Preface

Modern Critical Care Endocrinology and Its Impact on Critical Care Medicine

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Editor

Endocrinology and issues related to the role of hormones in critical care medicine remain a dominant component of physiologic investigations, pathophysiologic manipulation, and treatment in patients admitted to intensive care units (ICUs) worldwide. As an example, only in the last 12 months, three major multicenter phase 3 randomized controlled trials (RCTs) have been published, which involved the assessment of hormonal therapy (hydrocortisone and angiotensin II) in patients with septic shock.^{1–5}

However, until now, there has not been any dedicated attempt to introduce critical care physicians to modern ideas and recent evidence in this rapidly evolving field. This issue of *Critical Care Clinics* aims to do just that, by taking clinicians into a critical care endocrinology world many would not be familiar with. Yet, this is a world that brings important new pathophysiologic insights and promising new therapies into the field. Such insights and therapies should already shape the practice of intensive care medicine and may well shape much of the future treatment of our patients.

For the purpose of this issue, we have specifically chosen aspects of critical care endocrinology that have seen major changes in our understanding of how specific hormones work, how disorders of hormonal function should be diagnosed, and how hormones should be used for therapy in the ICU. We have started from issues related to the inadequate and/or excessive antidiuretic hormone secretion (ADH),⁶ where modern endocrinology has delivered new diagnostic tools to our understanding of ADH (vasopressin) pathophysiology and where RCTs have provided new information about its use in septic shock⁷ and the possible beneficial renal effects of ADH in this setting. We have then focused on emerging evidence for the possible role of hormone therapy in the management of trauma.⁸ However, the most dramatic new entrant in critical care endocrinology has been the arrival of angiotensin II therapy and its Food and Drug

Administration approval as therapeutic agent after the completion and publication of the ATHOS-3 trial.⁹ Accordingly, two articles in this issue are dedicated to angiotensin II. One is focused on new insights into the physiology and pathophysiology of angiotensin II, angiotensin-converting enzyme (ACE) and ACE2, and the growing family of angiotensin hormones.¹⁰ The other is focused on its use for the treatment of vasodilatory shock.¹¹ Given the approval of this agent for the treatment of refractory vasodilatory shock, such articles are mandatory reading for critical care physicians. Similarly, a reassessment of another treatment of septic vasodilatory shock comes from the ADRENAL and APROACCHSS trials,^{1,3} which together randomized more than 5000 patients with septic shock. In this issue, the primary investigators of the ADRENAL trial review the powerful evidence derived from such studies and highlight their implications for clinical practice.¹²

The interaction between hormonal therapy and trauma is further developed in an article dedicated to the therapeutic potential and RCT data regarding erythropoietin (EPO) therapy for trauma and traumatic brain injury, where strong biological data, RCT-derived data, and meta-analytical data show a clear signal that EPO treatment might increase survival in trauma patients.¹³

The management of hyperglycemia in critically ill patients has been a major field of investigation for almost two decades, with multiple studies and several major RCTs. However, the field is now focusing on diabetic patients as a unique group of critically ill patients where the lessons learned from undifferentiated cohorts of critically ill patients may not apply, especially when preadmission glycemia (assessed by HbA1c levels) has been poorly controlled.^{14,15} In this group of patients, permissive hyperglycemia may be both a rational approach and one capable of delivering significant benefits.¹⁵ This is especially true as new technologies of semicontinuous glucose monitoring are becoming available for diabetic patients.¹⁶ This controversial but rapidly evolving area is reviewed in a dedicated article.¹⁷ However, these are not the only changes sweeping through the world of diabetes management. Several large RCTs have now established the potential for novel oral hypoglycemic agents to modify the risk of major adverse clinical outcomes in patients with diabetes. In particular, two classes of agents have now become widely used as a result of such trials: the sodium-glucose 2 cotransporter inhibitors (so called “flozins”) and the dipeptidyl peptidase-4 inhibitors (so-called “gliptins”). These new drugs and the evidence behind their use are presented in this issue,¹⁸ together with a review of a new class of hormones (the “incretins”)¹⁹ that appear to have a powerful role in regulating glucose absorption and blood glucose concentration.²⁰

Other areas of ICU endocrinology are rapidly expanding. The regulation of disturbed sleep and the prevention of delirium have become major priorities in the care of ICU patients. Accordingly, the use of melatonin and melatonin receptor agonists has grown and has attracted attention as a novel pharmacologic development in intensive care treatment.²¹

Novel insights into the regulation of iron movement in and out of cells and the role of iron as a catalyst for oxygen radical species generation have led to renewed interest in hormones that regulate its extracellular availability. Of these, hepcidin, the master regulator of iron fluxes, is the most important. Its role in physiology and pathophysiology and the potential for its therapeutic effects are a crucial new development of great interest to ICU clinicians.²²

Finally, studies on the role of thyroid hormones²³ in the ICU, hormonal manipulation of organ donors,²⁴ and hormonal manipulation to prevent post-ICU accelerated osteoporosis²⁵ have markedly expanded our understanding of their pathophysiology and therapeutic potential. The implications of such new insights are reviewed in three key articles in this issue.

In summary, critical care endocrinology is a fundamental area of intensive care practice and is rapidly expanding in its knowledge base and therapeutic implications. Critical care physicians have a unique opportunity to update their knowledge and understanding through this dedicated issue of *Critical Care Clinics*. I am sure they will find it stimulating, provocative, and with multiple implications for their clinical practice.

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