Cyclophoshamide inhibits root development of milar teeth in growing mice

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Abstrak

Root development of permanent teeth is disturbed in survivors of childhood cancer. Cyclophosphamide (CY) is a cytostatic drug commonly used for chemotherapy in children with cancer. This study aimed to evaluate the effects of CY on the development of molar teeth until the completion of occlusion in young mice, focusing on Hertwig's epithelial root sheath (HERS). We treated thirty-two 12-day-old ICR mice with CY (100 mg/kg; 100-CY group), and 36 control mice with saline. At 12, 14, 16, 20, 24, 27, 39, 60, and 76 days of age, the mandibular molars were removed. Soft X-ray radiographs were obtained in lateral projection. The root/crown length (R/C) ratio of the first molar was calculated. Serial sagittal sections were prepared and histomorphological hematoxylin and eosin (HE) staining and immunohistochemical (cytokeratin) studies were performed. The R/C ratio of the 100-CY group (0.78) was smaller than that of the control group (1.23) at 76 days ($p < 0.05$, t test). While all roots developed further after injection, microscopic examination showed that the roots of the first molars that developed in the 100-CY group were shorter than those in the control group. In addition, experimental mice showed apical closure of the roots. By 20 days after injection, the HERS had disappeared from the root surface in the 100-CY group. In conclusion, this study indicates that CY can induce a defect in HERS and cause early loss of HERS. Disruption of the epithelial sheath inhibits normal root formation, and it could cause irreversible short-root development.