

## Atorvastatin Medullar Thyroid Cancer Over Tt Cell Line Impact Of Apoptosis And Calcitonin Over Gene Expression

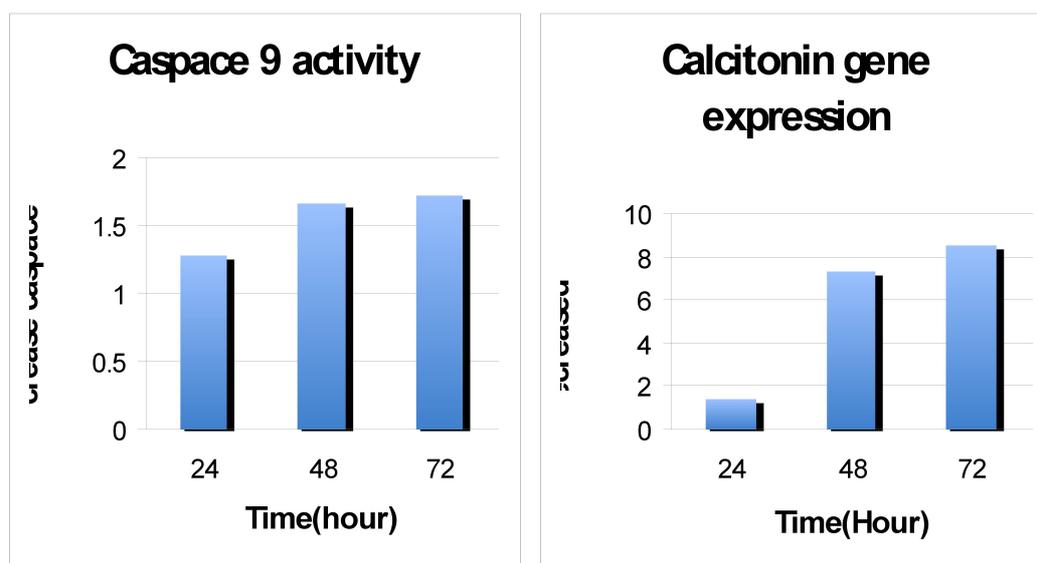
Emine Kartal Baykan(1), Çığır Biray Avcı(2), Mehmet Erdoğan(1), Şevki Çetinkalp(1), A. Gökhan Özgen(1), Cumhuri Gündüz(2), L. Füsün Saygılı(1)

1-Ege University Medical Faculty, Department of Endocrinology and Metabolism

2- Ege University Medical Faculty Department of Medical Biology

Medullar thyroid cancer (MTC) constitutes 5% of thyroid cancers. 25% of MTC are familial. Mutations activating “germ-line” in RET protooncogene are responsible from genetic inheritance. RET mutation causing tyrosine kinase activation result in oncogenic cell proliferation. Persistent and recurrence disease management is complicated in medullary thyroid cancer because it is unresponsive to chemo, radio and radioactive iodine therapy. Agents targeting tyrosine kinase and RET receptor activity can be used in this case. Tyrosine kinase inhibitors have potential to stabilize metastatic disease, but has no effect on survival, they have many serious side effects. Many studies show that statins, inhibit cancer growth by inhibiting HMG Co A reductase through suppressing mevalonate pathway. In the present study, through TT cell line we investigated atorvastatin’s apoptotic impact in MTC cells and also its effect on calcitonin gene expression.

TT cells were treated with varying doses of atorvastatin (12,5-25-50-60-70-80-90-100-125-150-200  $\mu$ M). IC 50 values at 24 hrs was 90  $\mu$ M, at 48 hrs was 80  $\mu$ M, at 72 hrs was 80  $\mu$ M. The apoptotic effect of atorvastatin was evaluated according to caspase 9 activity. Compared to controls atorvastatin increased caspase 9 activity 1.27 times at 24 hrs, 1.660 times at 48 hrs and 1.716 times at 72 hrs. Calcitonin gene expression decreased 1.377 times at 24 hrs, 7.290 times at 48 hrs and 8.494 times at 72 hrs after treating with atorvastatin when compared with controls.



The result of this study shows that atorvastatin increases apoptosis in TT cell line depending on dose and duration, decreases calcitonin gene expression. In conclusion, atorvastatin, which has low side effects, may be a remedy for advanced MTC patients.

**Key words:** Atorvastatin, TT cell line, Apoptosis, Calcitonin