SIGNA VITAE 2008; 3 Suppl 1: S 10 - 12

REVIEW

Analgesia and sedation in hemodynamic unstable patient

VIŠNJA MAJERIĆ KOGLER • JUDITH DEUTSCH • SANJA SAKAN

VIŠNJA MAJERIĆ KOGLER (✉) •
JUDITH DEUTSCH •
SANJA SAKAN
Department for Anesthesiology,
Reanimatology and Intensive Care
University Hospital Zagreb
Kišpatičeva 12,
10000 Zagreb, Croatia
Phone: + 385 1 2388 204
Fax: + 385 1 24 21 601
E-mail: vkogler1944@yahoo.co.uk

ABSTRACT

Pain, restlessness, tension and delirium are almost always encountered while treating hemodynamic unstable critical patients in the intensive care units. Usually in critical patients, the evaluation of the nature and pain intensity (VAS scale) are often impossible. During the last 10 years intense nociceptor somatic and visceral post operative pain is believed to be the most crucial factor in the development of endocrine and neurohumoral disorders, within the postoperative period. Chronic post operative pain is appearing often (30%-40%), with great influence on the quality of patients life. The modern principal in treating acute pain is the use of multimodal balanced analgesia approach, which is individually catered with drug and dose for each patient. Modern systemic analgesia is understood to be the continuous use of opiates or opioids, titrated towards pain intensity, with a minimum number of complications even in hemodynamic unstable patients. The combined use of opioids with NSAID and paracetamol reduces the overall dosage of opioids by 20% - 30% and therefore significantly contributes to hemodynamic and respiratory stability. Effective and safe epidural analgesia in hemodynamic unstable patients can be optimized by simultaneous use of various drugs with different mechanisms of action (local anaesthetic, opioid, adrenalin, ketamin). The accepted concept of analgosedation in critical patients is understood to be the use of short acting drugs (fentanyl, sufentanil, remifentanil, midazolam, propofol) in which drug dosage can be quickly adjusted in respect to the present clinical state of the patient.

Key words: acute postoperative pain, multimodal balanced analgesia, analgesia drugs

Introduction

Pain, restlessness, tension, and delirium are almost always encountered while treating hemodynamic unstable critical patients in the intensive care unit. Due to the critical state of these patients, symptoms are often masked and are difficult to observe and are often underestimated, not completely and without efficacy treated.

During the last 10 years intense nociceptor somatic and visceral post operative pain is believed to be the most crucial factor in the development of endocrine and neurohumoral disorders, within the postoperative period. Therefore, this period is marked by an increase in catabolism, increased secretions of stress hormones, increased stress on the cardiovascular system, pulmonary function disorders, hyper coagulative states, decreased fibrinolysis, immunosupression, paralytic ileus, and post operative nausea and vomiting. The effects of the previously mentioned events lead to a dysfunction in the homeostasis of glucose, lipid and protein metabolism.

The intensity and persistence of these dysfunctions depends upon the intensity of surgical injuries, effectiveness of treating post operative pain, and the use of numerous methods which can speed up rehabilitation of patients. (1,2)

A particular problem is the inadequate effectiveness in controlling the dynamic and static pain during thoracic surgery and the development of chronic pain syndrome with central and peripheral sensitization within the upper abdomen. Chronic post operative pain appearing often, with great influence on the quality of life in patients, is very high and accounts for about 40% of patients.

Usually in critical patients, the evaluation to the nature and intensity of pain

(VAS patient information) are often impossible. In the assessment of pain intensity we often rely on physiological clues, the development of restlessness, vegetative clues, and facial mimicry and expression (faces scale).
The modern principle in treating acute pain is with the use of a multimodal balanced analgesia approach, which is individually catered with drug and dose for each patient.

