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DEXMEDETOMIDINE-INDUCED PYREXIA- A CASE REPORT

Anaesthesiology

Dr. Nirmala B. C	Professor
Dr. Uthkala Shetty	Professor
Dr. Thathi Reddy Thrinadh Reddy	Junior Resident
Dr. Liqayatul Wadud Al Hadi*	Junior Resident *Corresponding Author

ABSTRACT

Drug-induced fever presents a formidable challenge, given the array of medications capable of eliciting this response. Its prevalence is notably heightened within critical care environments, where the concurrent administration of multiple drugs is routine. This circumstance amplifies the complexity of diagnosing fevers in such settings, as each new instance could suggest either an emerging infection or a deterioration of existing health conditions. Consequently, the necessity for exhaustive investigations into fever origins arises, a process that entails significant time investment, invasiveness, financial costs, prolonged hospital stays, and heightened risks of morbidity and mortality. To illustrate this phenomenon, we delve into a documented case of Dexmedetomidine-induced fever in a critical care patient. The patient in question, a 79-year-old male, was urgently admitted under the surgical department due to an incarcerated umbilical hernia then underwent emergency Laparotomy.

KEYWORDS

INTRODUCTION

Drug-induced fevers account for approximately 3-5% of all adverse drug reactions [1]. The body's intricate temperature regulation mechanisms maintain core temperatures within a narrow range, typically between 35.3°F to 37.7°F. The hypothalamus plays a pivotal role in moderating the body's response to various fever-inducing stimuli, including pyrogens, interleukins, interferons, hypersensitivity reactions, and idiosyncratic responses [2].

Drug-induced fever manifests as a febrile reaction triggered by the introduction of a medication and typically subsides upon discontinuation of the offending drug. It often necessitates a diagnosis of exclusion, given the myriad potential causes. These may include hypersensitivity reactions to the medication, pharmacological extensions of the drug's mechanism of action, contamination of intravenous fluids or medications, presence of pyrogens in infusion sets, pyrogenic properties of certain drugs, or inflammation at the site of intravenous medication administration. Among the classes of medications frequently associated with drug-induced fever are antimicrobials, anticonvulsants, heparin, allopurinol, and biological agents.

Dexmedetomidine, a highly selective alpha-2 adrenergic receptor agonist and sympatholytic, is commonly used for light to moderate sedation via intravenous infusion in intensive care units (ICUs) [3]. Its unique pharmacokinetic profile includes a distribution half-life of six minutes, an elimination half-life of two hours, and the ability to cross the blood-brain barrier. Dexmedetomidine is favoured in ventilated patients due to its minimal respiratory depression effects compared to other sedatives, potentially aiding in early weaning and extubation. It proves beneficial in managing delirium, agitation, or non-compliance, producing sedation akin to natural deep sleep following sleep deprivation [4-5].

The sedative and sleep-promoting effects of dexmedetomidine stem from its actions on central pre- and postsynaptic α2-receptors within the locus coeruleus [4-5]. Despite its numerous benefits, there have been documented cases of drug-induced fevers associated with dexmedetomidine infusions in critical care settings, often attributed to allergic reactions. Both the FDA and dexmedetomidine labels acknowledge fever and hyperpyrexia as potential side effects [6].

Case Presentation

A 79-year-old male patient presented to the emergency department with diagnosis of an incarcerated umbilical hernia. On admission, the patient did not exhibit fever, and pre-emptive measures were taken by initiating broad-spectrum antibiotic therapy. An emergency exploratory laparotomy was subsequently performed, after which the patient was transferred to the intensive care unit (ICU) for postoperative monitoring and care.

In the ICU, the patient exhibited signs of postoperative agitation, prompting the initiation of dexmedetomidine therapy. This intervention commenced with a loading dose of 1 mcg/kg followed by a continuous intravenous infusion at a rate of 0.4 mcg/kg/hr. However, shortly after the commencement of dexmedetomidine infusion, the patient manifested a fever spike, reaching a notable temperature of 105.8°F as measured via sublingual temperature monitoring.

