

CHRONOBIOLOGICALLY MODULATED CHEMOTHERAPY IN ORAL CANCER

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Chronobiology is the study of the temporal relationship of biologic phenomena. All living things evolved in a milieu characterized by constant change based upon the cyclic relationships of the sun, earth, and moon. The circadian periodicity is genetically retained by all living organisms. Circadian organization is such a basic property of life that, derangements may have lethal consequences. Mammalian circadian rhythms result from a complex organization involving molecular clocks within nearly all normal cells and a dedicated neuroanatomical system which coordinates the so called peripheral oscillators. The core of the central clock system is constituted by the suprachiasmatic nuclei that are located on the floor of the hypothalamus. This circadian organization is responsible for predictable changes in the tolerability and efficacy of anticancer agents. The circadian rhythm dependent chemotherapy provides indirect evidence for time-dependent variability of the response of the human and murine to anticancer drugs. Doxorubicin, cisplatin, 5-fluorouracil and floxuridine (FUDR) have been studied in oral cancer for their circadian pharmacodynamics and toxicology. The outcome of these studies clearly concluded that circadian dependent administration of anticancer drugs reduces drug toxicity and allows substantial increase in the maximally tolerated dose which results in better treatment efficacy and greater comfort for oral cancer patients. Thus chronobiologically modulated chemotherapy hold promising results in treatment of oral cancer and other cancer with increased efficacy and decreased toxicity. In coming years, the future of cancer treatment lies in circadian rhythm dependent chemotherapy.

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