Systemic drug use

Modern systemic analgesia is understood to be the continuous use of opiates or opioids, titrated towards pain intensity, with minimal effects on patient mobilization and with a minimum number of complications. The therapeutic goals are to reach enough analgesia and patient comfort.
Opiates and opioids remain the cornerstone in treating intense postoperative pain even in hemodynamic unstable patients. However, over generalized treatment plans in prescribing drugs and inadequate individualization for each patient are often the reasons for developing cardiorespiratory complications and drug overdoses. (3,4)
Systemic intramuscular drug treatments due to the unpredictable speed of absorption, unknown start and length of effectiveness, as well as patient discomfort, are not applied in critically patients.
The most frequently used opiate analgesics within the intensive care unit are morphine, fentanyl, and sufentanyl.
In the hemodynamic unstable patient the recommended dosage of fentanyl as a bolus is 25 – 100μ g every 5 – 15 minutes until reaching the desired analgesic effect. Due to the short drug half life, a continuous infusion is recommended at 0,0125-0,1mg/h, thereafter.
The advantages of fentanyl over morphine are the reduced release of histamine and its elimination which is independent of the kidneys.
Bolus dose of sufentanyl is 0,01-0,05mg and 0,01-0,05 mg/h for continuous infusion.
Morphine intravenously causes additional vasodilatation and hypotension, due to the release of histamine. The effects in patients with damaged liver and kidney functions are pronounced and prolonged. The bolus dosage in hemodynamic unstable patients is 1 – 2 mg i.v. every 5 – 15 min. until reaching desired effects, and then there 0,01-0,10 mg/kg i.v. every 1 – 2 h.
When using patient controlled analgesia (PCA) in the hemodynamic unstable patient it is important to set the morphine limit at 1 mg at a lockout interval of 5 – 10 minutes. The usual PCA dose of fentanyl is 10 – 20 μg, at a lockout interval of 5-10 minutes.
The combined use of NSAID's and paracetamol, as long as there are no contraindications of usage, it is possible to achieve adequate analgesia for moderate pain using dosages of paracetamol (1 g per os every 6 hours for adults or 2 g rectal, and in children 40 mg/kg bolus then 20 mg/kg every 6 hours per os).
The combined use with opioids reduces the overall dosage of opiods used, by 20 – 30 %, and therefore significantly contributes to hemodynamic and respiratory stability. (5)
Non-opioid analgesic protocols which perform additively or synergistically with opiates and opioids are the following:

- Diclofenac 50 mg / 8 h i.v., orally, or rectally
- Ketoprofen 100 mg / 8 h i.v., orally, or rectally
- Ketorolac 10 – 30 mg / 8 h i.v. or orally
- Ibuprofen 400 mg / 8 h orally or rectally

In geriatric patients, the need for the use of opiates and opioids (morphine, fentanyl) are reduced two to four times, in effectively treating acute pain. The reduced requirements are unexplainable, except for the physiological changes that occur in older life years, rather than important pharmacological dynamic components.
In patients older than 75 years of age, the drug half life of tramadol is greatly increased, which greatly reduces the daily dosage requirements.
Kidney dysfunction increases risks of active metabolite build up of morphine – 6, morphine – 3 – glucorinide, normoperidine, hydromorphone – 3 – glucuronide and O desmethyltramadol. (6)
In geriatric patients, the reduction of nausea, vomiting and pruritus has been observed.
Reduced states of confusion and less cognitive dysfunction have been noted with the use of fentanyl, rather than with morphine.

Epidural analgesia

Thoracic epidural analgesia (TEA) dilates constricted coronary arteries, increases myocardial oxygenation, reduces cardiac oxygen consumption, reduces frequent ischemic coronary incidences, improves pulmonary oxygenation and overall function, and also positively influences bowel motility.
Lumbar epidural analgesia leads to the dilation of arteries in the lower half of the body, constricts coronary arteries, decreases myocardial oxygen delivery, does not improve bowel motility, and often leads to urinary retention.
From the above mentioned, it is clear to see that lumbar epidural analgesia can increase the risk of occurrence of coronary incidences.
Most authors mention the use of small volume amounts of 4 – 6 ml / h of local anesthetics, which will keep favorable hemodynamic stability. Perioperative factors which reduce venous return such as hypovolemia and vena cava compression require quick correction of hypotension with intravenous fluid volumes. Venous dilation, the result of remarkable hypotension can be reduced with the use of alpha 1 agonists, ephedrine or dopamine at a dose of 4 – 8 μg / kg / min. In patients being treated for hypertension and ischemic heart disease caution is necessary. Patients on ACE inhibitors, the hypotensive effects are great and prolonged. Positive hemodynamic outcome and moderate sympathic blockade of cardiac nerve segments (T3 – T5) results in the decrease of after load. TEA can reduce compensatory increases of heart rate with the appearance of hypovolemia.
Patients with unstable angina pectoris, TEA (T1 – T5) greatly eases the pain suffered in angina attacks while main-

taining minute heart volume, systemic vascular resistance, and coronary perfusion pressure.
Effective and safe epidural analgesia in hemodynamic unstable patients can be optimized by simultaneous use of various drugs with different mechanisms of action (a multimodal action principle).
Brevik recommends for an optimal and safe combination to use a mixture of bupivacaine 1 mg/ml, fentanyl 2 microgram/ml, and adrenalin 2 microgram/ml.
The sub anesthetic dose of bupivacaine inhibits excitatory synaptic mechanisms in specific areas of the spinal cord, while fentanyl and adrenalin inhibit pre and post synaptic opioid and alpha 2 adrenergic receptors in the posterior horn, of the spinal cord. Documented synergism using such combinations enables significant reductions of individual drug dosages, while achieving maximal results and minimal side effects.
Sufentanil is more potent than fentanyl it is well documented and approved for epidural administration.
Ropivacain is a good alternative to bupivacain and levobupivacain for hemodynamic instable patients because is less cardiotoxic.
Not only does adrenalin provide analgesic effects, but it also slows down systemic absorption of fentanyl and bupivacine, reducing their systemic side effects. (7)

