

GROWTH AND DEVELOPMENT

Dwarfism linked to hypertension treatment

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Treatment of female mice with an $\alpha 1$ -adrenergic antagonist during pregnancy results in dwarfism and insulin resistance in male offspring, according to new findings published in *Molecular Metabolism*. “As combined $\alpha 1/\beta$ -adrenergic blockers are currently recommended as first-line and second-line treatments for gestational hypertension, the findings have immediate clinical relevance,” asserts lead investigator Jens Mittag.

Mittag and his team at the University of Lübeck, Germany, treated wild-type (C57BL6) mice with $50 \mu\text{g ml}^{-1}$ of prazosin (an $\alpha 1$ -adrenergic antagonist) in drinking water shortly before mating and

during pregnancy, and analysed male and female offspring for endocrine and metabolic abnormalities. Male offspring of prazosin-treated dams had reduced body length (indicative of dwarfism) at 4–5 months and insulin resistance (evidenced by a reduced glucose clearance rate and a diminished response to insulin) compared with control mice.

Focusing on the growth hormone (GH)–insulin-like growth factor 1 (IGF1) axis (genetic defects in which are the main cause of dwarfism), the researchers were able to show that the growth and metabolically impaired phenotype of male offspring was accompanied by reduced serum levels of IGF1, which was mediated by reduced hepatic expression of the GH receptor gene (*Ghr*). Moreover, increased CpG methylation at the

transcriptional start site of the *Ghr* promoter in offspring of prazosin-treated dams inversely correlated with hepatic levels of *Ghr* mRNA. Together, the findings indicate that maternal $\alpha 1$ -adrenergic blockade during pregnancy can epigenetically modify levels of IGF1 and subsequently body length and insulin sensitivity in male offspring.

“As our study was performed in mice, we cannot draw any immediate conclusions about patient care but we hope that our findings will stimulate further research in this area and that retrospective studies in human cohorts will follow shortly,” comments Mittag. “If a similar connection between maternal use of $\alpha 1$ -adrenergic antagonists and height or an elevated risk of insulin resistance is observed in human offspring, use of this class of drugs in pregnant women will need to be re-evaluated.”

David Holmes

ORIGINAL ARTICLE Oelkrug, R. *et al.* Dwarfism and insulin resistance in male offspring caused by $\alpha 1$ -adrenergic antagonism during pregnancy. *Mol. Metab.* <http://dx.doi.org/10.1016/j.molmet.2017.06.016> (2017)



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