Medications and malignancy in inflammatory bowel disease

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Do not overstate the risk of non-melanoma skin cancer when prescribing thiopurines in inflammatory bowel disease

- Ariyaratnam J, Subramanian V. Association between thiopurine use and nonmelanoma skin cancers in patients with inflammatory bowel disease: a meta-analysis. *Am J Gastroenterol* 2014;109:163–9.

The risk of developing non-melanoma skin cancers (NMSC) doubles for those patients with inflammatory bowel disease (IBD) who receive thiopurine. This is lower than previously published. Ascertainment bias may be responsible for some of this increased risk.

The data regarding risk of NMSC with thiopurines in IBD are conflicting. In this meta-analysis, a search was performed of electronic journal databases for full articles reporting the risk of developing NMSC in patients with IBD on thiopurines. HR, publication bias and heterogeneity were calculated.

Eight studies (four nested case-control and four retrospective cohort) involving 60 351 patients met the study eligibility criteria. The HR of developing NMSC with thiopurines was 2.28. There was heterogeneity in the studies, significantly so for the population under study and for the duration of follow-up. Hospital based studies found a greater association than did population based studies. Ascertainment bias (patients on thiopurines receive greater clinical follow-up than those who are not) may be partially responsible for the increased risk.

Comment

The increased risk of NMSC with thiopurines may be less than previously published. This is reassuring for prescribers and patients and should improve adherence to this effective class of medications. This editor disagrees, however, with the authors' assertion that a 2.28 HR is only 'modestly elevated'. NMSC are common (UK age standardised incidence rate 105/100 000), therefore doubling the HR leads to a significant numerical increase in incident cases. As the authors note, all patients started on thiopurines must still be counselled regarding the increase in risk of NMSC, and the importance of universal skin precautions.

Do not overstate the increased risk of malignancy when prescribing anti-TNF in Crohn's disease

- Lichtenstein GR, Feagan BG, Cohen RD, *et al.* Drug therapies and the risk of malignancy in Crohn's disease: results from the TREATTM registry. *Am J Gastroenterol* 2014;109:212–3.

While patient age, duration of disease and smoking were independently associated with an increased risk of malignancy, no such risk was demonstrated for infliximab therapy.

Analysing data from the Crohn's Therapy, Resource, Evaluation, and Assessment Tool (TREAT) prospective cohort registry, Lichtenstein *et al* calculated the relative risk of malignancy based on patient, disease and medication factors. The study cohort included all patients exposed

to infliximab recently before or during the study and the control cohort included all patients who were not exposed to infliximab.

A total of 6273 patients with a median of 5.2 years' follow-up were included. No significant increase in overall cancer rate was seen in the infliximab cohort or in the infliximab and immunosuppressant cohort. Sub-analysis showed no significant increase in lymphoma or NMSC in the infliximab group. Age, disease duration and smoking all correlated with excess incidence of cancer.

Comment

This well powered study provides reassuring data about the addition of anti-tumour necrosis factor (anti-TNF) to standard medications for Crohn's disease (CD); however a single study with reassuring outcomes should not make clinicians blasé about the risk of malignancy. Clinicians should be especially vigilant for malignancy in patients on anti-TNF who are elderly, smokers or have a long history of CD. The difference in numbers between the combined infliximab and immunosuppressant group (3517) and the 'neither' group (96) renders any conclusions drawn between these two groups redundant. The registry and study were funded by the manufacturer, introducing the potential of funding bias.

Competing interests None.

Provenance and peer review

Commissioned; internally peer reviewed.