Grade III-IV toxicities among elderly stage III colon cancer patients receiving CAPOX or capecitabine

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Introduction: Little is known about the prevalence of toxicities among elderly stage III colon cancer patients receiving adjuvant chemotherapy (adjCT) and the influence of these toxicities on treatment intensity.

Methods: Stage III colon cancer patients aged ≥70 years diagnosed in southern-Netherlands between 2005-2012 who received adjCT, comprising of capecitabine and oxaliplatin (CAPOX, n = 193) or capecitabine monotherapy (CapMono, n = 164), were included. For toxicity grading, Common Terminology Criteria for Adverse Events version 4.0 were used. Grade III-IV toxicities that appeared in >5% of patients were reported and investigated whether these toxicities were related to patient, tumor and treatment characteristics using χ2-tests, Fisher’s Exact tests and T-tests. Characteristics included were gender, age, comorbidity, ASA score, pT-pN, tumor subsite, differentiation grade, period of diagnosis, completion of planned cycles and mean total dosage (MTD).

Results: The number of grade III-IV toxicities differed between CAPOX and CapMono (p < 0.0001). For CAPOX, 20% developed no toxicity; 32% developed 1 toxicity; 22% developed 2 toxicities; and 26% developed ≥3 toxicities. For CapMono, these proportions were 49%, 31%, 13% and 7% respectively. For CAPOX, most common grade III-IV toxicities were diarrhea (n = 40, 21%); neurological complications (n = 21, 11%); vomiting/nausea (n = 21, 11%); thrombocytopenia (n = 16, 8%); and hypokalemia (n = 15, 8%). For CapMono, most common toxicities were dermatological complications (n = 28, 17%); diarrhea (n = 14, 9%); and fatigue (n = 11, 7%). 8% of reported toxicities was grade IV; the other toxicities were grade III. Higher ASA score was associated with diarrhea and thrombocytopenia among patients receiving CAPOX (p = 0.015 and p = 0.048 respectively). Diagnosis in later periods was associated with dermatological complications and diarrhea among patients receiving CapMono (p = 0.0003 and p = 0.015 respectively). No other patient or tumor characteristics appeared related to toxicity. For CAPOX, patients with diarrhea or vomiting/nausea less often completed all planned cycles as compared to patients without these toxicities (10% vs. 39%, p = 0.0006 and 10% vs. 35%, p = 0.017 respectively). Furthermore, MTD of capecitabine within the CAPOX regimen was lower for patients with diarrhea (85,576 vs. 157,890mg/m2, p < 0.0001), vomiting/nausea (80,573 vs. 151,284mg/m2, p < 0.0001), and hypokalemia (75,295 vs. 149,621mg/m2, p < 0.0001) but higher for patients with neurological complications (173,583 vs. 135,868mg/m2, p = 0.043) and thrombocytopenia (159,278 vs. 135,099mg/m2, p = 0.025). MTD of oxaliplatin was lower for patients with diarrhea (358 vs. 603mg/m2, p < 0.0001), vomiting/nausea (358 vs. 580 mg/m2, p = 0.0009) and hypokalemia (369 vs. 572mg/m2, p = 0.008) but higher for patients with thrombocytopenia (655 vs. 501mg/m2, p = 0.0005). For CapMono, MTD of capecitabine was lower for patients with diarrhea (114,373 vs. 175,548mg/m2, p = 0.005).

Conclusion: A large majority of elderly treated with CAPOX and half of elderly treated with CapMono developed grade III-IV toxicities, which had a pronounced impact on completion of all planned cycles and mean total dosage.