**OC001—A PROMISING PREDICTOR FOR HEART DISEASES AND DIURETIC DRUG THERAPY IN THE ALDOSTERONE RECEPTOR GENE**

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**Introduction:** Aldosterone mediates sodium and water retention in hypovolemia. In normovolemia, aldosterone primarily mediates kaliuresis. To mediate kaliuresis, aldosterone downregulates the sodium chloride cotransporters NCC and up-regulates the epithelial sodium channel ENaC. NCC downregulation increases sodium chloride transport to ENaC, where it is reabsorbed in turn for potassium, which is then excreted. We investigated whether kaliuresis is associated with the aldosterone receptor polymorphism rs3857080 in normovolemic healthy volunteers.

**Patients (or Materials) and Methods:** We genotyped 195 healthy young men for rs3857080. In a triple-crossover study, 101 of them had ingested a sodium-chloride restricted diet 3 times for each a diet run-in day, a second diet day and a third diet plus verum day. Verums had ingested a sodium-chloride restricted diet 3 times for each a diet.

**Results:** Potassium excretion was in both studies associated with rs3857080, which had a minor allele frequency of 0.111. Comparatively high potassium excretion was associated with the minor A-allele under most conditions (Table). After torsemide, which is a loop diuretic such as bumetanide and furosemide but in addition blocks the aldosterone receptor, potassium excretion was similar between the A- and the G-allele of rs3857080.

**Table. Urinary potassium excretion over 24 hours and rs3857080.**

<table>
<thead>
<tr>
<th></th>
<th>A/A</th>
<th>G/G</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl restriction</td>
<td>3.7 (0.2)*</td>
<td>2.8 (0.1)</td>
</tr>
<tr>
<td>HCT 25 mg</td>
<td>4.8 (0.6)</td>
<td>3.7 (0.1)</td>
</tr>
<tr>
<td>HCT 100 mg</td>
<td>5.5 (0.6)</td>
<td>4.3 (0.1)</td>
</tr>
<tr>
<td>Triamterene</td>
<td>3.3 (0.5)</td>
<td>2.2 (0.1)</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>3.5 (0.3)</td>
<td>2.8 (0.1)</td>
</tr>
<tr>
<td>Furosemide</td>
<td>3.5 (0.3)</td>
<td>3.1 (0.1)</td>
</tr>
<tr>
<td>Torsemide</td>
<td>2.5 (0.3)</td>
<td>2.6 (0.1)</td>
</tr>
</tbody>
</table>

*Mean (SEM) of gram amounts normalized to 120 mL/min creatinine clearance.

**Conclusion:** Taken together, our findings indicate that the A-allele of rs3857080 marks a comparatively active aldosterone receptor. Carriers of the A-allele may be prone to hypokalemia and its devastating consequences. The A-allele of rs3857080 may predict less optimal outcome of diuretic therapy and of heart diseases. Antialdosteronergic drugs such as spironolactone, eplerenone, and torsemide may be especially indicated in carriers of the A-allele. In consequence, rs3857080 is a highly promising candidate for in vitro studies as well as for clinical research.

**Disclosure of Interest:** N. Dalila: None declared. M. Tzvetkov: None declared. J. Brockmöller: None declared. S. Vormfelde: None declared.

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**OC002—CYP2R1 GENETIC POLYMORPHISMS ARE ASSOCIATED WITH LOWER 25-HYDROXY VITAMIN D LEVELS IN LEBANESE SUBJECTS**

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**Introduction:** Despite plentiful sunshine in the Middle East, populations in general, and in Lebanon in particular, have some of the lowest levels of 25-hydroxy vitamin D (25-OHD) worldwide. Our group has demonstrated such findings across the lifespan; predictors include gender, season, and clothing style (http://staff.aub.edu.lb/~webcnop/publications.html). However, the possibility of an underlying genetic modulation of circulating 25-OHD levels remains unexplored. 25-Hydroxylation is mainly driven by cytochrome P-450 2R1 (CYP2R1) drug metabolizing enzyme; we therefore hypothesized that carriage of CYP2R1 single nucleotide polymorphisms (SNPs) may be associated with variability in 25-OHD levels.

