Areca nut extract up-regulate prostaglandin, cyclooxygenase-2 mRNA and protein expression of human oral keratinocytes.

何元順
Jeng JH;Ho YS;Chan CP;Wang YJ;Hahn LJ;Lei D;Hsu CC;Chang MC.

Abstract

There are about 600 million betel quid (BQ) chewers in the world. BQ chewing is associated with increased incidence of oral cancer and submucous fibrosis. In this study, areca nut (AN) extract (200-800 microg/ml) induced the prostaglandin E(2) (PGE(2)) production by 1. 4-3.4-fold and 6-keto-PGF(1 alpha) production by 1.1-1.7-fold of gingival keratinocytes (GK), respectively, following 24 h of exposure. Exposure of GK to AN extract (>400 microg/ml) led to cell retraction and intracellular vacuoles formation. At concentrations of 800 and 1200 microg/ml, AN extract induced cell death at 21-24 and 32-52% as detected by MTT assay and cellular lactate dehydrogenase release, respectively. Interestingly, AN-induced morphological changes of GK are reversible. GK can still proliferate following exposure to AN extract. Cytotoxicity of AN extract cannot be inhibited by indomethacin (1 microM) and aspirin (50 microM), indicating that prostaglandin (PG) production is not the major factor responsible for AN cytotoxicity. PGE(2) exhibited little effect on the growth of GK at concentrations ranging from 100-1000 pg/ml. Stimulating GK production of PGs by AN extract could be due to induction of cyclooxygenase-2 (COX-2) mRNA expression and protein production. These results suggest that AN ingredients are critical in the pathogenesis of oral submucous fibrosis and oral cancer via their stimulatory effects on the PGs, COX-2 production and associated tissue inflammatory responses. AN cytotoxicity to GK is not directly mediated by COX-2 stimulation and PG production.