Given the sudden onset of fever in this context, a comprehensive diagnostic approach was undertaken to investigate potential etiologies. This included a thorough assessment of the patient's clinical status, laboratory analyses, and imaging studies. Notably, all investigations, including blood cultures, yielded results within normal parameters and demonstrated no evidence of microbial growth or infectious processes.

In response to the fever and the absence of discernible infectious causes, a series of therapeutic interventions were implemented. Firstly, the dexmedetomidine infusion was promptly discontinued. Additionally, the patient received a therapeutic dose of intravenous paracetamol (1 gram) for antipyretic effect. Concurrently, measures aimed at physical cooling were employed, including a tepid sponge bath to facilitate heat dissipation from the patient's body surface.

The collective effect of these interventions was observed over a period of approximately four hours, during which time the patient's fever gradually subsided. Ultimately, the patient's temperature normalized, indicating a successful resolution of the fever episode following the cessation of dexmedetomidine infusion and the administration of appropriate antipyretic measures.

DISCUSSION

Dexmedetomidine, a commonly used sedative in intensive care units (ICUs), has been associated with drug-induced fever in numerous documented cases, highlighting a significant drawback of its clinical application [6][7]. While dexmedetomidine offers considerable benefits in routine sedation protocols, its potential to trigger drug fever, particularly in ventilated patients, poses a diagnostic challenge that can be initially overlooked [6][7].

Our patient's case exemplifies this dilemma, compounded by the concurrent administration of prophylactic antibiotics and the myriad potential causes of fever in the ICU setting, including nosocomial infections [6][7]. In such scenarios, the consideration of drug fever often emerges as a diagnostic consideration of exclusion, following the

exhaustive exploration of other potential differentials. This sequential approach can lead to a cascade of investigations, contributing to diagnostic delays and prolonged ICU stays, each carrying its own set of challenges [6][7].

Echoing our observations are findings from studies such as Okabe et al. (2009) and Reeve and Cooper (2013), where dexmedetomidine infusion correlated temporally with fever onset, with fevers resolving upon discontinuation of the drug [6][7]. Okabe et al. reported fever onset approximately 22 hours post-infusion initiation, escalating to 40.6°C despite fever control measures, and resolving within hours of drug cessation [6]. This pattern was consistent across various studies, highlighting the importance of recognizing the temporal association between dexmedetomidine administration and fever onset, in conjunction with ruling out other potential fever etiologies [6][7].

The pharmacokinetic profile of dexmedetomidine further supports these observations, with a distribution half-life of six minutes and an elimination half-life of two to three hours in ICU patients [8][9]. This aligns with the observed resolution of fever within hours post-infusion cessation [8][9].

Despite the fever-related challenges, dexmedetomidine remains a favored sedative in the ICU due to its efficacy in facilitating early weaning from mechanical ventilation and reducing ICU lengths of stay [10]. However, it is crucial to note that fever and hyperpyrexia are listed as potential side effects on the FDA and dexmedetomidine labels [11]. To aid in diagnosing drug-induced fever, the Naranjo Scale, an Adverse Drug Reaction Probability Scale, can be utilized, assigning scores based on specific criteria to determine the likelihood of drug causality [2][12].

CONCLUSION

It's important to think about drug-induced fevers, especially when starting medications like dexmedetomidine in the ICU that can cause fevers. Dexmedetomidine is often used because it's better than other sedatives like propofol and benzodiazepines, but it can still lead to fevers. Being aware of this can help us avoid unnecessary tests, treatments, and longer stays in the ICU, which can be costly and increase the risk of complications.

We should consider stopping dexmedetomidine first if a patient develops a fever, rather than waiting until we've ruled out other causes. This can save time, money, and reduce the patient's discomfort. It's a reminder that we may need to update our guidelines for managing fevers in critical care to improve patient care overall.

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