

activity should be encouraged not only to reduce dyspnoea but also to delay development, progression and death from COPD.'

DR PETER SAUL

Hansen GM, Marott JL, Holtermann A et al. Midlife cardiorespiratory fitness and the long-term risk of chronic obstructive pulmonary disease. *Thorax* Epub ahead of print. 17 June 2019 doi: 10.1136/thoraxjnl-2018-212821

Mental health

Gabapentinoids may increase risk of suicidal behaviour in young patients

A large Swedish study has suggested that gabapentinoid medications are associated with an increased risk of suicidal behaviour and unintentional overdose in adolescents and young adults.

The investigators conducted a population-based cohort study using data from Swedish registers with complete national coverage. The population of almost nine million (8,945,712) individuals aged 15 years and over was assessed for gabapentinoid treatment episodes (two consecutive dispensed prescriptions for a gabapentinoid) between 2006 and 2013.

Information on suicidal behaviour, unintentional overdoses, injuries and road traffic incidents was collected from the Swedish Patient Register; deaths from the Swedish Death Register; and criminal activity from the Register of People Suspected of Offences.

Follow-up time was divided into periods of treatment and non-treatment, and the gabapentinoids were analysed both together and individually. Those with identified substance misuse

disorders and those who were taking other antiepileptic medication were excluded from some analyses.

Over the study period, 191,973 patients collected two or more consecutive prescriptions for a gabapentinoid, and around 60% of these were for pregabalin.

When treatment and non-treatment periods were compared for the same participant, gabapentinoid prescribing was associated with an increased risk of:

- Suicidal behaviour and death from suicide; age adjusted hazard ratio (HR) 1.26 (95% CI: 1.20-1.32)
- Unintentional overdose HR 1.24 (95% CI: 1.19-1.28)
- Head or body injury HR 1.22 (95% CI: 1.19-1.25)
- Road traffic incidents and offences HR 1.13 (95% CI: 1.06-1.20)

There was no statistically significant association with arrest for violent crime HR 1.04 (95% CI: 0.98-1.11).

When stratified by gabapentinoid type, pregabalin was associated with increased hazards for all outcomes. However, gabapentin treatment was associated with reductions in road traffic incidents and offences HR 0.81 (95% CI: 0.70-0.94) and arrests for violent crime HR 0.80 (95% CI: 0.67-0.95) but not for other outcomes. Results for men and women followed the same general patterns.

Periods of gabapentinoid treatment were associated with increased hazards of suicidal behaviour in people younger than age 55, with the highest risk in those aged 15-24 years, HR 1.67 (95% CI: 1.52-1.84) but reduced or no association in those aged 55 and older. Patterns were similar for other outcomes i.e. younger participants (15-34 years) showed increased hazards, whereas older participants (≥ 55 years) did not.

Over recent years the number of prescriptions issued for gabapentin and pregabalin have risen sharply. Adverse effects with these drugs have been noted including dizziness, somnolence, balance problems, blurred vision, coordination problems and impairment in cognitive performance, and earlier reports have suggested a link to overdose-related death and increased suicidal thinking. However, good quality evidence on the risks of these medications has been relatively limited. Earlier this year gabapentin and pregabalin were reclassified as class 3 controlled drugs in the UK.

The study authors conclude:

'Overall, gabapentinoids seem to be safe for a range of outcomes in older people. However, the increased risks found in adolescents and young adults (ages 15-24 years) prescribed gabapentinoids, particularly for suicidal behaviour and unintentional overdoses, warrant further research.'

DR JEZ THOMPSON

Molero Y, Larsson H, D'Onofrio BM et al. Associations between gabapentinoids and suicidal behaviour, unintentional overdoses, injuries, road traffic incidents, and violent crime: population based cohort study in Sweden. *BMJ* 2019;365:l214

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