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Review

Treating chronic non-cancer pain in older people – More questions than answers?

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ABSTRACT

There is little evidence specifically relating to drug treatments for pain in older people, but much can be extrapolated from what we already know. The evidence about drug treatments for chronic non-cancer pain is changing, driven by major improvements in understanding of clinical trial analysis and by the adoption of patient-centered outcomes of proven economic benefit. There is clear evidence of lack of useful effect, or insufficient evidence of effect for a number of commonly used drugs, including paracetamol, topical rubefacients, low concentration topical capsaicin, and for strong opioids in chronic non-cancer pain. In musculoskeletal pain there is evidence of efficacy for NSAIDs, tramadol, and tapentadol, and in neuropathic pain for duloxetine, pregabalin, and gabapentin, with weak evidence for amitriptyline. The new perspective is of drugs that work well in a minority of patients, but hardly at all in the remainder. The goal of treatment is large reductions in pain, by 50% or more. This outcome, and only this outcome, is associated with large benefits in terms of improved sleep, reduced depression, and large gains in function and quality of life. It is not possible to predict which patient will benefit from which drug, but early success or failure appears to be predictive of long-term success or failure. The emphasis is on stopping treatments that do not work and switching to other drugs in the same or different class, so that any potential future risk of treatment is balanced by very large and immediate benefit.

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1. Introduction

1.1. What is CNCP and why is it important?

Chronic non-cancer pain (CNCP) is pain that is not caused by malignant disease and persists over a period of time. Although there is no widely accepted definition of minimum duration, three months is often arbitrarily used to differentiate between acute or subacute pain (intermittent migraine, for example), and chronic pain.

In older people CNCP is often associated with musculoskeletal disease, or conditions affecting the somatosensory nervous system (neuropathic pain). In addition, pain in itself can be associated with depression, impaired function in activities of daily living, and increased mortality. Unfortunately it is a common problem for patients, their families/carers, health professionals and of course there are implications for delivery and cost of health care services. Assessment and treatment of pain in patients who cannot readily communicate (e.g. in dementia) are very important issues but will not be explored in this paper.

CNCP can be continuous; while it often varies in intensity over time, it is characterised by pain that is typically moderate or severe in intensity over many years. Systematic reviews of CNCP prevalence agree that chronic pain (usually defined conservatively in studies as moderate or severe pain lasting six months or more) affects about 1 adult in 5 [1,2]. This is mostly musculoskeletal pain (especially osteoarthritis), that increases with age [3], thought about a third of older people with CNCP have neuropathic pain [1]. Most people (66%) with CNCP have it for five years or longer: it rarely goes away spontaneously [4]. Over half of people aged 65 years or older in a study in the USA had bothersome pain [5].

The detrimental impact of CNCP on a whole range of associated problems, including quality of life and function, is immense [1]. CNCP has a greater negative impact on quality of life than any other chronic condition for people living in the community [6]. There is also growing evidence that CNCP can affect the *quantity* of life [1], particularly in those with the most severe pain [7], or with walking disability [8]; cardiovascular or respiratory death contribute most to excess mortality.

This review concentrates on new thinking on drug therapy. Here there is at least some evidence, but for intervention management or complementary therapies, evidence is notable by its absence. For example, a broad review of interventional therapies for neuropathic pain could make, at best, four very weak recommendations that particular treatments might work [9]. For complementary therapies and devices, there are many problems with the evidence, as typified by acupuncture [10].

1.2. Evidence on CNCP in older people? Can we extrapolate evidence from younger patients?

There is clear evidence that CNCP is more prevalent in older populations, driven largely by osteoarthritis and other musculoskeletal conditions [3]. Other surveys suggest that prevalence may decline somewhat with age [4].

As is often the case with conditions affecting patients with a wide age range, there is little evidence on CNCP specifically in older people, and much of the available data come from observational studies. Reasons for the lack of inclusion of older patients in clinical trials in general have been discussed elsewhere; in CNCP, many trials recruit patients from specialist clinics in secondary care attended by relatively few older people. As a result, clinical trials in CNCP, particularly in osteoarthritis, often have a majority of patients of late middle age and some older patients but tend not to include many of the "oldest-old".

There is some clinical trial evidence that shows similar efficacy for treatment of CNCP in patients of different ages. In osteoarthritis, for example, one randomised trial of rofecoxib recruited 341 patients with an average age of 83 years [11], and another compared the effects of rofecoxib and celecoxib in hypertensive osteoarthritis patients aged 65 years or older [12]. A post hoc assessment of pregabalin efficacy in 2516 patients with painful diabetic neuropathy or postherpetic neuralgia compared older patients (65–74 years, and ≥75 years) with those aged 18–64 years [13] (Fig. 1).

To our knowledge no study shows any large difference in response, as in Fig. 1, though more analyses would be very useful because it is tempting to see greater efficacy for pregabalin in older people, compared with placebo. In the absence of age-specific data, information from younger patients is often used to guide treatment in older patients, although with caution as older people tend to be more likely to experience adverse effects. It is likely that extrapolation is appropriate for analgesic efficacy, but may not be for adverse events.

1.3. There are significant developments in understanding data from clinical trials in treating CNCP

Several recent insights show that much of the existing clinical trial evidence on CNCP may be unreliable as a guide to treatment.

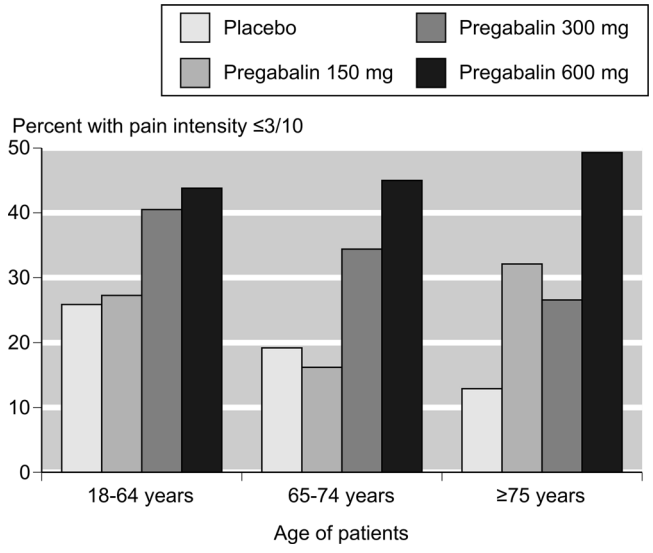

Fig. 1. Percentage of patients with pain scores of ≤30/10 (mild or no pain) on a numerical rating scale at the end of 12 weeks studies of pregabalin at various doses in painful diabetic neuropathy or postherpetic neuralgia, originally with moderate or severe pain (from Ref. [13]).