stopped their treatment because of adverse events, and only four patients had to reduce their dose.

Conclusion

In this study, oral dronabinol reduced central pain in patients with multiple sclerosis. It should be available as a treatment option to patients whose central pain does not respond adequately to other drugs.

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Science commentary: High hopes for cannabinoid analgesia

Geoff Watts

Several decades of irrational prejudice may have hampered clinical research on cannabis as a medicine, but work on the pharmacology of its active ingredients has been making steady progress. Just as the body has a natural counterpart to the opiate drugs, so too it makes its own endogenous cannabinoids. These act through receptors, of which two variants—CB₁ and CB₂—have been definitely identified and at least one other is suspected. The CB₁ receptors are located only in the brain; their CB₂ counterparts are found peripherally, and

especially on the cells of the immune system. Cannabinoid receptors are present not just in vertebrates but also in molluscs, leeches, and other invertebrate groups that have been evolutionarily separate for 500 million years. The fact that natural selection has for so long conserved these receptors is an indication of their physiological importance.

Anandamide, the first natural cannabinoid to be isolated, came to light in 1992. Its precise role, and those of the other cannabinoids that have since been

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identified, remains uncertain; but evidence exists that all play a part in memory, appetite, the control of movement, and, especially, the modulation of pain.¹ With respect to the last of these, the sites of cannabinoid action in the central nervous system are confined to specific areas, most of which—the dorsal horn of the spinal cord, for example^{2–3}—are involved in processing pain signals. Clear parallels exist between cannabinoid and opioid receptors, and evidence is accumulating that the two systems sometimes interact,⁴ and may operate synergistically. One unproved but intriguing idea is that endocannabinoids may set the “analgesic tone” of the body, with the level of their production acting as a kind of pain thermostat.

The perception of pain is controlled by neurotransmitter systems within the central nervous system, but peripheral tissues also have mechanisms for relieving and preventing pain. Cannabinoids may therefore have two distinct roles in relation to pain. The evidence comes from animal experiments showing that cannabinoids lower the response of pain neurones in the spinal cord and also in parts of the thalamus in the brain. The possibility that cannabinoid receptor subtypes act synergistically hints at a potentially valuable strategy: the development of a new class of analgesic drug comprising a mixture of synthetic CB₁ and CB₂ agonists. Alternatively, devising agents to slow the breakdown of natural cannabinoids might potentiate their analgesic effects.⁵

The brain has many more CB₁ than opioid receptors, and interest in the therapeutic potential of cannabinoids has prompted the development of several synthetic variants, of which dronabinol is one.¹ Many of these compounds bind to both CB₁ and CB₂ receptors, but differences between the two suggest that it should be possible to design drugs that would attach to only one of them. This might offer a means of producing more selective biological actions, including analgesia without some of the psychotropic effects that might disturb people whose wish was to be pain-free but not “high.”

A review by the US Institute of Medicine has commented on how little we know about cannabinoids in comparison with opiates.² A comparison between the history of research into the two groups, the review added, “suggests good reason for optimism about the future of cannabinoid drug development.”

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Randomised controlled trial assessing the impact of a nurse delivered, flow monitored protocol for optimisation of circulatory status after cardiac surgery

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Abstract

Objective To assess whether a nurse led, flow monitored protocol for optimising circulatory status in patients after cardiac surgery reduces complications and shortens stay in intensive care and hospital.

Design Randomised controlled trial.

Setting Intensive care unit and cardiothoracic unit of a university teaching hospital.

Participants 174 patients who had cardiac surgery between April 2000 and January 2003.

Interventions Patients were allocated to conventional haemodynamic management or to an algorithm guided by oesophageal Doppler flowmetry to maintain a stroke index above 35 ml/m².

Results 26 control patients had postoperative complications (two deaths) compared with 17 (four deaths) protocol patients (P = 0.08). Duration of hospital stay in the protocol group was significantly reduced from a median of nine (interquartile range 7-12) days to seven (7-10 days; P = 0.02). The mean duration of hospital stay was reduced from 13.9 to

11.4 days, a saving in hospital bed days of 18% (95% confidence interval – 12% to 47%). Usage of intensive care beds was reduced by 23% (– 8% to 59%).

Conclusions A nurse delivered protocol for optimising circulatory status in the early postoperative period after cardiac surgery may significantly shorten hospital stay.

Introduction

Hypovolaemia and tissue hypoperfusion can pass undetected during and after major surgery.¹ These are often not clinically apparent for several days, and may lead to increased morbidity and mortality.

Several perioperative studies have used invasive (pulmonary artery catheterisation) or minimally invasive (oesophageal Doppler flowmetry) monitoring technologies to optimise circulatory variables,² and

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