The role of pentoxifylline as a modifier of radiation therapy.

Abstract:

Pentoxifylline (Ptx), a hemorrheologic methylxanthine derivative, is of interest in radiation oncology for several reasons. First, improvement of tumor perfusion might result in better oxygenation and thus radiosensitivity. In addition, the drug also influences cytokine-mediated inflammation. The role of cytokines in the progression of radiation reactions in both tumor and normal tissues therefore provides further opportunities to combine Ptx with ionising radiation in order to improve the therapeutic ratio. This review summarizes preclinical and clinical data in both tumor and normal tissues. Regarding radiosensitization of tumors, a large body of evidence suggests that Ptx improves tumor oxygenation and sensitizes p53 mutant tumors. However, these findings have not translated into positive clinical studies to date. None of three published clinical trials attempting to enhance the effectiveness of radiotherapy with Ptx had a satisfactory design. There is also little evidence to prove that Ptx reduces acute side effects of radiotherapy. The only possible exception is a small randomized trial of lung radiotherapy. Regarding established late sequelae, numerous non-randomized clinical trials described healing of soft tissue necrosis and improvement of trismus and fibrosis after several weeks of Ptx or Ptx plus vitamin E. However, is not unequivocally clear that the combination with vitamin E indeed is superior. The literature data suggest that radiation necrosis can be treated
more effectively than fibrosis and that certain improvements might be functional and transient, with less influence on the chronic structural damage induced by ionising radiation. The ultimate individual outcome might depend, for example, on the stage of fibrosis progression, the size of the lesion and comorbid conditions such as diabetes and arteriosclerosis. Some of these factors will influence the actual amount of drug available in the targeted region. It is therefore necessary to evaluate Ptx in larger clinical trials with less baseline variation and to improve the recording of long-term results.