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ORIGINAL

Hemodynamic and antipyretic effects of paracetamol, metamizol and dexketoprofen in critical patients☆

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KEYWORDS
Fever;
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Abstract
Background: The objective was to study the antipyretic and hemodynamic effects of three different drugs used to treat fever in critically ill patients.
Methods: Design and setting: Prospective, observational study in a 16-bed, general ICU of a university hospital. Patient population: We studied 150 patients who had a febrile episode (temperature >38° C): 50 received paracetamol, 50 metamizol and 50 dexketoprofen. Interventions: None. Body temperature, systolic, diastolic and mean arterial pressure, heart rate, central venous pressure and oxygen saturation were determined at baseline and at 30, 60 and 120 minutes after infusion of the drug. Additionally, we recorded temperature 180 minutes after starting drug infusion. Diuresis and the need for or change of dose of vasodilator or vasoconstrictor drugs were also recorded.
Results: Patient characteristics, baseline temperature and hemodynamics were similar in all groups. We observed a significant decrease of at least 1 °C in temperature after 180 minutes in 38 patients treated with dexketoprofen (76%), in 36 with metamizol (72%), and in 20 with paracetamol (40%) ($p < 0.001$). After 120 minutes, the mean decrease in mean arterial pressure was 8.5 ± 13.6 mmHg with paracetamol, 14.9 ± 11.8 mmHg with metamizol, and 16.8 ± 13.7 mmHg with dexketoprofen ($p = 0.005$).
Conclusions: Dexketoprofen was the most effective antipyretic agent at the doses tested. Although all three drugs reduced mean arterial pressure, the reduction with paracetamol was less pronounced.

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PALABRAS CLAVE
Fiebre;
Paciente crítico;
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Efectos hemodinámicos y antipiréticos del paracetamol, metamizol y dexketoprofeno en pacientes críticos

Resumen
Objetivo: El objetivo fue estudiar los efectos antipiréticos y hemodinámicos de 3 fármacos diferentes utilizados para tratar la fiebre en pacientes críticos.
Material y método: Diseño: estudio prospectivo, observacional, en una UCI de 16 camas de un Hospital Universitario. Pacientes: 150 pacientes que tuvieron un episodio febril (temperatura > 38° C). Intervención: 50 recibieron paracetamol, 50 metamizol y 50 dexketoprofeno. Se determinaron la temperatura axilar, presión arterial sistólica, diastólica y media, frecuencia cardíaca, presión venosa central y saturación de oxígeno, en situación basal y a los 30, 60 y 120 minutos tras la administración del fármaco. También se registró la temperatura a los 180 minutos después de haber iniciado el fármaco. La diuresis y las necesidades de tratamiento vasodilatador y vasoconstrictor durante el tratamiento también se registraron.
Resultados: Las características de los pacientes, la temperatura y la hemodinámica basal fueron similares en todos los grupos. Observamos un descenso significativo de al menos un grado en la temperatura después de 180 minutos en 38 pacientes tratados con dexketoprofeno (76%), en 36 con metamizol (72%), y en 20 con paracetamol (40%) ($p < 0{,}001$). Después de 120 minutos, la media del descenso de la presión arterial media fue de $8{,}5 \pm 13{,}6$ mmHg con paracetamol, $14{,}9 \pm 11{,}8$ mmHg con metamizol y $16{,}8 \pm 13{,}7$ mmHg con dexketoprofeno ($p = 0{,}005$).
Conclusiones: Dexketoprofeno fue el fármaco antipirético más efectivo, a las dosis estudiadas. Aunque los 3 fármacos redujeron la tensión arterial media, la reducción con paracetamol fue menos pronunciada.

Introduction

Fever is common in critical patients, and is observed in 90% of all septic patients.[1,2] A febrile episode may be of infectious or non-infectious origin. Pneumonia, sinusitis and bacteremia (primary or catheter-related) are the most frequent infectious causes of fever, while the non-infectious origins include cancer, drugs, transfusions and allergic reactions.[3]

The initial management of fever includes treatment of the cause and the administration of antipyretic (fever-lowering) drugs. Antipyretic treatments are effective in lowering temperature, but can have important side effects.[4] Such drugs should not be used on a routine basis in the Intensive Care Unit (ICU). The risks and benefits should be evaluated individually in each fever episode. Paracetamol is simple to administer and is safe, with a high therapeutic index and a low risk of side effects in the form of renal, gastrointestinal or hematological disorders.[5] Metamizol in turn is usually used to treat postoperative pain and fever. Dexketoprofen is a water-soluble salt of ketoprofen, a dextrorotary enantiomer belonging to the group of nonsteroidal antiinflammatory drugs (NSAIDs). It is used as an analgesic and antiinflammatory agent, and *in vitro* constitutes one of the most potent inhibitors of prostaglandin synthesis.[6] To date, the antipyretic effect of dexketoprofen has only been described in animal models.[7] This drug substance has been compared with other NSAIDs in the management of postoperative pain. It appears to be better tolerated than other NSAIDs,[8] but its antipyretic effect and hemodynamic profile in critical patients have not been described.

The present study compares the antipyretic and hemodynamic effects of paracetamol, metamizol and dexketoprofen–the main drugs used to treat fever in critical patients.

Patients and methods

A prospective observational study was carried out in the 16-bed ICU of a University hospital between 2005 and April 2007, involving 150 patients with an episode of fever (over 38 °C) which the supervising physician decided to treat using one of the three drugs employed in the Unit for this purpose. Each patient was included in the study only once. The decision to treat was established in each patient based on the clinical repercussions of fever: tachypnea, tachycardia, changes in blood pressure and increased production of carbon dioxide or oxygen consumption. The antipyretic treatments commonly used in our Unit for fever are paracetamol 1000 mg, metamizol 2000 mg and dexketoprofen 50 mg – all administered as an intravenous infusion during 30 minutes. An ethics committee of our hospital approved the study without the need for informed consent. The following variables were monitored at baseline (immediately prior to the start of treatment) and 30, 60 and 120 minutes after infusion of the drug: axillary temperature, systolic blood pressure, diastolic blood pressure, mean blood pressure (MBP), heart rate (HR) and oxygen saturation ($SatO_2$) measured by pulsioximetry. Temperature was monitored 180 minutes after infusion of the drug to determine a decrease of at least 1 °C. Blood pressure was recorded using an invasive system in those patients in which such a system was already in place, based on a femoral or radial arterial catheter, and noninvasively using a digital arm sphygmomanometer in the rest of the cases.