Fluoroquinolones and aortic aneurysm or aortic dissection: is there an associated risk?

Professor Mark Wilcox, reviewing Dong Y-H, *et al*. *JAMA Intern Med* e204192 and Gopalakrishnan C, *et al*. *JAMA Intern Med* e204199, both published online 8 September 2020.

Two observational studies raise important questions about the previously reported association between fluoroquinolone use and subsequent aortic aneurysm or dissection

Previous observational studies highlighted a potential association between fluoroquinolone use and the occurrence of aortic aneurysm (AA) or aortic dissection (AD).[1-4] In 2018, regulatory authorities in the USA and Europe issued drug safety warnings regarding the use of fluoroquinolones in patients with or at risk of AA/AD.[5-6] Adding another chapter to this story, two important recent studies (reported in the September 2020 issue of *JAMA Internal Medicine*) question the association between fluoroquinolone use and subsequent aortic pathological changes.

First, Dong *et al*.[7] found no increased risk of AA or AD for inpatients prescribed fluoroquinolones compared with other antibiotic classes; this nested case-control study used the same Taiwan National Health Insurance Research Database as in one of the earlier studies that observed the potential association between drug exposure and aortic rupture (2). Second, Gopalakrishnan *et al*.[8] found a small, absolute increased risk of AA/AD in patients with pneumonia but not in those with urinary tract infection, using a propensity-matched cohort design in an analysis of a US commercial claims database.

The study by Dong *et al*.[7] included only patients with infections for which fluoroquinolones are indicated. After adjusting for baseline covariates and concomitant antibiotic use, infection was found to be a risk factor for AA/AD, with septicaemia and intra-abdominal infections having the highest increased risk. Elevated risk for AA/AD was associated with multiple antibiotics, which the authors considered was reflective of residual confounding due to risk factors for AA/AD, such as tobacco use and frailty. Gopalakrishnan *et al*.[8] speculate that although fluoroquinolone use increased the rate of AA/AD compared with azithromycin and amoxicillin, surveillance bias, as well as residual confounding, could not be excluded.

Comment

Observational studies provide important real-world assessment of treatment effects, but have intrinsic strengths and limitations. Such studies may reveal associations between observed exposure baseline variables or outcomes, but cannot be used to demonstrate causality. As pointed out in the editorial[9] accompanying these two study reports, the results are sensitive to design parameters, especially to the choice of appropriate comparison groups. All antibiotics including fluoroquinolones, should be used only for appropriate indications, with careful consideration of well-established adverse effects. Concern about AA/AD with antibiotic treatment is justified, and avoiding fluoroquinolone use in patients with AA/AD or who are at risk for these conditions remains appropriate. However, Gopalakrishnan *et al*.[8] note that the rates of AA/AD were <0.1% across the cohorts they studied. In this respect, the low risk of AA/AD should not preclude patients with indicated infections from receiving necessary treatment, because the benefits of choosing fluoroquinolones for treatment, when appropriate, may outweigh a small possible increased risk of AA/AD.

References

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