Antiproliferative effects of imatinib mesylate on ZR-75-1 and MDA-MB-231 cell lines via PDGFR-β, PDGF-BB, c-Kit and SCF expression

Authors:
- Ali Kadivar
- Mohamed Ibrahim Noordin
- Arya Aditya
- Behnam Kamalidehghan
- Ehsan Taghizadeh Davoudi
- Reihaneh Sedghi
- Hamid Akbari Javar

View Affiliations

Published online on: March 27, 2018  https://doi.org/10.3892/ijmm.2018.3590

Metrics: HTML 0 views | PDF 0 views  Cited By (CrossRef): 0 citations

Abstract

Imatinib mesylate is an anti-neoplastic targeted chemotherapeutic agent, which can inhibit tyrosine kinase receptors, including BCR-ABL, platelet-derived growth factor receptors (PDGFRs) and c-Kit. Cellular processes, including differentiation, proliferation and survival are regulated by these receptors. The present study aimed to evaluate the antiproliferative effects of imatinib mesylate, and its effects on apoptotic induction and cell cycle arrest in breast cancer cell lines. In addition, the study aimed to determine whether the effects of this drug were associated with the mRNA and protein expression levels of PDGFR-β, c-Kit, and their corresponding ligands PDGF-BB and stem cell factor (SCF), which may potentially modulate cell survival and proliferation. To assess the antiproliferative effects of imatinib mesylate, an MTS assay was conducted following treatment of cells with 2-10 µM imatinib mesylate for 96, 120 and 144 h; accordingly the half maximal inhibitory concentration of imatinib mesylate was calculated for each cell line. In addition, the proapoptotic effects and cytostatic activity of imatinib mesylate were investigated. To evaluate the expression of imatinib-targeted genes, PDGFR-β, c-Kit, PDGF-BB and SCF, under imatinib mesylate treatment, mRNA expression was detected using semi-quantitative polymerase chain reaction and protein expression was detected by western blot analysis in ZR-75-1 and MDA-MB-231 breast carcinoma cell lines. Treatment with imatinib mesylate suppressed cell proliferation, which was accompanied by apoptotic induction and cell
cycle arrest in the investigated cell lines. In addition, PDGFR-β, PDGF-BB, c-Kit and SCF were expressed in both breast carcinoma cell lines; PDGFR-β and c-Kit, as imatinib targets, were downregulated in response to imatinib mesylate treatment. The present results revealed that at least two potential targets of imatinib mesylate were expressed in the two breast carcinoma cell lines studied. In conclusion, the antiproliferative, cytostatic and proapoptotic effects of imatinib mesylate may be the result of a reduction in the expression of c-Kit and PDGFR tyrosine kinase receptors, thus resulting in suppression of the corresponding ligand PDGF-BB. Therefore, imatinib mesylate may be considered a promising target therapy for the future treatment of breast cancer.