**Patients (or Materials) and Methods:** Baseline 25-OHD levels were obtained for 172 elderly Lebanese patients: 60% female; age, 70.9 (4.3) [mean (SD)] years; BMI, 30.3 (4.8) kg/m²; with vitamin D, 25-OHD, 18.7 (7.9) ng/mL. Genotyping was performed for 4 functionally important SNPs (rs12794714, rs10741657, rs1562902, and rs10766197) in CYP2R1 gene by using real-time PCR. Means were first compared with univariate analysis, and then multivariate regression analysis was run adjusting for age, gender, BMI, and season.

**Results:** Mean allele frequencies were 0.50, 0.29, 0.36, and 0.49 for rs12794714, rs10741657, rs1562902, and rs10766197, respectively; proportions comparable to those reported in Caucasian populations. Univariate analysis showed that carriers of the rs12794714 and rs10766197 variant alleles are associated with baseline 25-OHD that was 3.24 ng/mL and 4.48 ng/mL lower, respectively ($P = 0.018$ and 0.004). This significant association remained for rs10766197 after adjusting for covariates ($β = –6.401$ [95% CI, –11.775 to –1.027]; $P = 0.020$).

**Conclusion:** This is the first study that shows the association of genetic polymorphisms in CYP2R1 with hypovitaminosis D in the Middle East. Further analysis is ongoing to evaluate the effect of these SNPs on 25-OHD levels achieved after supplementation with different doses of vitamin D.

**Disclosure of Interest:** None declared.

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**OC003—PREGNANCY OUTCOME FOLLOWING MATERNAL EXPOSURE TO MIRTAZAPINE: PRELIMINARY RESULTS OF A COLLABORATIVE ENTIS STUDY**

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**Introduction:** Despite significant efforts, the teratogenic potential of mirtazapine, a commonly used antidepressant, is still unexplored. Mirtazapine is a potent antagonist of the α2-adrenergic and 5-HT2C receptor. A single nucleotide polymorphism rs12794714 in the CYP2R1 (CYP2R1) drug metabolizing enzyme; we therefore hypothesized that carriage of CYP2R1 single nucleotide polymorphisms (SNPs) may be associated with variability in 25-OHD levels.

**Patients (or Materials) and Methods:** Baseline 25-OHD levels were obtained for 172 elderly Lebanese patients: 60% female; age, 70.9 (4.3) [mean (SD)] years; BMI, 30.3 (4.8) kg/m²; with vitamin D, 25-OHD, 18.7 (7.9) ng/mL. Genotyping was performed for 4 functionally important SNPs (rs12794714, rs10741657, rs1562902, and rs10766197) in CYP2R1 gene by using real-time PCR. Means were first compared with univariate analysis, and then multivariate regression analysis was run adjusting for age, gender, BMI, and season.

**Results:** Mean allele frequencies were 0.50, 0.29, 0.36, and 0.49 for rs12794714, rs10741657, rs1562902, and rs10766197, respectively; proportions comparable to those reported in Caucasian populations. Univariate analysis showed that carriers of the rs12794714 and rs10766197 variant alleles are associated with baseline 25-OHD that was 3.24 ng/mL and 4.48 ng/mL lower, respectively ($P = 0.018$ and 0.004). This significant association remained for rs10766197 after adjusting for covariates ($β = –6.401$ [95% CI, –11.775 to –1.027]; $P = 0.020$).

**Conclusion:** This is the first study that shows the association of genetic polymorphisms in CYP2R1 with hypovitaminosis D in the Middle East. Further analysis is ongoing to evaluate the effect of these SNPs on 25-OHD levels achieved after supplementation with different doses of vitamin D.

**Disclosure of Interest:** None declared.