Eicosapentaenoic acid and aspirin for colorectal adenomas

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Colorectal cancer (CRC) is the third most common cancer and the fifth leading cause of death in both men and women in Turkey, and 60%-70% of CRCs develop from adenomas; the remaining 25%-35% develop from sessile serrated polyps (1). Tubular adenomas represent approximately 75%-85% of adenomatous polyps and have < 5% chance of harboring a malignancy. Tubulovillous adenomas represent 10%-15% of polyps, and usually, 20%-25% harbor a malignancy. Villous adenomas constitute the remaining 5%-10%, and 35%-40% of the polyps are malignant (2). CRC screening programs are being performed in most countries, including Turkey. In addition, one strategy to reduce CRC incidence and mortality is the prevention. Both eicosapentaenoic acid (EPA) (an omega-3 polyunsaturated fatty acid) and aspirin have been shown to reduce CRC development (3,4).

A newly published article in Lancet, entitled "EPA and aspirin, alone and in combination, for the prevention of colorectal adenomas (seAFOod Polyp Prevention trial): a multicentre, randomised, double-blind, placebo-controlled, 2x2 factorial trial," researched the effect of EPA and aspirin for the prevention of colorectal adenomas (5). In this study, the authors investigated the efficacy of EPA and aspirin in individuals with sporadic colorectal neoplasia detected during colonoscopy. In total, 709 participants aged 55-73 years, either men or women, were identified as being at high risk (≥3 adenomas if at least one was ≥10 mm in diameter or ≥5 adenomas if these were <10 mm in diameter) and brought together from 53 Bowel Cancer Screening Program (BCSP) units in England, UK between November 11, 2011 and June 10, 2016. The exclusion criteria were the requirement for more than one repeat colonoscopy or flexible sigmoidoscopy within the 3 months of the BCSP screening window, the use of regular (>3 doses per week) aspirin or non-steroidal anti-inflammatory drug, and the use of concominant anticoagulant of antiplatelet drug. All appropriate participants were randomly divided into four groups: 1) EPA plus aspirin, 2) EPA plus placebo, 3) aspirin plus placebo, and 4) placebo plus placebo (1:1:1:1 ratio). EPA group received either 2 g 99% EPA-free fatty acid (FFA) per day or an equivalent FFA dose as 2780 mg 90% EPA-triglyceride per day. Enteric-coated aspirin dose was 300 mg per day. Four groups received the capsules, either placebo or drugs, during 12 months until the day before surveillance colonoscopy that was performed after 12 months of screening colonoscopy. The primary outcome was the adenoma detection rate (ADR) in participants detected at surveillance colonoscopy. The secondary outcomes were 1) the rate of participants with advanced (≥10 mm diameter, high-grade dysplasia, or villous histology) colorectal adenomas and with conventional (tubular, tubulovillous, and villous), serrated, left-sided, and right-sided colorectal adenoma subtypes; 2) the mean number of colorectal adenomas per participant for all colorectal adenomas and for advanced, conventional, serrated, left-sided, and right-sided colorectal adenoma subtypes; 3) the number of participants at high risk; 4) the development of CRC; 5) dietary fish and other seafood intake at baseline and at 12 months; 6) red blood cell and rectal mucosa polyunsaturated fatty acid concentrations; and 7) adverse events, including clinically significant bleeding episodes (hemorrhagic stroke or gastrointestinal bleeding).

In total, 709 appropriate participants were enrolled in this study: 176 participants in the placebo group, 179 participants in the EPA alone group, 177 participants in the aspirin alone group, and 177 participants in the EPA plus aspirin group. The mean age of participants was 65 years, and 80% of them were men. Totally, 641 participants underwent a surveillance colonoscopy, and 640 of them had enough data for adenomas.

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ADR (primary outcome) was similar among the four treatment groups. The risk difference and risk ratio of having at least one colorectal adenoma did not differ between EPA and placebo, and it also did not differ between aspirin and placebo. Numerically, fewer colorectal adenomas were detected in participants who used both aspirin and EPA rather than the other three groups, and this decrease was observed particularly for left-sided lesions. Aspirin treatment reduced the incidence of all colorectal adenomas and conventional colorectal adenomas and the incidence rate ratio (IRR) (the mean number of adenomas per participant) for right-sided and serrated lesions. EPA treatment reduced IRR for conventional colorectal adenomas and left-sided colorectal adenomas.

The majority of adverse events were mild and related to gastrointestinal system (diarrhea, abdominal pain, and nausea), particularly for the EPA alone group. The most frequently reported serious adverse events were cardiac events, mostly atrial fibrillation, particularly observed in EPA alone group. Six acute upper gastrointestinal bleeding events were reported; three of them were in the aspirin group, two in the EPA group, and one in the placebo group.

There was no difference in colorectal adenoma size either in EPA or aspirin group. One interesting finding of this trial was the relationship of rectal mucosal EPA concentration and the number of colorectal adenomas. Higher rectal mucosal EPA concentrations were related with lesser numbers of colorectal adenomas, particularly conventional adenomas.

In conclusion, EPA (2 g per day) and aspirin (300 mg per day) did not reduce the proportion of participants with at least one adenoma at 1-year surveillance colonoscopy in individuals at high risk for CRC. However, both agents have some chemoprevention effects for adenoma burden. Aspirin reduced the incidence of all and conventional colorectal adenomas and IRR for right-sided and serrated lesions, whereas EPA reduced IRR of left-sided and conventional colorectal adenomas.

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