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Dexmedetomidine in Sepsis

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Abstract

Activation of adrenergic alpha-2 receptors causes hypotension, bradycardia, sedation, arterial and venous vasoconstriction, decrease in presynaptic transmitter release, thrombus stabilization, hypothermia, decrease in gastric acid secretion and motility, inhibition of lipolysis, inhibition of insulin release from pancreas. It has been determined that it reduces short-term mortality without affecting İntensive care stay. It is stated that the number of clinical studies is insufficient and further studies are required.

Keywords: Dexmedetomidine; Sepsis; IL6

Mini Review

Activation of adrenergic alpha-2 receptors causes hypotension, bradycardia, sedation, arterial and venous vasoconstriction, decreased presynaptic transmitter release, thrombus stabilization, hypothermia, decreased gastric acid secretion and motility, inhibition of lipolysis and insulin from pancreas [1]. Endogenous noradrenaline release increases due to increased sympathetic activity in septic shock. According to the hypothesis of Pichot et al., Blinding of sympathetic activity with an alpha-2 agonist in septic shock improves vascular reactivity by creating alpha-1 receptor upregulation and thereby decreases the need for vasopressors [2]. It has been found that the response to norepinephrine decreases with the application of lipopolysaccharide in rats, and administration of alpha-2 agonists increases this response [3].

In human whole blood cultured with lipopolysaccharide, dexmedetomidine suppresses the release of tumor necrosis alpha (TNF-α) interleukins 6 and 8 (IL-6, IL-8), high mobility group box 1 (HMGB-1), and this effect is reversed with yohimbine. respectively. It has been reported that dexmedetomidine is suppressed by alpha-2 adrenergic receptors on the production of proinflammatory mediators [4]. HMGB-1 is a proinflammatory mediator closely associated with mortality in septic patients. Dexmedetomidine has been found to inhibit the translocation of HMGB-1 from nucleus to cytoplasm and HMGB-1 mRNA expression in lipopolysaccharide-activated macrophages [5]. Dexmedetomidine has been found to decrease mortality and decrease serum IL-6 and TNF-α levels in the experimental sepsis model and decrease HMGB-1 mRNA in the lung [6]. Dexmedetomidine has been reported to reduce acute kidney damage due to lipopolysaccharide in septic rats. In this study, plasma creatinine, IL-6 and 8, TNFα and HMGB-1 levels were found to be significantly lower in the dexmedetomidine group [7]. Dexmedtoimide has been found to significantly reduce mortality and pulmonary inflammation in septic rats and inhibit toll like receptor / myeloid differatiation factor 88 (TLR-4 / MyD88) expression and nuclear factor kap B (NFkB) activation. Dexmedetomidine has been reported to reduce mortality and lung inflammation by suppressing the TLR-4 / MyD88 / NFkB pathway [8]. Dexmedetomidine reduces TNF-α and IL-6 levels in septic rats bronchoalveolar lavage fluid and plasma, and inhibits TLR-4 and MyD88 expression in mRNA and inhibits extracellular signal-regulated kinase 1/2 phosphorylation (ERK1 / 2) and NFkB activation in lung tissue. is shown [9].

Dexmedetoimidine has been shown to activate the cholinergic anti-inflammatory pathway linked to alpha7 nicotinic acetylcholine receptors [10,11]. The spleen plays an important role in the neural cholinergic anti-inflammatory pathway. Dexmedetoimide has been shown to decrease NFkB activation due to lipopolysaccharide in septic rats and reduce TNF-α and IL-6 production at the level of mRNA in the spleen [12]. Atakan et al. Examined the effects of dexmedetomidine on liver histopathology in the model of sepsis in rats [13]. They found that hepatic central venous congestion, congestion and dilatation in hepatic sinusoids, and inflammation in the portal area were significantly lower in the dexmedetomidine + sepsis group compared to the sepsis group. It has been reported that dexmedetomidine is an option to prevent liver dysfunction due to sepsis [14].

The effects of propofol and dexmedetomidine on inflammatory response and intraabdominal pressure in patients with severe sepsis after abdominal surgery were compared. TNF-α and IL-1 and 6 and intraabdominal pressure were found to be significantly lower at the 24th and 48th hours compared to the propofol group in the dexmedetomidine group [15]. The

effects of dexmedetomidine on survival in septic patients were investigated by systematic review of 6 studies involving 242 patients. Dexmedetomidine has been found to reduce short-term mortality without affecting the length of stay in intensive care. They stated that the number of clinical studies is insufficient and further studies are required [16]. Clinical studies are needed to examine the effects of dexmedetomidine on survival, organ functions and vasopressor requirement in sepsis.

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