## The effect of antenatal betamethasone exposure on diaphragm contractile function in young rat progeny

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Premature infants are a major paediatric problem due to the high incidence of mortality and morbidity. The functional and structural immaturity of the respiratory system of premature infants can lead to the development of respiratory distress syndrome (RDS). Mothers at risk of preterm delivery are treated antenatally with glucocorticoids to increase fetal lung maturity and surfactant production. In adults, glucocorticoids are known to induce skeletal muscle atrophy and intrinsic muscle weakness (Schakman *et al.*, 2008), raising the possibility that maternal glucocorticoid treatment may adversely impact neonatal diaphragmatic force production, that may exacerbate the onset of RDS. This study aimed to investigate how antenatal maternal glucocorticoids effect the contractile function of diaphragm muscle preparations from 21 day old rat progeny.

Pregnant Wistar rats were treated with two single intramuscular doses of 0.5 mg/kg of betamethasone (Celestone,Shering Plough) 7 days and 3 days before estimated pup delivery. The control group received no treatment. Twenty one days after birth, rats were euthanized by an overdose of pentobarbitone (>120 mg/kg). The diaphragm was removed from the animal and diaphragm muscle strips were excised and mounted on an *in vitro* muscle test system. The muscles were maintained in a bath containing Kerbs mammalian Ringer solution (pH 7.3) bubbled with carbogen (95% $O_2$ and 5% $CO_2$) at 25°C. Twitch force characteristics, the force frequency relationship (force expressed as a percentage of maximum force as a function of stimulation frequency), and maximum specific force were measured in diaphragm strips from both groups.

Antenatal betamethasone treatment decreased maximum twitch force in diaphragm strips from 21 day old progeny compared to the untreated control sample (betamethasone: 1.54 ± 0.36 N/cm$^2$; control: 2.89 ± 0.49 N/cm$^2$, $P$<0.05). The mean time to peak (TTP) and half relaxation time (½ RT) values of the twitch responses also decreased in diaphragm strips from the betamethasone treated group (betamethasone TTP: 0.05 ± 0.01 s; control TTP: 0.09 ± 0.01 s, p<0.05)(betamethasone ½ RT: 0.06 ± 0.01 s; control ½ RT: 0.13 ± 0.01 s, $P$<0.05). The force frequency relationship measured in diaphragm strips from the betamethasone treated group was shifted to the right compared to that measured in the control group. Relative force output was significantly lower at stimulation frequencies of 5, 10 and 20 Hz in the betamethasone treated group compared to controls ($P$<0.05). The maximum specific force output was similar in the diaphragm strips from both groups (betamethasone: 12.12 ± 2.01 N/cm$^2$; control: 15.10 ± 1.18 N/cm$^2$).

These findings indicate that antenatal administration of glucocorticoids has significant and persistent detrimental effects on postnatal diaphragm sub-maximal force production in exposed progeny. If similar effects occur in humans, antenatal maternal glucocorticoid treatment could contribute to diaphragmatic dysfunction and RDS in premature infants.

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