Impact of Erythropoietin on Arterial Hypertension

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Abstract

Cardiovascular and renal diseases constitute two pathophysiological contexts of progressive fatal recognitions worldwide and as priorities in terms of health in its entirety. Erythropoietin is a glycoprotein hormone which produces red blood cells, which carry oxygen in the blood. The objective was to know the most prevalent modifiable risk factors found in arterial hypertension, since this disease is the third cause of death in the world, the bibliographic search and the inductive-deductive method were used. The result was that treatment with recombinant human erythropoietin-stimulating agents is considered effective in improving the management of anemia associated with chronic kidney disease, since it has cardioprotective, renoprotective and neuroprotective functions.

Introduction

Cardiovascular, renal, and other immunosuppressive diseases are among the main reasons for death and morbidity in the world today (Gómez et al., 2019). The main function of the cardiovascular system is the supply of oxygen. Atherosclerosis is a disease linked to insufficient oxygenation in the tissues that can increase the risk of cardiovascular events, whether they are myocardial infarction or stroke (Tanaka & Eckardt, 2018). Erythropoietin (EPO) is a glycoprotein of 165 amino acids that is synthesized in hypoxic growth conditions, for which it is the only hematopoietic growth factor that is regulated by hypoxia, which is the decrease in oxygen in the blood induced by the synthesis of EPO by peritubular cells of the kidney (Kaufner et al., 2020). Just as it indirectly regulates oxygen levels by controlling the production of new red blood cells through erythropoiesis (Brar et al., 2021).

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Materials and Methods

A bibliographic search related to the effects of erythropoietin on blood pressure was carried out, in addition to the inductive, deductive and analytical methods.

Results

Hypertension (HBP) is defined as a sustained elevation of blood pressure above normal limits, being a silent disease that can cause apparent symptoms, although it can cause lesions in the target organs that are involved in the blood pressure (BP) control (BTA, 2020). Patients with AHT show elevated serum levels of various pro-inflammatory cytokines such as the interleukin IL-17A produced by TCD4+ (Th17) lymphocytes. Its main function is defense against pathogens in infectious, inflammatory, and autoimmune diseases (Maiese et al., 2004; Nekoui & Blaise, 2017). The changes induced by IL-17A in small arteries could be responsible for the increase in BP, which demonstrates a new mechanism with which IL-17A could contribute to the development of hypertension (Rodrigues et al., 2021).

The kidneys are a key organ for the regulation of BP and a target for the actions of IL-17 since, from physiology, the little elimination of salt and water by the kidney can already raise BP levels (Rodrigues et al., 2021). The kidney is responsible for the synthesis of EPO, which is because 20% of the blood from the heart goes to the kidney and the partial pressure of oxygen in the renal tissue drops to 50mmHg to 5mmHg from the cortex to the medulla (SEQCML, 2021). The pathogenesis of AHT associated with treatment with recombinant human erythropoietin (rHuEPO) is not well understood, but increases in peripheral vascular resistance have been described, presenting mechanisms for the treatment of (rHuEPO), which are shown in Figure 1.

rHuEPO has become the most therapeutically used cytokine in the world due to the success obtained in patients with end-stage renal failure due to its usefulness in therapies, it can also improve anemia in pediatric and neonatal patients, which led to a significant reduction in the number of transfusions and in exposure to donors (Ozkurt et al., 2018). EPO can cause an increase in blood pressure; the mechanisms of this effect are not entirely clear. By optimizing dialysis treatment, paying close attention to volume regulation, administering EPO subcutaneously, and in a manner that gradually increases hematocrit, the occurrence of increases in blood pressure can be minimized. Hypertension has not been shown to be a serious general problem in the patient treated with EPO (Gradman et al., 2010; Kumar, 2013).

Structure and physiology of human erythropoietin

Erythropoietin (EPO) is a class I cytokine of a pleiotropic and proangiogenic nature that exerts protective effects on multiple organs of non-hematopoietic origin (Takagi et al., 2007; Katavetin et al., 2007). It is also a glycoprotein hormone that acts as a primary regulator of erythropoiesis. EPO binds to two identical receptors (EPOR) that exist as homodimers. Two molecules of Janus kinases 2 (JAK2) tyrosine-kinase, which are in contact with the cytoplasmic region of the EPO receptor that are activated channeling of various transduction signals.

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Hypertension as a side effect of EPO or its stimulating agents (ASE)

Cloning of human erythropoietin (EPOHuR) is a side effect of HTN since it is associated with polycythemia. EPOHuR administration increases peripheral vascular resistance and decreases cardiac output; all this due to an increase in endothelins, angiotensin, ineffective relaxation of the vascular endothelium, alteration of calcium levels in the smooth muscle tissue of the vascular endothelium and the release of serotonin by platelets (Ozkurt, et al., 2018).

ASE treatment causes a worsening of BP in 30% of patients. In Germany, a study was carried out in which an intensive antihypertensive therapy regimen was used with maximum doses of beta-blockers, angiotensin II blockers and ACE inhibitors, which achieved normal BP measurements before the start of renal replacement therapy sessions. The results showed that the normalization of serum hemoglobin levels was accompanied not only by a lack of increase in BP, but also by a decrease in its values (Vittori et al., 2016).

The antihypertensive effect of EPO may be independent of the hematopoietic effect, where there are specific sites in the EPO molecule that determine this hypertensive effect, which allows the creation of animal genetic models that eliminate this effect while preserving hematopoietic action (Vittori et al., 2016).

Erythropoietin protects renal tissue against hypertension by preventing apoptotic effects. EPO is an ideal treatment for patients with anemia and kidney failure, which positively influences cardiac function and allows regression of cardiac hypertrophy (Staessen et al., 2003; Chiong et al., 2008). EPO can cause an increase in blood pressure, by paying close attention to volume regulation, administering EPO subcutaneously, and in a manner that gradually increases the hematocrit, the occurrence of BP increases can be minimized. Hypertension has not been shown to be a serious general problem in patients treated with EPO.

Conclusion

Treatment with recombinant human erythropoietin-stimulating agents is considered effective in improving the management of anemia associated with chronic kidney disease.

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References


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