Introduction
Adrenal lesions that are found incidentally during routine imaging of people who do not have any complaints or physical findings related to adrenal gland are called adrenal incidentaloma (1,2). Incidentalomas appear more frequently with the increasing use of imaging techniques and increasing age. It is unclear why most of these masses emerged. It is controversial whether nonfunctional adrenal incidentalomas (NFAI) increase the risk of cardiovascular disease or metabolic syndrome or are more common in people with these diseases. In this study, we aimed to investigate whether lifestyle and body fat have an impact on the occurrence of NFAI.

Materials and Methods
100 patients with NFAI were included in the study. Control group consisted of 50 healthy and similar age groups. Physical activities of these groups (with the International Physical Activity Questionnaire Short Form), smoking were questioned and anthropometric measurements were made (Height, body weight, body mass index (BMI), neck, hip, waist circumference and body fat mass, fat percentage, total body water, fet free mass with bioimpedance method). Laboratory tests were examined from the patient file.

Results
Female dominance was observed in patients with NFAI. BMI, waist circumference, hip circumference, neck circumference, total body fat percentage and mass and smoking were found to be higher in the patient group compared to the healthy group and a statistically significant difference was found. When a subgroup of patients with similar age and BMI among the patients and the control group were constituted (25-29,99 kg / m²) waist circumference and total fat mass were again significantly higher in the patient group compared to controls. In addition, there was a significant positive correlation between mass size and waist circumference, BMI, neck circumference, cortisol after 1 mg dexamethasone suppression test and a significant negative correlation with ACTH.

Conclusion
The data obtained showed that body adiposity and smoking were higher in patients with NFAI. Also, it was shown that although the patients were regarded as nonfunctional, suppressibility of the cortisol decreases as the mass size of the incidentaloma increase.

Resources
1. Turkey Endocrinology and Metabolic Diseases Society of Adrenal and Gonadal Working Group. Adrenal and Gonadal Diseases Guide. 2019, pages 77–84.
2. Fassnacht M, Arlt W, Bancos I, Dralle H, Newell-Price J, Sahdev A, et al. Management of adrenal incidentalomas: adrenal tumors. 2016; 175 (2): G1-G34.

Reproductive Endocrinology

FEMALE REPRODUCTION: BASIC MECHANISMS

Effects of Delta-9-Tetrahydrocannabinol (THC) on Oocyte Competence and Early Embryonic Development

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MON-010
Cannabis is the highest used recreational drug amongst individuals of reproductive age. Fertility clinics advise against cannabis use when undergoing fertility treatments, but the literature backing this statement is weak. This rise in cannabis use has occurred simultaneously with the increase in the percentage of the main psychoactive component of cannabis, delta-9 tetrahydrocannabinol (THC) (1). Current literature suggests that THC mimics the effects of endogenous cannabinoids, binding to cannabinoid receptor 1 (CB1), which has been identified in reproductive tissues (2).

Our research aims to study the impact of THC on oocyte maturation and pre-implantation embryonic development. An in vitro bovine system was used as it is the most appropriate translational model to humans for in vitro reproductive toxicity studies. Bovine oocytes were collected and matured under five treatment groups: control, vehicle (1:1:18 ethanol: TWEEN: saline), low THC (0.032uM), mid THC (0.32uM) and high THC (3.2uM). These doses mimic plasma concentrations reached after therapeutic (0.032uM) or low/high recreational (0.32uM and 3.2uM) cannabis use (3). We hypothesise that THC affects oocyte competence and proper early embryonic development in vitro.

A negative THC dose-dependent response in cleavage rate was observed, with the highest THC group cleaving at 70.2% rate compared to 86.8% and 85.5% of control and vehicle groups, respectively (p<0.0001, n=7). There was no significant difference in blastocyst rate, suggesting that oocyte THC exposure affects the numbers of oocytes capable of development, but those able to cleave will properly reach blastocyst stage. We analyzed changes in gene expression, i) by a full RNA transcriptome analysis (24,128 transcripts screened) and ii) by quantification of Connexin 37 (CX37) and 43 (CX43) mRNA levels. Connexin expression is correlated to oocyte competence (4). RNA transcriptome analysis showed 62 genes that were significantly downregulated only in the low THC group. CX mRNA levels were measured via droplet digital PCR in both cumulus-oocyte complexes (COCs) and blastocysts. No significant differences were detected in blastocysts, however, a significant decrease in both CX37 and CX43 levels was measured in the low THC group in COCs (p<0.05, n= 9). Differences seen exclusively at the low THC dose suggest a role of THC as partial agonist of CB1.

This research aims to understand the effects of cannabis on fertility, as current knowledge during pre-implantation development is limited, making it difficult for physicians to properly advise patients undergoing IVF.

