**Placental expression of epithelial sodium channels and NEDD4-2 throughout gestation in human pregnancy**

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**Objective:** The epithelial sodium channel (ENaC) is an important regulator of blood pressure due to its role in sodium ion transport. The aim of this study was to characterise expression of a number of key genes involved in blood pressure regulation throughout gestation. These include the four ENaC subunits α, β, γ, δ and the ubiquitin ligase NEDD4-2, which is an important regulator of ENaC activity.

**Methods:** Following ethical committee approval and informed patient consent placental tissue was obtained from 6 early (6-9 weeks gestational age [GA]) and 7 mid (10-14 weeks GA) pregnancy terminations (TOP) and from women undergoing elective Caesarean section following normal pregnancy (n=6; mean gestational age[standard deviation] 39.5 [1.02] weeks). Quantitative real-time PCR was used to determine expression of ENaCα, ENaCβ, ENaCγ, ENaCδ, NEDD4-2 and the housekeeping genes GAPDH and β-actin.

**Results:** Placental ENaCα, ENaCβ, ENaCγ, ENaCδ and NEDD4-2 expression were unchanged during the first trimester. However, with the exception of ENaCα expression was significantly decreased at term for all genes examined compared to both early and mid TOP.

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|  | ENaCα | ENaCβ | ENaCγ | ENaCδ | NEDD4-2 |
| Early TOP (n=6) | 1135  [478.9, 2125] | 356.3a  [274.5, 2735] | 958.3a  [671.5, 2211] | 3698a  [762.2, 10106] | 76079a  [45441, 132288] |
| Mid TOP (n=7) | 758.9  [542.8, 1474] | 713.2b  [467, 2318] | 899.8b  [716.5, 1238] | 1251b  [790.4, 2589] | 42980b  [35438, 58016] |
| Term (n=6) | 54.5  [48.4, 60.6] | 14.8a,b  [4.5, 82.4] | 18.2a,b  [9.0, 73.9] | 305.6a,b  [51.3, 719.5] | 1403a,b  [1036, 2026] |

Data presented as median [IQR] normalised copy number. Significant differences (P<0.05) between groups are indicated by corresponding superscripts.

**Conclusion:** These data clearly suggest that ENaC channels and their regulator are important in early pregnancy, which implies that they have an important role in the plasma volume increase that is essential for healthy pregnancy. Future work will confirm these changes at the functional level.