Endocannabinoids and fertility: Anandamide induces apoptosis of human granulosa cells

Lia Costa 1,2, Beatriz Pinto 2, Eduarda Felgueira 1, Irene Rebelo 2, Bruno Fonseca 2

1 Unidade de Medicina da Reprodução Dra Ingeborg Chaves, Centro Hospitalar de Vila Nova de Gaia/Espinho
2 UCIBIO, REQUIMTE, Laboratório de Bioquímica, Departamento de Ciências Biológicas, Faculdade de Farmácia da Universidade do Porto

INTRODUCTION

The major endocannabinoid (eCBs) anandamide (AEA) has already been suggested as biomarker of reproductive potential of male and female gametes [1]. The endocannabinoid system (ECS) has been recognized as a crucial player in human reproduction and changes in AEA levels affect reproductive events [2]. Cannabinoid-receptor 1 (CB1) was already identified in the granulosa cells (GC) of antral follicles, and in the luteal cells of functional corpus luteum of rat ovary [3]. GC interact directly with the oocyte during its development, being crucial for its reproductive potential [4]. However, the ECS was not characterized on COV434 nor the effects of AEA on GC depicted. Therefore, the aim of this work was to explore the effects of AEA on COV434 granulosa cell line and on human granulosa cells (hGC) obtained from follicular fluid of patients enrolled in IVF treatments.

RESULTS

Our results reveal that AEA induce a reduction on GC viability in a concentration and time-dependent manner (figure 1). That effect on hGC was only observed at higher concentrations of AEA. This eCB did not induce ROS release nor mitochondrial membrane potential changes (figure 2) on both cell models, however it induced morphological changes (figure 3), presenting chromatin condensation at 72h. Both cell models exhibit an increase in caspase -3/7 and 9 activity (figure 4), suggestive of apoptosis.

CONCLUSION

This study supports the idea that ECS balance is crucial for folliculogenesis and oocyte quality, also indicating that deregulated AEA levels may compromise female fertility.

REFERENCES


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