Among those, 813 had no tumor, 329 had adenomas, and 23 had carcinomas. In a univariate analysis, older age, male gender, lack of digestive symptoms, and previous polyps were more common in patients with colorectal tumors. In contrast, previous Forlax intake was more common in tumor-free patients (odds ratio (OR) any use/no use, 0.52; 95% confidence interval, 0.27-0.94). More people used Forlax, which contains a higher dose of PEG than the other PEG-laxatives, whose ORs were smaller than 1, but did not reach significance. In multivariate analysis, older age and male gender were associated with higher risk, and NSAIDs use with lower risk, of colorectal tumors. CONCLUSION: Forlax users had a halved risk of
Colorectal tumors in univariate analysis, which suggests that PEG may prevent carcinogenesis.

PMID: 17075478

Induction of multinucleated cells and apoptosis in the PC-3 prostate cancer cell line by low concentrations of polyethylene glycol 1000.


Biochemistry Division, National Cancer Center Research Institute, 5-1-1, Tsukiji, Chuo-ku, Tokyo 104-0045, Japan.

Polyethylene glycol (PEG) has been reported to inhibit the development of colonic lesions in carcinogen-treated rats when administered orally. However, the precise mechanism for the chemopreventive activity of PEG remains largely elusive. Based on a characteristic feature of PEG as a 'fusogen', we investigated its potential as a chemotherapeutic agent through the induction of multinucleated cell formation and apoptosis induction in PC-3 prostate cancer cells. When PC-3 cells were treated with 0.5 and 1.0% PEG 1000, multinucleated cells were induced at a frequency of 8.4 and 13%, respectively, 36 h after PEG treatment under high cell density (1 x 10^6 cells in 100 microL PEG solution) in vitro. Although abnormality of cell cycle progression was not evident in PEG-treated PC-3 cells, multinucleated cells substantially disappeared at around 38 h due to apoptosis. In contrast, no apparent growth suppression was observed when PC-3 cells were exposed to up to 1.0% PEG at a much lower cell density, namely under ordinary culture conditions. Furthermore, injection of 0.5% PEG solution in vivo into PC-3 xenografts implanted in BALB/c-nu/nu male mice significantly suppressed tumor growth compared to phosphate-buffered saline injection. Multinucleated TdT-mediated dUTP-biotin nick end-labeling (TUNEL)-positive cells were observed inside the PEG-injected tumors. PEG was here demonstrated to have anticell proliferation and antitumor effects via induction of apoptosis, possibly by cell fusion. PEG injection therapy could therefore be adopted as an alternative chemotherapeutic strategy for localized prostate cancers, including those that become refractory to androgen-deprivation therapy.

PMID: 18380794

Cytostatic effect of polyethylene glycol on human colonic adenocarcinoma cells.


Laboratoire des Xénobiotiques, Institut National de la Recherche Agronomique, Toulouse, France.

Polyethylene glycol (PEG 8000) is a potent cancer chemopreventive agent. This osmotic laxative polymer markedly suppresses colon cancer in rats. To explain the mechanism, we have tested the in vitro effect of PEG on four human cell lines. Two poorly differentiated adenocarcinoma lines (HT29 and COLO205), a fetal mucosa line (FHC) and a differentiated line (post-confluent Caco-2) were incubated with various PEG concentrations for 2-5 days. Results show that PEG markedly and dose-dependently inhibited HT29 and COLO205 cell growth. This cytostatic effect was associated with a blocking of the cell cycle in G0/G1 phase. In addition, PEG decreased the viability of HT29 and COLO205 adenocarcinoma cells. In contrast, post-confluent intestinal-like Caco-2 cells and normal FHC cells were, respectively, not or little affected by PEG. Moreover, the lactate concentration increased twofold in the medium of PEG-treated HT29 cells compared with untreated cells. Microscopic observations showed that PEG induced cell shrinking, membrane blebbing and the condensation of nuclear chromatin. However, because no DNA ladder and no annexin staining were detected, we presume that PEG did not induce apoptosis. PEG increased the osmotic pressure of the culture medium. Hyperosmotic media with added NaCl or sorbitol also inhibited HT29 cell growth, and increased lactate release. These results suggest that PEG may be selectively cytostatic for proliferating cancer cells. This growth inhibition may be due to the high osmotic pressure induced by PEG in vitro. Because the osmotic pressure is high in feces of PEG-fed rats, it may explain the suppression of colon carcinogenesis by PEG. Copyright 2001 Wiley-Liss, Inc.

PMID: 11279607