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MINIMAL MODEL FOR METRONOMIC CHEMOTHERAPY: MATHEMATICAL ANALYSIS AND MEDICAL IMPLICATIONS

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ABSTRACT

In the last years, a new era in the fight against cancer has began, fueled by biochemical deciphering of many sub and intracelular interactions involved in the tumor microenvironment, and by new technologies in medicine [1]. New strategies and new treatment targets have come as an alternative to traditional chemotherapy, which prevailed over the last five decades. An important example of new treatment strategy is metronomic chemotherapy, which consists in the frequent application of low doses of cytotoxic agents, with few or no interruptions [2]. In this work, we propose and analyze in details an ODE model for metronomic chemotherapy with three equations: for normal cells, cancer cells and the drug. This simple model takes into account the drug deactivation by cancer and normal cells, an interaction generally disregarded by other models. Also, the inclusion of normal cells allow us to measure the toxicity of a given treatment. Biological implications are discussed and we conclude that the model reproduces well realistic scenarios. A lower bound is obtained to the drug infusion rate in order to the system has a unique stable equilibrium, which corresponds to a complete cure. Finally, by investigating occurrence of bifurcations, a condition is obtained which gives a way to classify the toxicities of diverse treatments.

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