EDITORIAL

Do statins raise the risk of depression?

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STATIN USE IS ASSOCIATED WITH A REDUCED RISK OF DEPRESSION AND DOES NOT INCREASE THE risk of suicide, anxiety or seizures, a Swedish national cohort study has found.[1]

Linked prescription, healthcare and mortality data were obtained from national registers. The cohort comprised all individuals aged 15 years and over who were prescribed statins between January 2006 and December 2013. A within-subjects design was used whereby each participant served as his/her own control. The incidence of the defined outcomes during periods of treatment and non-treatment was compared. Neuropsychiatric outcomes were identified by ICD-10 codes from hospital emergency and specialised outpatient settings; depression diagnoses were only included when they originated from unplanned or emergency visits.

Overall, 1,149,384 statin users were included in the study. Most (88.4%) were aged 50 years or over and 54.4% were male. In total, there were 2,053,310 non-treatment periods and 2,997,545 treatment periods. During the study, 6,372 individuals (0.6%) presented with suicidal behaviour or completed suicide, 23,745 (2.1%) were diagnosed with a depressive disorder, 30,100 (2.6%) were diagnosed with an anxiety disorder and 28,844 (2.5%) presented with seizures.

Compared with non-treatment periods, periods of statin use were associated with a lower risk of depression diagnosis, hazard ratio (HR) 0.91 (95% CI: 0.87-0.94), and this result was not affected by adjustment for concurrent antidepressant use. Statin use was not associated with suicide outcomes HR 0.99 (95% CI: 0.90-1.08), anxiety HR 0.99 (95% CI: 0.95-1.02) or seizures HR 1.00 (95% CI: 0.97-1.04).

The restricted inclusion criteria account for the low prevalence of depression and could have reduced the power of the study to detect associations, although similar results were obtained when data from planned hospital visits and primary care were analysed. The within-subjects design minimised the risk of confounding by indication.[2]

In 2009 the MHRA reviewed the evidence from randomised controlled trials, observational studies and case reports and recommended that depression should be listed as a possible adverse effect of statins.[3] Statins inhibit HMG-CoA reductase and reduce the level of LDL cholesterol. Cholesterol is essential for cell membrane stability and cholesterol deficiency may disrupt serotonin signalling. There is evidence from cross-sectional studies of a link between depression and low LDL.[4] A recent Mendelian randomisation study found a significant association between genetic inhibition of HMG-CoA reductase and the risk of depression: for each 1-SD reduction in LDL there was a 12% increase in the risk of depression.[5]

The finding that statin use is associated with a reduction rather than an increase in the risk of depression is therefore surprising, although consistent with a meta-analysis of observational studies.[6] It is suggested that statins may exert an antidepressant effect through their ability to reduce oxidative stress and inflammation.

'The finding that statin use is associated with a reduction in the risk of depression is consistent with a meta-analysis of observational studies'

However, in the present study use of thiazide diuretics and antihistamines was also associated with a reduced risk of depression, although this did not reach statistical significance, HRs 0.61 (95% CI: 0.38-1.00) and 0.84 (95% CI: 0.67-1.06) respectively. This implies that the reduced risk of depression associated with statin use may be the result of non-specific treatment factors rather than a direct neuroprotective effect.

The authors conclude that 'statin treatment is a safe therapeutic option with regard to some neuropsychiatric outcomes.'

However, until we have a better understanding of their complex and opposing effects on brain function and mood, I think it is sensible when prescribing statins to identify and follow up patients who are considered to be at increased risk of depression.[3]

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