Keloid keratinocyte proliferation and gene expression changes with exposure to omega-3 fatty acids

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Background

Keloid scars are often refractory to current treatments. Prolonged inflammation is thought to contribute to keloid scar development. Omega-3 polyunsaturated fatty acids (ω-3-PUFAs), such as eicosapentaenoic acid (EPA) and docosohexaenoic acid (DHA), are nutritional supplements and have anti-inflammatory effects *in vitro* and *in vivo*. Traditional West African medicine uses ω-3-PUFAs to prevent and reduce keloid scarring. Previous studies focused on ω-3-PUFA effects on keloid fibroblasts.

Aims/Hypothesis

We focused on keloid keratinocytes, which influence fibroblasts via paracrine interactions, to investigate gene expression and proliferation changes upon ω-3-PUFA treatment. Genes analyzed included IL1RN (IL-1 receptor antagonist), PTGS2 (cyclooxygenase-2), and IL1A (IL-1-alpha).

Methods

Two keloid and two normal keratinocyte cell strains obtained with IRB approval from patients at Shriner's Hospital for Children-Cincinnati and University of Cincinnati Medical Center were incubated 24 hours with EPA or DHA (0, 5, and 20μM); proliferation was quantified by counting cells. Gene expression was measured using quantitative PCR. The housekeeping gene GAPDH was used to normalize gene expression. One-way ANOVA and Holm-Sidak pairwise comparisons were used to determine statistical significance.

Results

Media containing 20μM DHA reduced cell growth for all cell strains ($p<0.05$); 20μM EPA reduced cell growth for both keloid and one normal cell strain ($p<0.01$). Incubation with 20μM DHA increased IL1RN expression in one normal and one keloid strain ($p<0.04$) while increasing PTGS2 expression in the same strains ($p=0.001$). Incubation with 20μM EPA increased expression of IL1RN and IL1A in one normal strain ($p<0.05$) and increased PTGS2 expression in both normal strains ($p<0.04$).

Conclusions

Although ω-3-PUFAs act as anti-inflammatory mediators in other inflammatory diseases, this small sample suggests that high doses of ω-3-PUFAs are cytotoxic to normal and keloid keratinocytes. ω-3-PUFAs variably affected expression of pro-inflammatory mediators IL1A and PTGS2 and anti-inflammatory molecule IL1RN in normal and keloid keratinocytes. The effects of ω-3-PUFAs on gene expression may be related to individual genetic variation rather than keloid pathology.

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