EFFECT OF SIMVASTATIN ON METASTASIS-SPECIFIC MOUSE MAMMARY CARCINOMA 4T1 CELLS IN VIVO SYSTEM

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Introduction: The use of lipophilic statins, like simvastatin, has been shown to significantly lower the risk of breast cancer. The present study was designed to assess the anticarcinogenic and antimetastatic effects of simvastatin in an in vivo model using 4T1 mouse mammary carcinoma cells, which closely resemble stage IV in human breast cancer.

Methods: 4T1 cells were inoculated in female BALB/c mice, randomly divided into three cohorts of 10 mice each. In two groups (Gl and Gll), simvastatin treatment (25mg/Kg and 50mg/Kg, respectively) was administered for 6 weeks, and one group (Gill) received vehicle alone without simvastatin. Tumor development rates, tumor volumes, proliferation (PCNA), and apoptosis (Bax, Caspase 3, and Bcl2) were evaluated. Immunohistochemistry techniques were used to assess PCNA and Caspase 3 marking intensity.

Results: The Gll presented a higher metastasis rate than Gl, while tumors of Gll presented a medium volume higher than in Gl (p=0.011). This volume increase in Gll was accompanied by an apparent increase in proliferation, demonstrated by the higher marking intensity for PCNA in Gll in relation to Gl (p=0.005). All groups presented an increase in apoptosis by higher marking intensity for Caspase 3 and Bax when compared to Gll (p=0.005). The Gl and Gll presented no significant differences in Caspase 3 and Bax marking; however, a slight increase in Bcl2 marking was observed in Gl (p<0.005).

Conclusion: This study suggests that simvastatin has the ability to prevent the development of breast cancer and related metastasis by decreasing proliferation and increasing apoptosis. Further studies are required to identify the molecular targets.