Sedation

Drugs most often used in influencing the level of consciousness and memory are:
Analgesics: Morphine, Fentanyl, Petidin, Sufentanil, Remifentanil, Alfentanil
Effects: analgesia, sedation, euphoria
Hypnotics: Thiopental, Propofol
Sedatives: Benzodiazepines, Phenothiazines, Butyrophenones
The accepted concept of analgosedation in critical patients is understood to be the use of short acting drugs (fentanyl, sufentanil, remifentanil, midazolam, propofol) in which drug dosage can be quickly adjusted in respect to the present clinical state of the patient. This provides the possibility of therapeutic intervention, and as necessary the ability to neurologically assess the state of the patient.
Routine guidelines of fixed drug combinations, used continuously (midazolam, fentanyl) cause drug accumulation and overdoses, dangerous side effects (respiratory depression, hypotension) and prolonged awakening.

Benzodiazepines

The most regularly used benzodiazepines in critical patients are diazepam, midazolam, and lorazepam.
The effective bolus dose of diazepam of 2 – 6 mg can be repeated after 2 – 5 minutes. Repeating diazepam in boluses every 5 – 15 minutes provides effective sedation of agitated patients. Unfortunately, due to the lengthy drug half life, patients with liver and kidney dysfunction, sedation is prolonged, as well as unpredictable in duration. Therefore, continuous infusions are not recommended.
Midazolam boluses of 2 – 5 mg cause quick sedations of short length, but hemodynamic instability are often unavoidable. Using continuous infusions for longer than 48 – 72 hours, critical patients are unpredictable for emergence, especially when hypo albuminemia and renal insufficiency are present.
Lorazepam boluses of 1 – 4 mg every 2 – 6 hours are favorable for long term sedation, since it is not lipid soluble and does not produce active metabolites. Due to the slow appearance of therapeutic effects, it is not possible to achieve a rapid response. However, recommendation from the Society for Critical Care (2002) is to use lorazepam, as the sedative of choice, in long term sedation of critical patients.
Propofol due to its speedy effects (1 – 2 minutes) and short duration of action (2 – 8 min) is effective in controlling acute agitation, and in instances when expedite awakening is necessary. However, due to the possibility of significant hypotension and myocardial depression it is not favorable for the sedation of hemodynamic unstable patients. Elevated doses of continuous infusions (>75μg / kg / min) can cause metabolic acidosis, serious arrhythmias, and heart failure.
The use of remifentanil in small doses with midazolam or propofol, also known as analgesia basis sedation, has provided acceptable analgesia and patient comfort. In addition, adequate hemodynamic stability, duration of analgosedation, predictability of awakening, and fewer side effects have also been observed. (8)

REFERENCES

1. Kehlet H, Holte K. Effects of postoperative analgesia on surgical outcome. Br J Anaesth 2001;87:62-72.
2. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. Am J Surg 2002;183:630-41.
3. Holte K, Kehlet H. Postoperative epidural analgesia et outcome-a research agenda. In: Tramer MR, editor. Evidence based resource in anesthesia and analgesia. 2nd ed. London: BMJ Books; 2003. p. 175-83.
4. Kehlet H. Procedure- specific postoperative pain management. Anesthesiol Clin N Am 2005b;23:203-10.
5. Jorgensen H, Wetterslev J, Moiniche S, Dahl JB. Epidural local anesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV et pain after abdominal nsurgery. Cochrane Database Syst Rev 2001;CD001893.
6. Rigg JR, Jambrozik K, Myles PS. Epidural anesthesia and analgesia and outcome of major surgery: a randomised trial. Lancet 2002;359:1276-82.
7. Breivik H. Occurens of chronic pain after surgery. In: Refresher Course Lectures. Vienna: Euroanesthesia Austria; 2005. p. 231-2.
8. Park G, Lane M, Rogers S, Bassett P. A comparison of hypnotic and analgetic based sedation in general intensive care unit. Br J Anaesth 2007;98(1):76-82.