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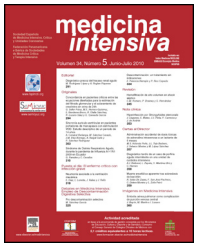

REVIEW

Indications of dexmedetomidine in the current sedoanalgesia trends in the critical patient☆

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Abstract Recently, dexmedetomidine has been marketed in Spain and other European countries. The published experience regarding its use has placed dexmedetomidine on current trends in sedoanalgesic strategies in the adult critically ill patient. Dexmedetomidine has sedative and analgesic properties, without respiratory depressant effects, inducing a degree of depth of sedation in which patients can open their eyes to verbal stimulation, obey simple commands and cooperate in nursing care. It is therefore a very useful drug in patients who can be maintained on mechanical ventilation with these levels of sedation avoiding the deleterious effects of over- or infrasedation. Because of its effects on α2-receptors, it is very useful for the control and prevention of tolerance and withdrawal to other sedatives and psychotropic drugs. The use of dexmedetomidine has been associated with lower incidence of delirium when compared with other sedatives. Moreover, it is a potentially useful drug for sedation of patients on non-invasive ventilation.

PALABRAS CLAVE
Sedación;
Dexmedetomidina;
Alfa2-agonistas;
Ventilación mecánica;
Paciente crítico

Indicaciones de la dexmedetomidina en las tendencias actuales de sedoanalgesia en el paciente crítico

Resumen Recientemente, la dexmedetomidina se ha comercializado en España y en otros países europeos. La experiencia publicada permite dar unas recomendaciones y situar este fármaco en las actuales tendencias de sedoanalgesia del paciente crítico adulto. La dexmedetomidina tiene efectos sedantes y analgésicos, sin causar depresión respiratoria, e induce un nivel de sedación donde el paciente puede abrir los ojos a la estimulación verbal, obedecer órdenes sencillas y cooperar en los cuidados de enfermería. Por tanto, es muy útil en enfermos ventilados que pueden ser mantenidos con estos niveles de sedación, evitando los efectos deletéreos de la sobresedación o la infrasedación. Por su acción sobre los α2-receptores, es eficaz en la

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prevención y en el control de los cuadros de tolerancia y/o abstinencia a otros sedantes y psicotrópicos. Comparada con otros sedantes, la dexmedetomidina se ha asociado con una menor incidencia de delirio. Además, puede ser útil en la sedación durante la ventilación no invasiva.

Introduction

Sedoanalgesia is a key element in the management of many critically ill patients, particularly those requiring mechanical ventilation (MV), and is useful for improving patient well-being, reducing anxiety and facilitating the performance of different procedures.[1] However, inadequate sedative use can cause potentially serious adverse effects.[2,3] On one hand, insufficient sedoanalgesia can give rise to serious agitation with the induction of myocardial ischemia, poor adaptation to the ventilator, or auto-extubation or catheter removal, and is associated with a prolongation of stay in the Department of Intensive Care Medicine, increased costs, greater morbidity and even mortality. On the other hand, excessive sedation prolongs the duration of MV and of patient stay in the DICM, increases the risk of complications such as ventilator-associated pneumonia or neuromuscular alterations, gives rise to a larger number of neurological diagnostic tests with the consequent risks and costs, and leads to a greater incidence of cognitive disorders[4] and even mortality.[5] Moreover, the administration of high sedative doses poses a risk of adverse and toxic effects (hemodynamic, gastrointestinal, infectious, metabolic, withdrawal symptoms, etc.).[3]

The discrepancies found in the literature regarding the recommended optimum sedation range, the variations in the methodology used to evaluate sedation, and the differences in the frequency of evaluation all make it difficult to establish the true incidence of inappropriate sedation. In this context, the published incidence of suboptimal sedation is 1–75%, and oversedation is more common than undersedation, with an estimated frequency of 33–57%.[6] In the DICM, a desirable aim of sedation is to keep the patient calm, comfortable, cooperative and communicative, with easy awakening, the capacity to interact with the healthcare personnel or relatives, and the maintenance of a normal sleep-waking cycle. However, because of their clinical condition, some patients may require deeper sedation (e.g., in situations of intracranial hypertension or acute respiratory distress syndrome).[7,8]

In order to prevent the deleterious effects of undersedation or oversedation, the administration of sedatives and analgesics should be based on an established protocol, with clearly defined sedoanalgesic objectives. Such objectives should be established according to the patient condition at the start of treatment, and must be revised on a regular basis. Collaboration of the nursing personnel is very important in this scenario, since social, personal and professional factors often influence individual interpretation of the patient needs.[9] It must be taken into account that the patient needs vary according to the clinical circumstances, and that the therapeutic objectives can change over time.[10]

Sedatives are to be adjusted to the individual needs of the patient, administering the minimum dose required to achieve the objectives. In attempting to optimize sedoanalgesia, when selecting the appropriate drug it is important to consider the specific characteristics of each agent, including the pharmacokinetics and possible adverse effects. It also must be taken into account that pharmacokinetic and pharmacodynamic alterations occur in the critical patient, secondary to an increased distribution volume, a decrease or increase in drug-binding proteins, possible receptor alterations, organ failure, etc., which modify the effects of sedatives and analgesics.

Theoretically, the ideal drug should offer rapid action, with a predictable pharmacokinetic and pharmacodynamic profile and, once suspended, it should allow fast patient physical and cognitive recovery. At present, the sedatives most commonly used in the DICM are benzodiazepines and propofol.[1] The characteristics of the benzodiazepines, including onset and duration of action, distribution, potency, and the presence or absence of active metabolites, are variable. Caution is advised when administering these drugs in continuous infusion, due to possible accumulation of the drug substance or its metabolites, which can give rise to inadvertent oversedation, the development of tolerance phenomena in a matter of hours or days, and withdrawal symptoms after prolonged use.[3,8] Propofol is the preferred sedative when rapid wakening is desired, or in neurological patients, since it allows the performance of intermittent neurological evaluations. However, its administration for long periods of time or in large doses can produce adverse effects (hypertriglyceridemia, propofol infusion syndrome).[3]

The α2-adrenergic receptor agonists, such as clonidine and dexmedetomidine (DEX), possess sedative and analgesic effects, and in some situations constitute an alternative to the aforementioned sedatives (benzodiazepines and propofol). Different authors have demonstrated the efficacy of DEX in critical patients, affording adequate sedoanalgesia and allowing a reduction of the doses of other sedatives and analgesics, and even a shortening of the duration of MV.[11–14] Since the year 1999, DEX is available in the United States and in other American countries for the sedation of ventilated patients, and is one of the most widely recommended drugs in the clinical guides of these countries.[15,16] However, DEX was only approved by the European Medicines Agency (EMA) in 2011–this representing the first step for its marketing in Spain. The cumulative experience gained with DEX allows us to make a series of suggestions regarding its current place in the sedoanalgesia of critically ill patients.

Pharmacological characteristics of dexmedetomidine

DEX is a selective α2-adrenergic receptor agonist that acts at both peripheral level and in the brain and spinal cord, with a selectivity approximately 7- to 8-fold that of