

Anxiety levels among oral cancer patients: A case-control study from Turkey

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ABSTRACT

The role of psychological stressors in cancerogenesis has been widely investigated and increased number of cancer cases in separated/divorced people, stressful and pessimistic women, and parents of deceased children are reported. This multicenter case-control study investigated the anxiety profile of a group of oral cancer patients in Turkey. Eighty-three patients with primary oral cancer were enrolled. Fifty-eight randomly selected subjects contributed as the healthy control group. A questionnaire containing State and Trait Anxiety Inventory Form-2 (STAI-2) was applied to both groups. Oral cancer patients filled the questionnaire after the diagnosis of the disease, but prior to initiation of any treatment. The scores of the groups were analyzed with independent sample t test. In all tests, p was set as 0.05. The mean scores provided for STAI-2 were 37.71 ± 7.53 for the cancer patients and 38.52 ± 7.84 for the healthy controls; the difference was insignificant ($p > 0.05$). The highest STAI-2 score provided by oral cancer patients was 3.072, whereas this was 3.241 in the controls. Our results revealed that STAI-2 scores were not different between oral cancer and control groups. Further determination of the factors associated with oral cancer would be helpful to establish efficient screening and prevention programmes. [Turk J Cancer 2009;39(2):56-61]

KEY WORDS: Oral cancer, psychometric assessment, anxiety

INTRODUCTION

Since 1950s, animal and human studies revealed the relationship between the brain and the immune system (1). With the emergence of a new scientific discipline termed neuroimmunomodulation or psychoneuroimmunology, the presence of bidirectional communication between the nervous, endocrine and the immune systems via the secretion of chemical messengers is now established (1-3). The response of the organism to stress is directed by the sympathetic-adrenal-medullary (SAM) and the hypothalamic-pituitary-adrenal (HPA) axes after the consequent rupture of the homeostasis (1,3).

The adaptive responses to stress begin with the activation of SAM and HPA axes. The neurosensory signals processed in the hypothalamus induce the secretion of corticotropin-releasing factor (CRF) and arginine vasopressin, which in turn activate the HPA axis in order to release adrenocorticotropic hormone (ACTH) and other pituitary peptides (1,3). The ACTH induces the secretion of glucocorticoids from the adrenal cortex. CRF activates the sympathetic nervous system (SNS), and this leads to the release of norepinephrine throughout the brain and the peripheral tissues. On the other hand, the activation of SNS stimulates the release of CRF by hypothalamus; thus, a bidirectional feedback loop results (1). So, as seen, both amygdala and hippocampus are involved within the onset of emotional reactions and also the regulation of CRF- ACTH-cortisol flow (3,4).

In addition to the immunosuppressive effects of glucocorticosteroids, many studies showed that catecholamines, histamine, opioids and cytokines -especially interleukin 2, 6 and 8- released during chronic stress and depression. These can contribute to the suppression of the cellular mediated immunity, including natural killer cells, cytotoxic T-lymphocytes, tissue macrophages and dendritic cells (1, 5-7). Likewise, behavioral stress activates catecholamines which subsequently induce the secretion of vascular endothelial growth factor. This significantly enhances the vessel density and leads to increased angiogenesis in malignant tumors (8,9). The disruption of these pathways by various physical and psychological stressors may promote the development of neuropsychiatric, cardiovascular and immunologic diseases (1,8,10). Among the psychological stressors, the prominent ones were described as major life events, losses, trauma, abuse, something related to the environment of home, workplace, family, neighborhood, social problems, depressive illnesses, and lack of confounding relations (1). In recent years, the role of psychological stressors in cancerogenesis has been widely investigated and increased number of cancer cases in separated/divorced people, stressful and pessimistic women, and parents of deceased children are reported (5, 11-14).

Stress contributes to development of carcinogenesis by disturbing various areas of the immune system and the suppression of natural killer cells activity may be sufficient enough to cause enhanced tumor development (1,10,15,16). Depression is pointed as an important factor of cancer progression that acts by modifying the modulation of the development and accumulation of somatic mutations and genomic instability (2,5,17). Additionally, inclination of stressful people to smoke and consume alcohol more frequently and heavily than controls has been reported as the indirect effect of stress on carcinogenesis (14,16).

