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Dear Editor

Drs' Goldstein and Sartor[1] raise some interesting observations based on the results of our analysis of opioid use in the English NHS over a 24 year period. It is important to reiterate that our study[2] is an observational cohort study and can only provide evidence of association rather than causality.

Dr's Goldstein and Sartor suggest that chronic rather than acute opioid use may be associated with disease exacerbation as another potential explanation for our results showing increased morality with regular opioid use in the IBD population. We have shown increased morality with greater than 3 opioid prescriptions per calender year and a similar Canadian population based study[3] showed that heavy opioid use (defined as continuous use for 30 days at a dose exceeding 50 mg morphine / day or equivalent) was significantly associated with mortality. These results would support but not confirm the hypothesis that chronic opiate use exacerbates IBD, but does not show that low dose or infrequent use ameliorates disease activity in the IBD population as suggested in their letter. We found no potential protective effect for lower strength, or lower dose opiate medications.

Opiate receptors are an attractive target for treating inflammatory bowel disease as they are abundant through the GI tract, and have direct effects on motility and potential immunological effects. Low dose naltrexone (a μ opioid receptor antagonist when used in higher concentrations) has been studied in an RCT in adult Crohn's disease patients compared to placebo by Smith et.al who found no statistically significant difference in the proportion of adult patients who achieved clinical remission.[4] The most recent Cochrane review on the use of low dose naltrexone in Crohn's disease did not find sufficient evidence to make firm conclusions on its efficacy suggesting that further randomized controlled trials are needed.[5]

We agree with Drs' Goldstein and Sartor that further prospective studies looking at chronic opioid use and disease exacerbations would be of interest but would require a large dataset of patients followed up for several years to be adequately powered. Given the current evidence of the association of mortality with chronic opiate use there would be ethical questions raised on continuing these patients on opioid medication (once chronic opioid use has been identified in a patient with IBD) making a prospective study difficult to justify. The effect of wound healing and low dose opiate therapy would, in our opinion, be best subject to a randomized controlled trial rather than looking at observational datasets where wound healing would be unlikely to be objectively and reliably assessed.

References

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