

Antineoplastic drug-induced morphological changes in the dental root development of young mice

In recent decades, improvements in therapies for childhood cancers have increased the number of survivors. The treatments for childhood cancer include chemotherapy, irradiation, surgery, stem cell transplantation, and any combination of these modalities, all of which are becoming increasingly effective. However, as the survival rate of children with cancer has improved considerably, the late effects of antineoplastic therapy deserve more attention.

Notably, late effects involving dental disturbances have been reported in a group of patients treated with childhood cancer therapy. Adverse effects of cancer and cancer therapy during childhood on dental health have been reported in terms of mineralization disturbances, dental caries, microdontia, hypodontia, root stunting, and taurodontism. Dental disturbances can result from chemotherapy, as well as radiation therapy. However, because multimodal therapy is used for almost all childhood cancers, it is difficult to attribute these effects to any single agent or treatment modality.

The effects of antineoplastic treatment, particularly those of alkylating drugs, on the oral health of childhood cancer survivors are well-known and widely documented. Cyclophosphamide, an N-mustard derivative, is an alkylating drug that is widely used in the treatment of cancer because of its capacity to interfere with cancer cell division. However, administration of Cyclophosphamide results in certain undesirable secondary effects caused by nonspecific actions on cells with a high mitotic index, which results in damage to both neoplastic and normal cells.

In our study, we examined the molar teeth of young mice treated solely with Cyclophosphamide, in order to evaluate the effects of Cyclophosphamide on root development until occlusion completion. We analyzed morphological changes in the molar roots of mice using 3D structural images to investigate the mechanism underlying the adverse effects of Cyclophosphamide on dental root formation. Our results showed that Cyclophosphamide administration in the early stages of root formation resulted in impaired root development and early closure of the apical foramen. Additionally, we showed that Cyclophosphamide inhibited the regular formation of Hertwig's epithelial root sheath and could cause disturbances to the developing root of the molar.

Further studies should elucidate how the dose, age, and time-related effects of anticancer treatment affect dental development. The number of long-term survivors of childhood cancer will increase steadily in the future. Therefore, a proper oral care program designed to prevent periodontal disease is needed, considering the irreversible short tooth roots of these survivors.