LEAD: 61.7%). Out of participants in both studies who used concomitant oral medication with LAN, this was commonly indicated for cardiovascular disorders including: renin-angiotensin agents (PRIMARYS: 33.3%; LEAD: 45.8%); antithrombotic agents (PRIMARYS: 10.7%; LEAD: 19.6%); beta-blocking agents (PRIMARYS: 22.7%; LEAD: 19.6%) and calcium channel blockers (PRIMARYS: 16.0%; LEAD: 22.4%). Diuretics (PRIMARYS: 16.0%; LEAD: 20.6%) and lipid modifying agents (PRIMARYS: 20.0%; LEAD: 39.3%) were also common concomitant oral medications, as were medications used in diabetes (PRIMARYS: 17.3%; LEAD: 20.6%) and for thyroid therapy (PRIMARYS: 28.0%; LEAD: 31.8%).

Conclusions: In this analysis, most patients with acromegaly receiving LAN, regardless of prior therapy, used ≥1 concomitant oral medication. An awareness of the ongoing burden of comorbidities requiring oral medications should help physicians in managing acromegaly.

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Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY BASIC RESEARCH ADVANCES

FOXA2 as a Candidate Gene Responsible for Congenital Panhypopituitarism: A Review of the Literature

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The pituitary gland produces hormones that regulate multiple functions including growth, metabolism, reproduction, and homeostasis. Thus, congenital hypopituitarism (CH) can have profound and widespread repercussions on physiological balance. Recent research identified the forkhead box A2 transcription factor (FOXA2) *as* a candidate gene responsible for CH. We sought to review the literature for mouse models and case reports describing *FOXA2* mutations, to shed more light on the potential role of this gene in CH. Using a pretested search strategy, we searched the PubMed database, including in the review only original research articles reporting *FOXA2* gene mutations in mouse models and human case reports. A total of 10 studies reporting different *Foxa2* mutations in mouse models were included. These works described the involvement of *Foxa2* in the regulation of murine organogenesis. *Foxa2* was found to participate in the development of ventral midline structures and endodermal-derived organs. In addition, when mutated, it was found to determine defects in node, notochord and the neural tube, precursors of the pituitary gland. *Foxa2* was also found to have important effects on glucose homeostasis and its deficiency is characterized by hyperinsulinemic hypoglycaemia. Regarding human case reports, a total of 5 cases describing nonsynonymous missense mutations of *FOXA2* were identified. All mutations were localized in the DNA binding domain, which might regulate the expression of tissue-specific genes important for cell differentiation. Panhypopituitarism was a prominent feature among the cases as well as hypoglycaemia in infancy with abnormal glucose homeostasis later in life. Additional 6 cases describing patients with varying deletions of 20p11.2 that encompasses *FOXA2* were selected. In addition to panhypopituitarism, the patients were found to have several other dysmorphic features, affecting the face as well as the cardiac, gastrointestinal and genital systems. Authors proposed a region of approximately 1.35 Mb that covers around 17 genes, among which *FOXA2,* as the critical region associated with hypopituitarism. However, the other genes also deleted from this region are associated with the development of the central nervous system and the pancreas and may be responsible of the observed phenotype of these patients. Considering this evidence, *FOXA2* seems to be a strong candidate for CH. However, further research is required to elucidate its involvement in pituitary development, as well as the genetic cause that drive *FOXA2* haploinsufficiency in determining CH.

Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY BASIC RESEARCH ADVANCES

In Silico Perspectives on Gonadotropin Crosstalk

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The pivotal role of the gonadotropins (GtHs) luteinizing hormone (LH) and follicle stimulating hormone (FSH) in vertebrate reproduction is well documented. LH and FSH bind to the leucine-rich repeats of the extracellular domains of their cognate receptors (R) in the gonads to actuate steroidogenesis and gametogenesis. Though these GtHs specifically bind only to their cognate receptors in mammals, this interaction becomes inconsistent in the case of fish. Whilst in some fish species the gonadotropins show receptor specificity much like their mammalian homologs, FSH and LH have demonstrated mutual and/or singular cross-activation of the FSH and/or LH receptors in several fish species. These complications regarding receptor specificity are further magnified by cross activation by orthologous GtHs from different species. So far no consistent pattern has been established to chart or predict this cross-talk in specific species or higher taxonomic orders. In the current study, we strived to understand the promiscuous nature of FSH and LH through *in silico* perspectives. While our studies in Russian sturgeon (*Acipenser gueldenstaedtii*) have shown FSH and LH to exhibit mutual promiscuity but of varying magnitude, in common carp (*Cyprinus carpio*) only LH showed singular cross-activation of FSHR. In