



## LETTER TO THE EDITOR

### **Hormonal stress and susceptibility to hematological diseases: impact of cortisol and catecholamines**

*Estrés hormonal y susceptibilidad a enfermedades hematológicas: impacto del cortisol y las catecolaminas*

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#### **Dear Director:**

Chronic stress has become an underestimated risk factor in the development and progression of various diseases, including hematologic diseases. <sup>(1)</sup> Hormones such as cortisol and catecholamines (adrenaline and noradrenaline), released in response to stress, exert profound effects on the immune system and blood homeostasis. Recent studies suggest that prolonged dysregulation of these hormones may predispose to disorders such as anemia, thrombocytopenia, leukemia, and lymphomas. <sup>(2-4)</sup> This letter seeks to discuss the pathophysiological mechanisms and clinical implications of this relationship, based on current scientific evidence.

#### **HPA Axis and Cortisol: Immunosuppression and Hematopoietic Disorders**

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Cortisol, released by activation of the hypothalamic-pituitary-adrenal (HPA) axis, has biphasic effects: in acute cases, it modulates inflammation, but in chronic excess, it suppresses immune function. Elevated cortisol levels have been observed to reduce the proliferation of B and T lymphocytes, impairing surveillance against malignant cells. Furthermore, it inhibits erythropoiesis by suppressing erythropoietin production, which could explain its association with anemia in patients with prolonged stress. <sup>(5)</sup>

## **Catecholamines and Their Role in Hematologic Progression**

Catecholamines, key mediators of the "fight-or-flight" response, alter the bone marrow microenvironment through adrenergic ( $\beta_2$ ) receptors. Chronic activation of these receptors promotes oxidative stress in progenitor cells, increasing DNA mutations. <sup>(5)</sup> Research such as that by Zhang R et al. <sup>(6)</sup> demonstrated that adrenaline accelerates the proliferation of pre-malignant leukemic cells in mouse models. Furthermore, noradrenaline increases the expression of proinflammatory cytokines (IL-6, TNF- $\alpha$ ), creating a favorable niche for the metastasis of hematologic malignancies.

## **Interactions with the Immune System**

Hormonal imbalance due to stress distorts neutrophil and macrophage activity, promoting opportunistic infections that complicate existing hematological diseases. Patients with lymphoma and high stress show a decreased response to monoclonal antibody therapies, possibly due to the downregulation of cortisol-induced apoptosis genes. <sup>(6)</sup>

Given this evidence, integrating multidisciplinary approaches is crucial. Stress management techniques (mindfulness, aerobic exercise) could reduce cortisol levels and improve chemotherapy outcomes. Furthermore, the use of beta-blockers (such as propranolol) is being investigated as an adjuvant to mitigate the protumor effects of catecholamines. It is urgent to include psychological and endocrine assessments in the standard management of hematological patients. The impact of hormonal stress on hematopoiesis and oncogenesis is an emerging field that requires further research.

Recognizing these mechanisms not only broadens our pathophysiological understanding but also opens the door to innovative interventions. The medical community must prioritize holistic strategies that address both biological and psychosocial factors in these diseases.

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**EJZA:** conceptualization, research, methodology, project administration, validation, original draft writing, review, editing.

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