Inhibition of adenosine deaminase and xanthine oxidase activities by sodium acetate ameliorates glucose dysregulation and defective antioxidant defenses induced by gestational excess androgen in rats

Lawrence A Olatunji¹, Emmanuel D Areola¹, Olufunto O Badmus¹, Taofeek O Usman¹, Inkyeom Kim²

¹University of Ilorin, Nigeria, ²Kyungpook National University School of Medicine, Korea

Background: Nutritional challenges and androgen excess have been implicated in the development of gestational diabetes and poor fetal outcome, but the mechanisms are not well delineated. The effects of short chain fatty acid (SCFA) on glucose dysmetabolism and poor fetal outcome induced by gestational excess androgen is also not known. We tested the hypothesis that blockade of androgen receptor (AR) and suppression of late gestational excess androgen prevents glucose dysmetabolism and poor fetal outcome through suppression of adenosine deaminase (ADA)/xanthine oxidase (XO) pathway.

Methods: Twenty-four pregnant Wistar rats were treated (sc) with olive oil, testosterone propionate (0.5mg/kg) singly or in combination with SCFA (sodium acetate; 200mg/kg; po) between gestational days 14 and 19.

Results: The results showed that late gestational excess androgen led to glucose deregulation, poor fetal outcome, increased plasma, and hepatic free fatty acid and lactate dehydrogenase, liver function marker enzymes, malondialdehyde, uric acid, ADA and XO activities. Conversely, gestational excess androgen resulted in reduced body weight gain, visceral adiposity, plasma and hepatic antioxidant defenses (glutathione peroxidase, glutathione/glutathione disulphide ratio, glucose-6-phosphate dehydrogenase, adenosine and nitric oxide). However, all these effects were ameliorated by either sodium acetate or flutamide treatment.

Conclusion: The study demonstrated that suppression of testosterone by SCFA or AR blockade protects against glucose deregulation and poor fetal outcome by the improvement of antioxidant defenses through alterations in ADA/XO pathway. Hence, utility of SCFA should be encouraged for improvement of glucose dysmetabolism and poor fetal outcome.