SO-25 Global rise in early-onset colorectal cancer: An association with antibiotic consumption?

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Background: Since the late 1980s, global antibiotic consumption and colorectal cancer (CRC) rates in those aged less than 50 years have soared. As the gut microbiome modulates many human processes, significantly altering microbiome structure and diversity with antibiotic therapy has previously been shown to influence CRC genesis in older adults. To our knowledge, no study before has investigated antibiotic usage in early-onset CRC (EOCRC). This study will investigate the association between exposure to antibiotics and risk of EOCRC predisposition, and also evaluate antibiotic usage in older adults with CRC for comparison.

Methods: A nested case-control study was conducted using Scottish primary care data. CRC cases, diagnosed between 1999 to 2011, were identified from GP records and matched with up to 5 controls. Analyses were conducted separately in EOCRC cases (diagnosed =50 years). Prescriptions for oral antibiotics (by drug class and by anaerobic/non-anaerobic effect) were extracted and total antibiotic exposure period determined for each matched set. Total exposure time in days was categorised into 0, 1-15, 16-60, and >60 days. Cases and controls were described and conditional logistic regression used to calculate odds ratios (OR) and 95% confidence intervals (CI) for the associations between each exposure and CRC (by tumour location), adjusting for comorbidities. Test for trend was used to evaluate any exposure-response relationship.

Results: 7,903 CRC (5,281 colon, 2,622 rectal) cases and 30,418 controls were identified. 445 cases were aged under 50 years. 45% were prescribed antibiotics during the exposure period. Use of antibiotics was associated with increased risk of colon cancer in both age-groups, particularly in the EOCRC cohort adj) 1.49 (95%CI 1.07, 2.07), p=0.018); >= 50 years (OR adj (95%CI) 1.09 (1.01, 1.18), p=0.029). Antibiotic use was associated with a significantly increased risk of proximal colon cancer (pCC) among the under 50s (OR adj (95%CI) 3.78 (1.60, 8.92), p=0.002), but not among the older age-group (OR adj (95%CI) 0.89 (0.72, 1.11), p=0.315). This difference was of statistical significance (p=0.001). Among both age-groups, most classes of antibiotic were not significantly associated with colon, rectal, or distal colon cancer. However, quinolones and sulfonamides/trimethoprim were associated with pCC in the EOCRC cohort only (quinolones OR adj (95%CI) 7.47 (1.40, 39.94), p=0.019; sulfonamides/trimethoprim OR adj (95%CI) 4.66 (1.66, 13.09), p=0.003). Rectal cancer was not associated with antibiotic usage in either strata, with the exception of non anti-anaerobic antibiotics in the EOCRC cohort (OR adj (95%CI) 1.70 (1.06, 2.74), p=0.029). There was limited evidence of a positive exposure-response relationship between antibiotic use and risk of CRC, with the exception of pCC in the younger cohort (p-trend 0.004).

Conclusions: Our findings suggest antibiotics may have a role in colon tumour formation across all age groups, particularly in those aged less than 50 years. It is possible that exposure to antibiotics could be contributing to the observed increases in EOCRC, particularly in the proximal colon. If confirmed, our study will provide further reasons to reduce, where possible, frequent and unnecessary antibiotic prescribing.

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