On the other hand, many studies failed to reveal a strong effect of stress on malignant changes, and indicated the possible effect of bias, and/or uncontrolled personal parameters on the results (2,4,14, 18-25). Additionally, up to date, the effect of personality factors on the risk for cancer has been controversial; some studies reported a positive correlation, whereas others have failed to reveal a strong association (16,23, 26-28). Interpretation of personality is entangled due to the lack of universally accept-

ed definitions and furthermore, the individual's perception of major life events that lead to psychological stress may vary widely (23). Due to the variations among the standards, measurements and methodologies, data within the literature may be quite heterogenous and may lead to different conclusions (1,2,11,16,29). Additionally, the clarity of the instructions, the sequencing and complexity of the questions, the complexity and duration of the task, the number and range of the responses also affect the validity of the self-report questionnaires (2,30,31).

In addition to stress, anxiety -which is another major accompanying dimension to stress- has been investigated in patients with chronic medical illnesses in order to find out the association between anxiety levels of the patients and the healthy controls (9,16,29, 32-36). The combination of low anxiety and high defensiveness was observed to affect the prognosis of cancer (16). Likewise, depression and anxiety were positively correlated with postoperative vascular endothelial growth factor levels, which are known as a major contributor to cancer progression (9).

Even though there have been reports about the psychiatric conditions and personality characteristics of the cancer patients and the effects of psychological status on cancer prognosis and on patient compliance to the cancer therapy, to the authors' knowledge, there is no study investigating the anxiety profile of the patients with oral cancer in Turkey (37-40). In this multicenter case-control study, the aim was to investigate the level of anxiety in a group of oral cavity cancer patients in Turkey by application of self-report measures of anxiety and to determine the presence of any differences between the healthy controls.

MATERIALS AND METHODS

Study design

The case and controls were formerly enrolled into a previous study that examined the association of the sociodemographic features, dietary habits, tobacco-alcohol consumption, and dental status with oral cavity cancer (41).

Case subjects were primary oral cavity cancer patients who were admitted to the Ear, Nose & Throat Departments of the following 4 major hospitals between 1998-2002: Ege University Faculty of Medicine, Dokuz Eylül University Faculty of Medicine, Tepecik SSK State Hospital, and Uludağ University Faculty of Medicine. Total

of 83 patients (57 males and 26 females) accepted to participate and only the patients with cancers of tongue, floor of the mouth, lips, gingiva, buccal mucosa, hard and soft palate were enrolled. They were assigned after receiving their written informed consents; but prior to initiation of any kind of therapy.

Fifty-eight randomly selected subjects (24 males and 34 females) who were among the dental patients or their attendants admitted to the Outpatient Clinic of Department of Oral Diagnosis and Radiology in Ege University, School of Dentistry have accepted to partake as the healthy controls. They had no history of cancer, no psychiatric condition/disease that was diagnosed, and they were not under any medication. The informed consents of the control group were also obtained.

Data collection

A trained interviewer consulted all cases and controls in person. A questionnaire was used to assess the sociodemographic features, weight and height of the partakers, tobacco and alcohol consumptions, dietary food intake and eating habits, and oral hygiene status of the participants prior to the hospital admission. The employment, monthly income, level of education, and marital status of each person were also recorded. The data and results of this study have been published previously (41).

The long-standing patterns of anxiety among the patients and controls were assessed with a self-report measure of anxiety by using State-Trait Anxiety Inventory Form 2 (STAI Form TX-2). The STAI is a self-report instrument that consists two self-reporting measures by using 20 statements: state anxiety represents a temporal and transient emotional state as a reaction to the environment whereas trait anxiety -which also contains 20 items- reflects a relatively stable, more permanent disposition developed during childhood, and reflects" the existence of stable individual variations in the tendency to respond with state anxiety in the anticipation of threatening situations" (42-44). It assesses subject's state anxiety (STAI-1) and trait anxiety (STAI-2) on a scale of 1 ("almost never") to 4 ("almost always"); higher scores reflect higher levels of anxiety (42,45). After reversing the positively worded items, the responses for each scale are summed to provide a score between 20-80. This score then undergoes an assessment process that is performed by using a manual of normative values (43).

The scores of the groups were analyzed statistically with independent sample t test and in all tests, p was set as 0.05.

RESULTS

The results must be interpreted cautiously since the results are valid only for this test population and the two groups are not large enough to draw definite conclusions.

Mean age of the oral cancer patients was 56.2 whereas this was 55.3 in the healthy control group. The mean scores provided for STAI-2 were 37.71 ± 7.53 for the cancer patients and 38.52 ± 7.84 for the healthy controls; the difference was insignificant ($p > 0.05$) (Figure 1). Only the 9th item (I usually worry for unimportant things) was significantly different between groups ($p = 0.029$). The cancer group scored this item as 1.8049 whereas the healthy controls scored it as 2.155. All other items were scored similarly between tests and controls.

