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Forward thinking: where next for delirium prevention research?

Delirium, like many of the syndromes associated with older age, is recognized as clinically important and yet has seen relatively little original research. Guidance from professional bodies and government policy in many countries highlights improving delirium as a priority.[1-3] Yet much of the available guidance remains based on expert opinion rather than empirical data, and fundamental questions around delirium management remain unanswered. Thankfully the landscape is changing, and an updated Cochrane Review provides a nice summary of what we know and gives some pointers as to where we need to go with delirium prevention research.[4]

It is generally accepted that prevention is better than cure. This adage is particularly pertinent to delirium and emphasizes the importance of the prevention focus in this review. Various pharmacological and non-pharmacological approaches to treatment of established delirium have been tested, yet a cure for delirium has proven elusive.[5] The potentially devastating outcomes associated with an episode of delirium provide further support for a prevention focus. Although often considered an 'acute' condition, we should not underestimate the potential longer-term effects of delirium, including chronic cognitive decline, institutionalization, and death.[6]

This scope of this review is broad, and the authors are to be congratulated for presenting a synthesis of such a complex area.[4] Of the various interventions described in the review, many have been evaluated in trials that are underpowered or have serious methodological limitations. However, the results concerning multicomponent interventions and certain pharmacological interventions are more compelling and have clear implications for policy and practice.

The most important finding was a clinically meaningful reduction in incident delirium with use of a multicomponent prevention package. The individual components of the interventions varied between studies but commonly included reorientation strategies, ensuring hydration/nutrition, and early mobilization. A defining feature across all the interventions was a person-centred, holistic approach with particular attention paid to creating a therapeutic environment. It could be argued that many of the interventions were simply operationalized versions of good basic medical and nursing care. This raises the question: why aren't we delivering these interventions in the first place? Future studies may benefit from an implementation science approach to explore the facilitators and barriers to delivery.

The review authors graded the supporting evidence for multicomponent interventions as moderate quality. Certainly there was potential for bias in the included studies, but overall the quality of the trials was reasonable for a complex healthcare intervention. The beneficial effect of multicomponent interventions was apparent across prespecified patient subgroups, and for those that developed delirium the intervention seemed to reduce duration and severity. These subgroup analyses are far from definitive, but together lend credibility to the efficacy of multicomponent prevention. This form

of intervention also has face validity. Delirium is a multifactorial syndrome, and various risk factors and predisposing conditions interact in a complex synergy.[6] It seems intuitive that for an intervention to have a meaningful impact it will need to be similarly multifaceted.

The complex pathophysiology of delirium suggests that single pharmacological interventions were always going to struggle to have a meaningful impact. The pharmacological agents studied had compelling basic research and preclinical data but failed to demonstrate any convincing effect in the messy reality of delirium. In a preplanned subgroup analysis, there was a signal that atypical antipsychotics may reduce incident delirium. However, these agents also seemed to increase severity and duration of delirium. It seems plausible that antipsychotics may simply change the clinical manifestations of delirium, from hyperactive delirium (easy to diagnose as a study outcome) to a more insidious, hypoactive form.

For a review with such a broad scope it is perhaps unsurprising that there was substantial heterogeneity. There was heterogeneity across the treatments studied (22 different interventions) and across the healthcare settings included. Studies recruited from orthopaedic, cardiothoracic, and colorectal surgical wards. Postoperative delirium is a common and feared complication, and the inclusion of surgical settings in the review is laudable.[7] However, delirium is prevalent across all the hospital disciplines, and the lack of studies recruiting from geriatric and general (internal) medicine settings is disappointing.[8] Indeed, generalizability of the study results to the typical older adult at risk of delirium is questionable. Several of the included studies had a relatively young patient population and many excluded dementia, despite age and cognition being important risk factors for development of delirium.

A striking and encouraging aspect of the review is the number of included studies. This review included 39 different trials (16,082 participants), a healthy number for a systematic review with a cognitive focus. The authors identified a further 27 ongoing trials. The previous iteration of the review, published less than 10 years ago, contained only six studies.[9] Looking ahead, a single review covering all preventative interventions is probably no longer useful, and there should be sufficient published evidence to justify individual reviews for pharmacological, non-pharmacological, and perioperative interventions. This substantial increase in delirium research activity is a positive sign, but we should not be complacent. To put the magnitude of evidence in context, the most recent Cochrane Review of preventing falls in hospital was able to draw on 60 trials including 60,345 participants.[10] This review challenges the therapeutic nihilism around delirium and suggests that prevention of delirium is possible. We need to keep up the momentum, support further research, and encourage implementation of effective strategies.

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