EXTRACELLULAR ATP LEVELS ALTER THE EFFECTS OF CONGENITAL HYPOTHYROIDISM IN CALCIUM INFLUX AND IN OXIDATIVE STRESS PARAMETERS IN IMMATURE RAT TESTIS

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INTRODUCTION: Our group previously demonstrated that congenital hypothyroidism inhibits extracellular ATP hydrolysis and leads to oxidative damage in immature rat testis. These events might be involved in impaired male fertility caused by hypothyroidism. The aim of this study was to investigate the involvement of purinergic system in the effect of hypothyroidism on oxidative stress and calcium influx in immature rat testis. METHODS: Congenital hypothyroidism was induced in rat dams by adding 0.05% 6-propyl-2-thiouracil in the drinking water during gestation and suckling period. Testis from 15 day-old pups were pre-incubated in HBSS buffer for 15 min and then incubated during 30 min with 100 µM ATP; then lipid peroxidation (TBARS), gamma-glutamyl transferase (GGT) activity and $^{45}$Ca$^{2+}$ influx were determined. For calcium influx assays, the testis 0.1 µCi/ml $^{45}$Ca$^{2+}$ was added in the incubation medium. The enzymatic activity of GGT was determined in testis homogenates carried out in Tris-HCl pH 8.5. RESULTS AND DISCUSSION: Hypothyroidism induced lipid peroxidation as well as stimulated $^{45}$Ca$^{2+}$ influx and GGT activity in immature rat testis. Short-term incubation with ATP reversed these effects. In order to investigate the mechanisms involved in the effects of ATP in hypothyroid testis, vitamin E (antioxidant), BAPTA-AM (intracellular calcium quelator) and PD98059 (MAPK inhibitor) were used. Results showed that only vitamin E and BAPTA-AM prevented the effect of ATP in hypothyroid rat testis. CONCLUSION: Extracellular ATP reversed the effects of hypothyroidism on oxidative parameters and on calcium influx in immature rat testis. The mechanism underlying ATP action involves the modulation of intracellular calcium levels and might be prevented by antioxidants. Further experiments are necessary to clarify the participation of extracellular purines in hypothyroid-induced effects on testis.

Word Keys: hypothyroidism, testis, purinergic system.
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