**Human myometrial artery function is critically affected by maternal BMI**

The incidence of obesity in the pregnant population is growing and is a well-recognised risk factor for adverse pregnancy outcome. We have studied human myometrial artery function in order to better understand the (patho)physiology of myometrial vessels and how obesity might affect this. We have therefore examined whether maternal BMI affects the ability of the human myometrial arteries to contract and relax in vitro.

Human myometrial biopsies were collected during elective c-section from women with uncomplicated singleton term pregnancies, after informed consent, at Liverpool Women’s Hospital. Small arteries were dissected (2mm sections), mounted in a wire myograph containing oxygenated physiological salt solution at 34°C and set to their normalized diameter (0.9 x IC100). Vessels were separated into 2 groups: BMI<25 (normal weight) and BMI≥25 (overweight/obese). There was no significant difference in vessel size between groups. Vessel function was assessed using contractile (AVP, U-46619) and relaxatory (bradykinin (BK), CCh, SNAP) agonists. In addition, vessels (BMI≥30) were treated with 2% methyl cyclodextrin (MCD), to sequester cell membrane cholesterol, for 20min prior to assessing function. Data are expressed as mean±sem, where n=vessels, N=biopsies.

Contractile responses were altered in the BMI≥25 group. U-46619 was significantly less potent (pEC50=6.83±0.13, n=21/N=11 v 7.14±0.15, n=22/N=11, t-test p=0.018) compared to BMI<25. AVP showed a similar trend (pEC50=8.94±0.09, n=17/N=9 v 9.20±0.09, n=21/N=13, p=0.054). When pre-contracted with AVP, all vessels relaxed equally well to BK (BMI<25: pEC50=7.71±0.14, n=12/N=9 v BMI≥25: pEC50=7.80±0.06, n=20/N=12). In contrast, only a subset of vessels relaxed when challenged with CCh (14 out of 44). The BMI of women whose vessels responded to CCh (23.64±0.72, N=14) was significantly lower than those not responding (29.22±1.11, N=30). Overall, 15% of BMI≥25 vessels (4/27) and 59% of BMI<25 vessels (10/17) responded to CCh. In fact, no vessels from obese women (BMI >30) responded to CCh, although they all relaxed to BK. The CCh pEC50 in responding vessels was 7.41±0.25 (n=9/N=6). No significant difference in response to SNAP was observed. Exposure to MCD failed to restore a response to CCh in vessels from obese women.

Vasoconstriction and vasodilation are impaired in myometrial arteries from overweight/obese women, although responses are agonist-specific: the CCh response is ablated and U-46619 is less potent. Full relaxation was observed with SNAP, suggesting no deficit in arterial smooth muscle responses with increased BMI. If hyperlipidemia caused the loss of the CCh response, then treatment with MCD could potentially restore sensitivity to CCh, however this was not the case. Impaired vessel function may contribute to the significant adverse pregnancy outcomes experienced by overweight/obese women.