Reference: (1) ElSohly et al., Biol Psychiatry. 2016 Apr 1;79(7):613–9. (2) El-Talatini et al., PLoS ONE. 2009 Feb 24;4(2):e4579. (3) Whan et al., Fertil Steril. 2006
Adrenal

ADRENAL - TUMORS

Trial in Progress Interim Report: A Phase II Clinical Trial Using Single Agent Cabozantinib in Advanced Adrenocortical Carcinoma

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SAT-175

Background: Adrenocortical carcinoma (ACC) in an aggressive malignancy with suboptimal response to frontline chemotherapy and without established second line treatment. c-MET activation is associated with ACC resistance to chemotherapy. Cabozantinib is a multi-kinase inhibitor that targets the VEGFR, c-MET, AXL, and RET receptors. We report interim data about using cabozantinib in ACC through a prospective phase II clinical trial. Methods: This is an investigator-initiated, open label clinical trial to evaluate the efficacy and safety of cabozantinib in patients with unresectable/metastatic ACC in patients with hormonally active ACC. Median number of prior lines of systemic therapy was 2 (range 0 -5). Median duration of cabozantinib therapy was 6.6 months (range 0.7 -11.3). Eight patients (80%) were without evidence of disease cut off, 1 patient had partial response (53% reduction), 3 patients had stable disease, and ongoing), 3 patients had stable disease, and 5 patients had progressive disease. Nine patients were alive with disease and one patient died (not drug related). Grade 3/4 clinical adverse events included thromboembolic events (3 patients), severe hypertension (1 patient), intracranial hemorrhage secondary to hypertensive crisis (1 patient), weight loss (1 patient), and abdominal pain (1 patient). Grade 3/4 laboratory adverse events included increased AST (2 patients), increased ALT (1 patient), increased GGT, increased amylase (1 patient), increased lipase (1 patient) and hyponatremia (1 patient).

Conclusions: In this interim analysis of phase II study, majority of subjects reached the study primary endpoint (PFS4). These data are in favor of continuing study accrual to assess magnitude of response to therapy and safety profile in ACC. Aggressive blood pressure management and close monitoring of liver enzymes are crucial to ensure the safety of study subjects.

Bone and Mineral Metabolism

PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS

Is Most “Primary” Hyperparathyroidism Both Tertiary and Preventable?

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SAT-403

Primary Hyperparathyroidism has reached epidemic proportions since the advent of mass screening for laboratory parameters including calcium. Secondary Hyperparathyroidism has been considered by some individuals as “Normocalcemic Primary Hyperparathyroidism” (4th International Workshop on The Management of Asymptomatic Primary Hyperparathyroidism, Florence, 2013 Bilszekan et al.-“Normocalcemic PHPT is a clinical presentation of PHPT: management approach is recommended.”) We report a single case of severe secondary hyperparathyroidism (with severe osteomalacia due to ileal resection) as well as 56 subsequent secondary hyperparathyroid cases treated with 1,25dihydroxy-D3 (calcitriol) which were associated with significant reduction of parathormone levels *and continued normalization of calcium levels* [as well as significant improvement in bone density.] We are instituting a long-term, double-blind, placebo controlled clinical trial - with design presented here - to determine whether or not the incidence of hypercalcemic hyperparathyroidism can be significantly reduced or even obliterated by treatment with calcitriol.

Mrs. K.E.

Date Ca++ PTH Calcitriol

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1997/05/01 8.5 344.0 0.25 i po qd
1997/05/28 8.5 388.0 0.25 i po qd
1997/07/21 9.3 102.0 0.50 ii po tid
1997/08/21 9.3 167.0 0.50 ii po qd
1997/11/14 10.4 11.4 0.50 ii po qd
1998/01/26 11.2 0 ( ) 0.50 i po tid
1998/04/28 9.7 8.6 0.50 i po tid
1998/06/26 9.5 11.4 0.50 i po tid
1999/04/28 9.4 15.2 0.50 i po tid
2000/02/04 8.7 16.0 0.50 i po tid
2000/05/01 9.3 15.1 0.50 i po tid

Baseline Values Statistic: Ca++ /PTH, Total: 910.70 / 4170.00, Average: 9.49/73.16, Count: 57/57, Minimum: 11.70/211.00, Minimum: 4.90 /12.00, Variance: 1.38 /73.16, SD: 2.47/59.34

Post-Treatment with Calcitriol Statistic: Ca++ PTH, Total: 910.70/4170.00, Average: 9.49/73.16,Count: 57/57, 11.70/211.00, Minimum: 4.90/12.00, Variance: 1.38/923.70, SD: 1.18/43.86