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ADRENAL – CLINICAL RESEARCH STUDIES

Comparative Transcriptional Analysis of Patient Responders Versus Non-Responders to Glucocorticoid Treatment for Bronchopulmonary Dysplasia

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Bronchopulmonary Dysplasia (BPD) is a common heterogeneous lung disease that can result from preterm birth at less than 28-weeks gestation, prenatal and postnatal inflammatory insults, ventilator associated lung injury, and oxygen-related injury. Synthetic glucocorticoids (sGCs) are commonly used pre- and postnatally to treat inflammation and improve lung physiology. Clinical responses to sGC therapy for BPD vary in patients. We hypothesize that genetic background differences in transcriptional response to sGC therapy dictate the efficacy in infants with BPD. Identifying pathways and genes that mediate these differences will allow prospective determination of which infants would respond to sGC treatment.

26 preterm infants that received sGC treatment for BPD were identified. Respiratory Severity Score (RSS), an indication of BPD severity, was measured at diagnosis, 4 days, and 7 days post-sGC treatment. Patients were stratified into Responders versus Non-Responders by improvement in respiratory function after treatment. Changes in RSS were used to discriminate Responders (R >3 decrease in RSS) to treatment from Non-Responders (NR <3 decrease). 13 Responders and 13 Non-Responders were selected. They included 7 females and 19 males with an average gestational age of 24.3 weeks, and were 46% Caucasian, 31% African American, 19% Hispanic, and 4% other. 100μL of blood was collected before and after seven days of a dexamethasone treatment course.

To examine differences in transcription response between Responders (n = 13) and Non-Responders (n= 13), RNA was isolated and analyzed using the Clariom S Human Transcriptome Affymetrix array. 21,500 expressed genes were profiled. **Results:** were imported into the Transcriptome Analysis Console (TAC) software, and genes with a significant difference (fold change >1.48 or < -1.48 and p-value <0.05) in Responders and Non-Responders were identified. Of those, 133 genes were upregulated and 74 downregulated. Ingenuity Pathway Analysis (IPA) was used to identify signaling pathways and disease processes that were uniquely altered in Responders versus Non-Responders. Non-Responders showed significant activation of neuroinflammatory signaling pathways, degranulation pathways, and lymphocyte activation disease pathways. Target genes in the top dysregulated pathways were evaluated using quantitative Polymerase Chain Reaction (qPCR). Expression changes in Matrix Metalloproteinase-25, Interleukin-12 Receptor beta, and Microsomal Glutathione Transferase-1, key mediators of inflammation, were validated in independent studies using qPCR. While response to systemic glucocorticoids in neonates with BPD is variable, these studies identified pathways that are altered in Responders versus Non-Responders and are a step towards developing pre-screening tools to stratify infants for response to sGC BPD therapy.

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Concomitant Pheochromocytoma and Primary Aldosteronism: A Case Series and Literature Review

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Objective: The detection and management of concomitant pheochromocytoma (PHEO) and primary aldosteronism (PA) is not well understood. Our objectives were to investigate varying presentations and outcomes of cases with coexisting PHEO and PA to provide an approach to its diagnosis and management. **Design:** Retrospective case series from 2000–2020 at a single institution tertiary center; additional review of previously known cases before 2000 and from the medical literature. **Patients and Measurements:** Adult patients with concomitant PHEO and PA. Clinical, biochemical, radiologic, and histologic parameters were reviewed. **Results:** Fifteen patients (53% men, median age 53 years) were diagnosed with concomitant PHEO and PA. The majority presented with hypertension (13, 87%) and hypokalemia (13, 87%), but only 6 (40%) presented with symptoms suggestive of catecholamine excess. All patients with preoperative work-up for catecholamine excess (14, 93%) were found to have elevated plasma or urinary metanephrines/catecholamines above the upper limit of normal. Adrenal vein sampling (AVS) was performed in 9 (60%) patients, where 5 (56%) were diagnosed with bilateral PA, and 4 (44%) with unilateral PA. All patients underwent either unilateral (12, 80%) or bilateral (3, 20%) adrenalectomy to treat their PHEO and/or PA. Postoperative catecholamines and/or catecholamine breakdown products normalized or improved in 13 (87%) patients and were not measured in 2. Recurrence of PHEO was not observed. Six (40%) displayed persistent PA postoperatively, where 4 required long-term mineralocorticoid blockade. **Conclusions:** Concomitant PHEO and PA is a rare but likely underreported condition. Hypertension with or without hypokalemia should prompt evaluation for PA, while any indeterminate adrenal mass should be worked up for PHEO. Coexisting disease warrants consideration of AVS to determine the laterality of PA to ensure appropriate management.

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Confirmation of Feasibility of Selective Glucocorticoid Replacement Following Unilateral Adrenalectomy for Hypercortisolism and Primary Aldosteronism

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