Recent Advances and Prospectives for Chemoprevention in Head and Neck Cancer

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Cancer development in the field exposed to tobacco-related carcinogens is likely a result of accumulation of molecular, cellular, and genetic alterations. The opportunity to prevent cancer formation has been illustrated by preclinical studies for squamous cell carcinoma of the head and neck (SCCHN) and in clinical studies, involving precancerous and cancerous lesions of the head and neck. Cancer chemoprevention has recently become a practical modality. Among the potential chemopreventive agents, retinoids have been extensively studied for chemoprevention of the head and neck. Double-blind randomized studies using either high-dose 13-cis-retinoic acid (13cRA) or placebo for the treatment of oral premalignant lesions and prevention of second primary tumors showed promising results, although toxicity was a concern. A study of long-term based (3years) low-dose retinoids (13cRA, 30 mg/day) vs. placebo in a large intergroup trial did not show any difference in the prevention of second primary tumor rates ; therefore, we clearly need a new strategy for the chemoprevention in the head and neck. Biochemoprevention (13-cRA, interferon-α [IFN-α], and vitamin E [Vit E]) has shown promising results in a previously conducted phase II study. After the patients receive definitive local treatment for stage III/IV SCCHN, 45 patients received 12-months treatment with 13-cRA (50mg/m^2/day), IFN-α 2a (3×10^6 IU, TIW) and Vit E (1200IU/day). Toxicity was mild to moderate. The median follow-up is now 49.4months. The overall survival rates are far superior to the historical control : 1-year, 98% ; 3-year, 89% ; 5-year, 81%. To confirm these phase II results, we are currently conducting a phase III randomized trial (13-cRA+IFN-α 2a+vit E vs. observation) with biomarker studies through Eastern Cooperative Oncology Group (E1301). COX-2 and EGFR signalings have also been a main focus in the carcinogenesis of SCCHN. Blocking of these molecular pathways would be highly desirable approaches in chemoprevention of the head and neck. Preclinical studies including animal models using COX-2 inhibitors and EGFR blocking agents will be discussed. Further molecular intervention and understanding of the interaction of these two pathways may be important approaches in clinical trials in the near future. Finally, molecularly tailored approaches, including genomics and proteomics in chemoprevention, would be highly desirable based on the heterogeneous and multifunctional gene profile in SCCHN.