ARIPIPRAZOLE EFFECTS ON TRIGLYCERIDE CONTENT OF *IN VITRO* DIFFERENTIATING ADIPOCYTES

Melinda Kolcsár [1], Zsolt Gáll [1], Tamás Tábi [2], László IstvánBába[3], Szabolcs Koncz [4], Imre Zoltán Kun [5]

1 Department of Pharmacology and Clinical Pharmacy, University of Medicine and Pharmacy of Tîrgu Mures, Romania
2 Department of Pharmacodynamics, Semmelweis University Budapest, Hungary
3 Resident in Clinical Pharmacy, County Hospital Mureș and University of Medicine and Pharmacy of Tîrgu Mures, Romania
4 Student of the Faculty of Pharmacy, University of Medicine and Pharmacy of Tîrgu. Mures, Romania
5 Doctoral School, University of Medicine and Pharmacy of Tîrgu Mures, Romania

Introduction

In vitro adipogenesis is a two-step developmental process in which an undifferentiated mesenchymal cell differentiates into a preadipocyte, which then undergoes a secondary differentiation step to become a lipid-filled adipocyte.

The triglyceride accumulation is influenced by various endogenous and exogenous factors.

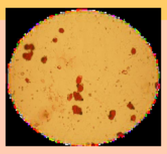
Objectives

In an attempt to understand the peripheral effects of some atypical antipsychotics on lipid accumulation during adipogenesis, aripiprazole and olanzapine effects on triglyceride content of isolated adipocytes were studied.

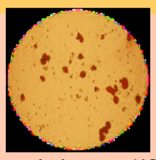
Methods

To induce adipocyte differentiation from mouse embryonic fibroblasts (MEF), these were grown to confluence and then cultured in adipogenic medium (DMEM + 5μM DEX + 0.2μM IBMX + 10μg/ml insulin) for 2 days and in a sustaining medium (DMEM + 10μg/ml insulin) for 12 days. Cells exposed to adipogenic medium±pioglitazone were used as absolute and positive controls, respectively. Aripiprazole and olanzapine were used as adipogenic triggers at different concentrations (0.5, 5 and 20□M). On the 7th and 14th days after induction, the cells viability test and Oil red O staining were performed. The accumulated Oil red O was dissolved in 1 ml 100% isopropanol and spectrophotometric absorbancy analysis was performed (results expressed in mAU). Oil red O staining is able for quantitation of intracitoplasmatic lipids (1). For statistical analysis Student's t test was used and the significance level was established at $p<0.05$.

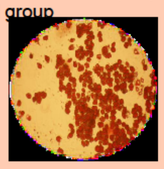
Results



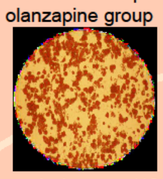
Microscopic image (100x) of the Oil red O stained adipocytes in the control group



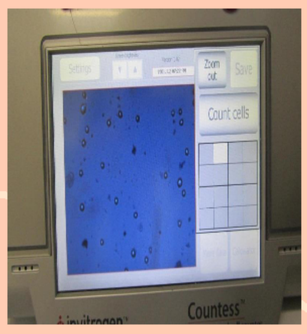
Microscopic image (100x) of the Oil red O stained adipocytes in the 5 uM olanzapine group



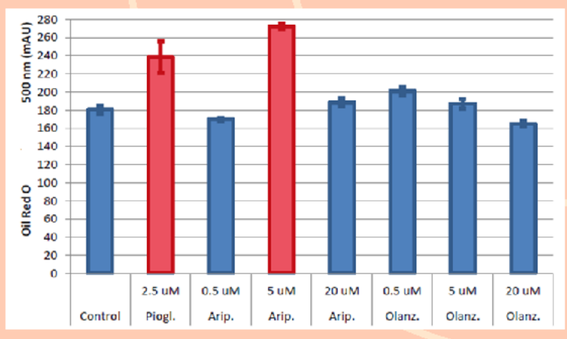
Microscopic image (100x) of the Oil red O stained adipocytes in the pioglitazone group



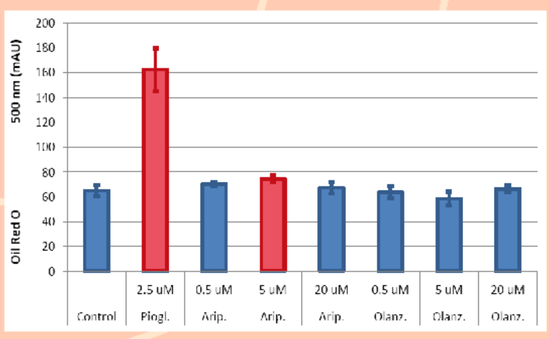
Microscopic image (100x) of the Oil red O stained adipocytes in the 5 uM aripiprazole group



Cell counter- no cytotoxic effect was observed



Oil red O absorbancy after 7 days



Oil red O absorbancy after 14 days

Aripiprazole and olanzapine had no cytotoxic effect at the concentrations tested.

After 7 days no significant differences were observed in the triglyceride contents of the cells, but higher mAU was obtained in pioglitazone (238 ± 23.2 vs.181 ± 34,5) and 5□M aripiprazole (272±65.7 vs. 181±34.5) added cultures, compared to the controls.

Although a decrease of lipid accumulation in all of the cells was observed in the 14th day, in pioglitazone and 5□M aripiprazole added cultures significantly higher triglyceride contents were present than in the control cells (162±17.2 and 75±2.9 vs. 65±4.6 mAU).

Discussion and conclusions

PPAR-γ agonists promote lipid retention in adipose tissue by directing triglyceride-derived fatty acids mainly to adipose tissue and prevent their recycling to the circulation and to other organs (2). Previous studies described that olanzapine induced fat accumulation both *in vivo* and *in vitro*. *In vitro* triacylglyceride accumulation during 3T3-L1 preadipocyte differentiation to mature adipocyte phenotype was accompanied by overexpression of fatty acid synthase (3,4). The aripiprazole effects on peripheral adipogenesis were not studied.

Our results demonstrate that aripiprazole, similarly to pioglitazone but surprisingly not to olanzapine, increased the triglyceride content of MEF-derived adipocytes after 14 days.

The effect of aripiprazole on the body weight may be induced not only through its influence on the CNS receptors, but also affecting the peripheral adipogenesis.

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References:

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