Ratiocination of ratios in endocrinology

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Abstract

Endocrinology is an ever-evolving almanac of science. Precise measurement of hormones and associated analytes are necessary to practice endocrine medicine. As the endocrine system depends upon feedback and cross-talk between various glands and hormones, it makes sense to assess ratios or proportions of related hormones. We review the ratiocination, or rationale, of ratios which have diagnostic and therapeutic utility in endocrine praxis.

Keywords: Feedback inhibition, hormonal assays, pituitary, thyroid, adrenal.

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Introduction

Endocrinology, the science of hormones, often depends on precise measurements of hormones and chemicals in blood and body fluids. These measurements are essential for screening, diagnosis, risk stratification, and disease monitoring. The endocrine system is regulated by various feedback mechanisms, and interpreting hormonal reports involves considering them in conjunction with each other. A single report of a hormone such as aldosterone or cortisol may not provide sufficient information for clinical decision making.[1,2] Analyzing these reports in conjunction with their antipodal counterparts provides a more nuanced understanding of the clinical status. At times products of two substances like calcium and phosphate may be more relevant. Despite this, the use of ratios is not common in endocrine practice. In this article, we share some ratios that may be pertinent, and offer ratiocination for them. "Ratiocination" refers to the process of logical reasoning or methodical thinking and is as a key aspect of endocrine care.

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Feedback and crosstalk

The functioning of the endocrine system is characterized by feedback and cross talk. While negative feedback operates in most hypothalamic-pituitary-organ axes, there are a few instances of positive feedback as well. These include the luteinizing hormone (LH) surge in ovulation, the effect of oxytocin on uterine contractions during parturition, and the role of prolactin on lactation. Cross-talk occur in other instances e.g. prolactin and growth hormone (GH).[3] At the same time, there are many aspects of endocrine regulation that are still not fully deciphered. Examples include the regulation of dehydroepiandrosterone (DHEA), and the pulsatility of gonadotrophin releasing hormone (GnRH).[4]

Advantage of ratios

In endocrinology, ratios are sometimes used to assess the balance or relationship between different hormones or substances within the body. Assessing endocrine function through ratios helps us understand physiology and pathology through a broader prism. This helps to gain insight about the etiology of a disease, its severity and its progress. It may also assist in reaching therapeutic decisions. From a larger perspective, ratios help the learner appreciate the interrelated character of the endocrine system. These ratios should be interpreted in the context of a comprehensive assessment of clinical and laboratory findings. The interpretation of ratios may vary based on individual patient characteristics and specific clinical scenarios.

Classification of ratios

One may classify hormones in various manners, according to chemical structure, the source of secretion, or their mode of action. Ratios, too, can be grouped in a systematic manner. We strongly suggest that ratios be assessed as per Table 1. While some ratios reflect a feedback relationship such as aldosterone-renin, others compare hormones secreted from the same gland such as different pituitary hormones. Sometimes ratios explore two seemingly diverse glands such as testosterone-cortisol ratio, and seek to unify endocrine functioning. Finally, comparison of hormones (cortisol) or substances (e.g. calcium) to creatinine in urine provides a more accurate estimation of their excretion.

Table: Ratios in endocrinology.

FEEDBACK-RELATED
• Adrenocorticotrophic hormone: cortisol
• Aldosterone: renin
SINGLE GLAND-RELATED
• Cholesterol ratios
• Estrogen: progesterone
• Luteinizing hormone: Follicle stimulating hormone
• Free T3: Free T4
• Insulin: C peptide
• Insulin: Glucagon
• Adrenal venous sampling
DUAL GLAND-RELATED
• Testosterone: cortisol
EXCRETION-RELATED
• Cortisol: creatinine ratio
• Calcium: creatinine ratio

Use in diagnosis

Some ratios may help in screening and diagnosis of endocrine syndromes. The LH-follicle stimulating hormone (FSH) has been traditionally used for diagnosis of polycystic ovary syndrome (PCOS).[5] Aldosterone-renin ratio is the screening modality for primary hyperaldosteronism.[6] An elevated alpha-subunit-thyroid stimulating hormone ratio is used for diagnosing thyrotropinoma.[7] Elevated serum testosterone-dihydrotestosterone is diagnostic of 5-alpha-reductase type 2 deficiency.[8] An elevated triiodothyronine (T3)-thyroxine (T4) ratio is suggestive of Graves' disease where as a lower ratio indicates possibility of thyroiditis.[9]

The lateralization of the tumour can be achieved by comparing hormones from bilateral samples of inferior petrosal sinuses and adrenal veins. Ratios such as those used in lipidology contribute to risk stratification of patients. This allows for appropriate counselling and care of persons with, or at risk of, coronary artery disease.

Use in choosing treatment

Insulin : C-peptide and insulin: glucagon ratio can help in diagnosing the predominant pathophysiology of diabetes, and in choosing appropriate therapy.[10] The renin-aldosterone phenotype in African-Americans predict their sensitivity to thiazide diuretics.[11]

Hormonal ratios as non-endocrine markers

Testosterone-cortisol ratio could be a marker of social aggression.[12] This ratio is also used to monitor health and functionality of elite athletes. Alterations in cortisol-dehydroepiandrosterone-sulphate (DHEAS) ratio are associated with psychiatric disorders.[13] A link between cardiovascular disease-related mortality and testosterone-estrogen ratio in men have also been demonstrated.[14]

Limitation of ratios

While the measurement of ratios is subject to the same limitations as measurement of single hormones, their interpretation must be done with caution. Though we continue to view endocrine physiology as a linear or binary construct, there are multiple factors that influence it. The concepts of quantum endocrinology or endocrine entanglement try to rationalize this situation[15]. Hormonal ratios should not be viewed in isolation, rather, they should be taken as an adjunct to clinical evaluation.

Summary

Science is characterized by change. As our tools of diagnosis such as hormonal assays- improve, so does our interpretation of the same. A fresh look at the ratiocination of ratios used in endocrinology will help us enhance our understanding of the subject, and the quality of care we offer our patients.

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