



Reducing delirium in elderly patients with femur fracture by adding dexamethasone to the local anesthetic in spinal anesthesia

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INTRODUCTION

Femur fracture is a common, mutilating and very expensive health problem. 10% of all fractures are femur fractures and these patients occupy more than 25% of beds in orthopedic hospitals. The mortality rate is very high, and only less than a half of injured people become mobile again after surgery (1). In Croatia, there are about 6000 fractures per year.

These are mainly elderly patients. Approximately 70% of patients will be of ASA physical status 3–4: 35% have one co-morbidity; 17% have two; and 7% have three or more. The most common comorbidities are cardiovascular disease (35%), respiratory disease (14%), cerebrovascular disease (13%), diabetes (9%), malignancy (8%) and treated renal disease (3%).

Approximately 25% of patients with hip fracture have moderate or severe cognitive impairment, and a further 15–25% have mild cognitive impairment.

Approximately 25% of patients with hip fractures have at least moderate cognitive impairment (abbreviated mental test score < 7), 20% are institutionalised, and 50% require walking aids or are immobile.

Mortality after hip fracture has remained relatively unchanged for the last two decades. Currently, 8.4% of patients die within 30 days of surgery. However, it has been suggested that up to half of postoperative deaths are potentially preventable. Thirty-day mortality is increased for older, sicker, male patients. Up to 15–30% of patients die within a year of surgery (2).

Neuroendocrine response and therapy in trauma patients

The injury is characterized by the activation of sympathetic nervous system, resulting an increased catabolism and hypermetabolism. Negative effects include pain, fatigue, bowel paralysis, reduced splanchnic perfusion, immunosuppression and prolonged recovery after surgery. In general, older patients have reduced functional organ supply, and are thus less tolerant to surgical stress, which explains the higher incidence of perioperative complications and death.

Cortisol secretion from the adrenal cortex increases rapidly following the start of surgery, as a result of ACTH stimulation. From baseline values of around 400 nmol/L, cortisol concentrations increase to a maximum at about 4–6h, and may reach >1500 nmol/L depending on the severity of surgical trauma (3). Studies have shown that plasma cortisol stays elevated two weeks after injury in patients with femur fracture.

Regional anesthesia is recommended in elderly patients.

Different adjuvants are used to prolong the duration of spinal anesthesia and postoperative analgesia.

Addition of dexamethasone significantly prolongs the duration of sensory block and decreases opioid requirements in postoperative management.

Dexamethasone relieves pain by reducing inflammation and blocking transmission of nociceptive C-fibers and by suppressing ectopic neural discharge (4). Dexamethasone sodium phosphate is a stable prodrug that is efficiently converted to free dexamethasone when delivered intrathecally. Low continuous intrathecal doses seem safe, but higher doses may lead to increased inflammation (5).

Steroids have powerful anti-inflammatory and analgesic effect, but the mechanism of analgesia still isn't entirely clear (6). Intrathecal dexamethasone may influence intraspinal prostaglandin production. Acute noxious stimulation of peripheral tissues leads to sensitization of dorsal horn neurons of the spinal cord by the release of substances such as glutamate and aspartate. These amino acids activate N-methyl-D-Aspartate receptors resulting in calcium ion influx which leads to activation of phospholipase A2, which converts membrane phospholipase to arachidonic acid. Corticosteroids are capable of reducing prostaglandin synthesis by inhibition of phospholipase A2 through the production of calcium-dependent phospholipid binding proteins called annexins and by the inhibition of cyclooxygenases during inflammation (7).

Intrathecal injection of steroids was frequently used for the treatment of mumps meningitis, chronic lymphocytic leukemia and central nervous involvement in lupus erythematosus (8).

Dexamethasone addition in a dose of 8 mg to ropivacaine does not cause greater neurotoxicity than ropivacaine alone (9). In addition, corticosteroids have a long history of safe use in the epidural space for treatment of radicular pain and dexamethasone was studied as an adjuvant in combination with local anesthetics administered epidurally (10,11). It is known that perineural application of steroids affects postoperative analgesia without adverse effects (12). Despite the hypothesis of a prolonged effect to the contrary, single shot of dexamethasone administered intrathecally for radicular pain indicates a short-term suppression of the pituitary-adrenal axis and lower plasma cortisol levels (13).

Postoperative cognitive disturbance

Delirium is a common complication seen after hip fracture, affecting approximately 10–16% of patients. It is associated with increased mortality within 1 year, delayed rehabilitation efforts, prolonged length of hospital stay, poorer functional outcomes, and increased risk of nursing home placement.

Predisposing factors to delirium include older age, diagnosis of dementia, depression, alcoholism, vision or hearing loss, history of mental status changes, mobility impairment, and dehydration. Hospital-related or iatrogenic factors include physical restraints, malnutrition, more than three medications added, use of a bladder catheter, hypoxia, metabolic disturbances, electrolyte imbalances, withdrawal syndromes, acute infection (systemic and intracranial), seizures, hyperthermia, head trauma, vascular disorders, immobilization, sleep deficiency, psychiatric medications, and intracranial space-occupying lesions.

Besides, hip fracture patients are at increased risk of delirium due to severe pain experienced upon arrival at the emergency department. Findings from laboratory studies indicate that unmanaged pain, both acute and chronic, can affect mental status and might precipitate delirium, especially in elderly patients with hip fractures, who usually report a 50–70% incidence of severe pain in the first 24 h post injury (14, 15).

Cognitive impairment has been associated with high levels of glucocorticoids, as documented in a variety of experimental and clinical settings (16, 17). Cortisol has been found to be toxic to cells in the hippocampus, a structure that plays a critical role in the consolidation of short-term into long-term explicit memory as well as descending control of the hypothalamic-pituitary-adrenal (HPA) axis (18). This gave rise to the proposal that repeated episodes of stress cause decreased hippocampal inhibition of the HPA axis and thus prolonged hyperactivation (19, 20). As well as a possible causal relationship, changes in cortisol secretion may reflect other metabolic changes. For example, an earlier study by Riis *et al.* (21) hypothesized that 'increased metabolic demands induced by the endocrine metabolic response to surgery', as measured by cortisol, contribute to postoperative cognitive dysfunction (POCD).

Postoperative confusion and cognitive problems are more common in the elderly (> 65 years) than in younger patients, and they can be categorized as postoperative delirium and postoperative cognitive dysfunction and dementia. Daily variation of cortisol concentrations are significantly associated with POCD.

Pain and disruption of cortisol circadian rhythm may be important mechanisms in the development of cognitive dysfunction after major surgery and affect the patient's outcome (22).

CONCLUSION

There is sufficient data that the effective pain management may reduce postoperative cognitive disturbances. The addition of dexamethasone to the local anesthetic administered intrathecally significantly prolongs the duration of sensory block and decreases opioid requirements in postoperative management.

Therefore, effective analgesia and the impact on the hypothalamic-pituitary-adrenal axis may reduce postoperative delirium in patients with femur fracture.

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