

Pathophysiological role of hormones and cytokines in cancer cachexia

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Background

Cancer-induced cachexia is the most common paraneoplastic syndrome and is recognized as an indicator of poor prognosis. Cancer cachexia differs from starvation, but has not been fully elucidated. We investigated the role of fasting hormones (adiponectin, ghrelin, and leptin) and pro-inflammatory cytokines (TNF- α , IFN- γ , and IL-6) in cancer patients.

Methods

Hormones (ghrelin, adiponectin, and leptin) and cytokines (TNF- α , IFN- γ , and IL-6) were measured by ELISA or RIA in lung cancer and colorectal cancer patients before the administration of cancer therapy, and measurements were repeated every 2 months for a total of three times. Statistical analysis was performed to determine the relationship of hormone and cytokine levels to weight change.

Results

From June 2006 to August 2008, 42 patients (19 with colorectal cancer and 23 with lung cancer) were enrolled. In total, 21 patients were included in the cachexia group and the others served as a comparison group. Similar distributions in terms of age, diagnosis, and levels of hemoglobin (Hb), CRP, glucose, and insulin were observed in both groups, but the cachectic patients included more males than females, and these patients had lower albumin levels. No significant difference in the initial adiponectin, ghrelin, TNF- α , IFN- γ , or IL-6 level was observed between groups, although leptin was significantly lower in cachectic patients than in the comparison group (15.3 ± 19.5 vs. 80.9 ± 99.0 pg/ml, $P = 0.007$). Hormone and cytokine levels did not differ between colorectal and lung cancer patients. During the follow-up, the patients who showed a $> 5\%$ weight gain had higher ghrelin levels (weight gain vs. no change vs. weight loss: 1223.1 ± 383.7 vs. 594.2 ± 218.1 vs. 654.3 ± 218.1 pg/ml, $P = 0.007$) after 6 months and lower cytokine levels (TNF- α , IFN- γ , and IL-6) than the control, but the differences were not statistically significant. Patients exhibiting elevated IL-6 levels typically showed a weight loss $> 5\%$ after 6 months.

Conclusions

A blunted adiponectin or ghrelin response to weight loss may contribute to cancer cachexia. Patients with initially higher levels of IL-6 experienced weight loss. After 6 months, those who had gained weight ($> 5\%$) showed elevated ghrelin levels, and therefore a clinical trial examining the effect of ghrelin treatment on cancer cachexia may be warranted.