EDITORIAL

Delirium linked to cognitive decline

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DELIRIUM IS ASSOCIATED WITH AN INCREASED RISK OF SUBSEQUENT COGNITIVE DECLINE AND there is evidence to suggest that the association is causal, a systematic review and meta-analysis has found.[1]

Relevant observational studies, from 1965 to 2018, were identified from electronic databases such as PubMed, Cochrane and Embase. Inclusion criteria were: comparison of groups with and without delirium; use of a validated delirium scale; measurement of cognition a minimum of 3 months after the delirium episode; and an objective measure of cognitive outcome.

A total of 24 studies comprising 3,562 delirious subjects and 6,987 controls were included in the analysis. The mean age of participants was 75 years and 47% were men. Most studies used the Confusion Assessment Method (CAM) to identify delirium. One study was excluded as an outlier.

Of the remaining 23, 15 used a continuous cognitive outcome measure such as the MMSE and eight used a binary outcome measure (dementia or cognitive impairment present/not present).

The combined effect size for the 23 studies was 0.45 (95% CI: 0.34-0.57; $P < 0.001$) indicating a medium effect. Every study found that those with delirium experienced greater cognitive decline than controls and the combined odds for a given cognitive decline were more than doubled in patients with delirium; OR 2.30 (95% CI: 1.85-2.86)

'The combined odds for a given cognitive decline were more than doubled in patients with delirium'

Dementia is the most important risk factor for delirium and it may simply be that delirium is an indicator of pre-existing cognitive impairment: delirium reflects cognitive decompensation under stress conditions and implies insufficient cognitive reserve. In some cases, delirium may unmask unrecognised dementia. Alternatively, an episode of delirium may cause permanent neuronal damage either as a direct effect of the precipitating factors (e.g. hypoxia, metabolic derangement) or as a result of the delirium process itself, which is thought to involve inflammatory dysregulation and neurotransmitter imbalance.[2,3]

Subgroup analyses provided evidence that delirium is a causative factor rather than a marker of vulnerability to dementia e.g. effect sizes were larger in the studies (17/23) which adjusted for baseline cognition.

The authors acknowledge that a significant limitation was the high level of heterogeneity ($I^2 = 81\%$). Meta-regression suggested that most of the variance derived from differences in follow-up duration, adjustment for baseline cognition and adjustment for other covariates. Only two of the included studies were community-based cohort studies. The others followed up hospitalised patients and most studies (14/23) were of postoperative delirium.

According to the CAM, delirium is characterised by: **1** acute onset with a fluctuating course (usually worse at night) AND **2** inattention AND **3** disorganised thinking (irrelevant conversation, illogical flow of ideas) OR altered level of consciousness (agitated/hyperactive or somnolent/hypoactive).[4] Tests of attention include asking the patient to spell *world* backwards, subtract serial 7s or recite the months backwards.[5] In addition to the core features, the long form of the CAM includes the following additional features of delirium: disorientation, memory impairment, perceptual disturbances (hallucinations, illusions), psychomotor agitation/retardation and altered sleep/wake cycle.

The authors recommend a focus on delirium prevention and conclude that 'additional research in this area may rather rapidly yield reductions in delirium and pari passu, postdelirium cognitive decline.'

GPs can play a key role in identifying older patients at risk of delirium – predisposing factors are mild cognitive impairment/dementia, previous delirium, functional or sensory impairment, multiple comorbidity, depression, cerebrovascular disease and alcohol abuse[6] – and instigating preventative strategies. Drugs which might cause delirium, such as benzodiazepines, anticholinergics and opioids should be avoided.[7] Carers should be provided with information on how to recognise and prevent delirium during intercurrent illness, including the importance of: maintaining orientation; ensuring adequate fluid intake; sleep hygiene; regular mobilisation; and access to glasses and hearing aids.[8]

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