39 Gender and Age Differences in Pain Perception

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Introduction

- The elderly population accounts for approximately 40% of 234 million surgeries performed each year worldwide. However, clinical studies typically do not include elderly subjects [1]. Therefore, recommendations for diagnosis and management of postoperative pain in older adults are derived from research in younger populations. This "one size fits all" approach to acute pain management is problematic for elderly patients. Specifically, empirical use of analgesic medications **without dosing modification for age** can lead to excessive sedation, delirium, and respiratory complication [2].
- Elderly patients have lower analgesic requirements; sufentanil, alfentanil, remifentanil, and **fentanyl are twice as potent in elderly patients** [3]. Remifentanyl's increased potency is due to a reduction in clearance. Additionally, the elderly have an increased duration of systemic and neuraxial effects of opioids.
- The etiology of increased sensitivity to opioids and anesthetics in the elderly is multifactorial. The combination of age-related degeneration of the sensory system, altered pharmacokinetics due to decreased volume of the central compartment and decreased clearance leads altered drug potency and increased duration of action.
- Epidemiological studies show that several **chronic pain conditions are more prevalent in women than men**, including fibromyalgia, migraine, auto-immune disease, eg. Systemic lupus erythematosus, rheumatoid arthritis, irritable bowel syndrome, temporomandibular disorders, and interstitial cystitis. There is also literature to suggest that women are more likely to report pain and describe pain affecting multiple sites as compared to their male counterparts.

Pain and Aging

- Multiple retrospective studies have reported that older patients report lower postoperative pain intensity and consume lower doses of opioids following surgery. In addition, older patients report minimal pain symptoms in several acute pain conditions. Approximately 35–42% of adults over the age of 65 experi-

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ence a silent or painless heart attack [4] and report little or no pain associated with peritonitis, intestinal obstruction, pneumothorax [5], and peptic ulcer diseases [6]. This data indicates a **fundamental change in pain regulation** associating with aging.

- Morphologic studies of the peripheral nervous system have shown that aged primary afferent nociceptors undergo several degenerative changes over time, including the loss of both myelinated and unmyelinated nerve fibers.
- The sensory system undergoes significant degenerative changes as a consequence of aging. Widespread disorganization and decreased myelin thickness has been demonstrated. There is a reduction of neurochemicals that are responsible for neurogenic inflammation, lower levels of growth factors necessary for ion channel synthesis as well as decreased expression of ion channels that convert noxious stimuli into electrical signals. It is very likely that such morphologic, biochemical and molecular changes in the sensory system are attributable to age-related diminished pain sensitivity [1].
- Although the prevalence of chronic pain is higher in the elderly population, **they have less pain symptoms** compared to their younger counterparts. For example, in a study of 193,158 patients aged 65 years and older, the mean reported pain score was lower with each increment in age (5 years) for men and women [7]. Further, older elderly individuals exhibited lower levels of pain compared with the younger elderly individuals after adjusting for a variety of potential confounding variables [7].
- Elderly patients on opiate therapy for chronic pain have a **higher incidence of adverse effects**. A cross sectional study [8] found that patients on long-term opioids performed significantly worse on attention tasks and had significantly lower self-efficacy beliefs over patients not receiving opioids. In a meta-analysis, opioids have shown to reduce attention of older patients when compared with patients who do not take medication that affects the central nervous system [9]. When opioids are used together with antidepressants and/or anticonvulsants, this effect increases [9].

Gender and Pain

- Both acute and chronic pain are reported more frequently by women than men, and several chronic pain conditions (eg, migraine, fibromyalgia, irritable bowel syndrome, and temporomandibular disorders) are considerably more common in women than in men [10] with female to male ratios ranging from 2:1 to 9:1. Females report higher numeric pain scores and a have a higher incidence of severe pain events after surgery [11].
- In basic science research, sex differences in the opioid receptor density, neurotransmitters, receptors and impact on pain of sex hormones have been documented [12]. It is possible that some chronic pain conditions that are common in females are genetic, likely transmitted via sex-linked inheritance. There are also differences in the prevalence of the psychosocial contributors to pain between men and women. There is a higher incidence of depression and anxiety among women, which increases the risk for pain. Pain catastrophizing, which is associated with greater pain intensity, (See Chap. 4) is also more common in women than in men,
- The mechanisms underlying sex differences in responses to pain is not clear. Existing hypotheses include genetic differences such as cognitive-affective factors, sex hormones, anxiety/depression, and familial factors.

Clinical Pearls

- Sensory system undergoes significant degenerative changes including widespread disorganization and decreased myelin thickness, reduction of neurochemicals that are responsible for neurogenic inflammation, reduction in the expression of ion channels that convert natural stimuli into electrical signals, and reduction in the levels of growth factors necessary for the synthesis of ion channels
- Although the prevalence of chronic pain is higher in the elderly population, **they have less pain symptoms** compared to relatively younger subjects.

- Elderly patients have lower analgesic requirements after surgery. Empirical use of analgesic medications without considering age as a risk factor can lead to excessive sedation, delirium, and respiratory complication.
- Female patients tend to report more pain compared to their male counterparts.

MCQ

1. After open exploratory laparotomy, severe acute postoperative pain is uncommon in the
   A. Middle age
   B. Adolescent
   C. Women
   D. Elderly
2. Which of the following is not a cause of increased sensitivity to opioid medications in the elderly?
   A. Age related degeneration of the nervous system
   B. Increased volume of the central compartment
   C. Decreased cardiac output in some elderly patients
   D. Altered pharmacokinetics of medications
3. Which of the following is not an effect of opioids in the elderly population?
   A. Increased incidence of respiratory depression
   B. Increased duration of systemic effects
   C. Increased incidence of pruritus
   D. Increased duration of neuraxial effects
4. Regarding gender differences in pain, which of the following statement is correct?
   A. No gender difference in the prevalence of migraine and temporomandibular joint disorder
   B. Females reports lower numeric pain scores than males
   C. Females are genetically more tolerant to pain
   D. Higher pain catastrophizing is associated with greater pain intensity.

Answers

1. D, 2. C, 3. C, 4. D

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