The highest score provided by the cancer group was 3.108 and it was granted to the 17th item; "I am a reasonable and determined person". This item was also the one that received the highest score (3.240) among the healthy controls. The second highest score was given to the 14th item "Generally I am satisfied with my life" (cancer patients=3.0723; controls=3.1404), and it was followed by the 10th item "I am generally happy" (cancer patients=2.9759; controls=3.1250).

The statistical analysis revealed that age and gender of the patients were not effective on the results ($p > 0.05$)

DISCUSSION

Limitations inherent to this study suggest that interpretation of the findings must be performed cautiously and shall be considered valid only for the samples of the current study.

It is reported that excessive stress consists of extremely strong negative affects whereas chronic stress is the state of stress experienced permanently or frequently. As a consequence of stress, changes in the organism occur that may result in physiological or biochemical disturbances expressed in psychosomatic diseases or other health problems (1,8,10,46). However, it shall be noted that not all states of stress lead to the negative consequences; rather,

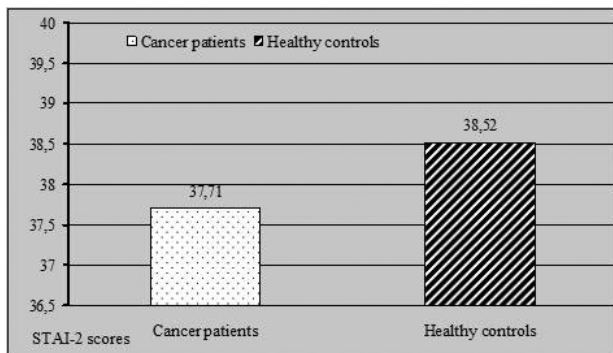


Fig 1. Mean STAI-2 scores provided by oral cancer group and the healthy controls

stress should be regarded as one of the many risk factors contributing to maladaptive functioning and disorders. When the state of stress acts together with other factors that decrease the outcomes of stress, these health problems may not be observed (46).

The popularity of self-reports originated from their properties such as being cheap and suitable for gathering the symptoms in the community, and having good psychometric virtue (47). On the other hand, self-reported questionnaires may lead to incompatible replies which are influenced by sociocultural norms, the setting in which the questionnaire is filled, the personal situation at the time of the data is collected, and the personal, cognitive and communication characteristics of the respondents such as the intelligence level, the need for approval, attitudes and beliefs, the desire to present oneself in a favorable manner (2,30,31). Since the self-report questionnaires include questions about emotional and/or behavioral difficulties, people may tend to inflate or minimize their degree of distress (48). In order to diminish the influence of diagnosis on the patients and remove their recall bias toward more negative events/items, some authors have suggested to use “limited prospective study design” where individuals with suspected lesions provide data regarding their psychological characteristics prior to the diagnosis of the lesions (2,49,50). However, in this study, our patients provided data about their psychological structure after the initial diagnosis, but prior to initiation of any therapy.

The STAI-2 scores of the oral cancer patients were similar to those of the healthy controls in this study. Considering that the scores are evaluated within the range of 20 to 80 and both groups had scores around 38, this finding could be commented as “both groups’ anxiety levels were low”. Stark et al. (51) reported that STAI-2 scores of

cancer patients with anxiety disorders were different than those of the patients without anxiety, and these were 47.6 and 36.3, respectively. Similar STAI-2 scores in various chronic diseases with immunological and psychological components have been reported in the literature (52,53). From Turkey, Gur et al. (45) used STAI in order to establish the anxiety levels of patients with Behçet’s disease with/without arthritis and reported that healthy controls’ scores were 31.41 and the patients were 44.00 and 48.00. Their healthy controls had corresponding STAI scores to our controls, revealing matching anxiety levels of different samples from the same society.

Even though statistically insignificant, cancer patients enrolled into this study provided lower scores to 17 out of 20 items when compared to those of the control group; revealing somewhat little bit more anxious state than the healthy controls. However, these differences failed to reach to significance. Only the scores granted to “I usually worry for unimportant things” statement was significantly different between the groups.

The complexity of the relationship between psychological factors and chronic illnesses, and the variations among the test parameters, groups and methods complicate the interpretation of the results (1,2,5,16,29). Grosarth-Maticek et al. (54) reported “the possibility that the disease process has affected the personality of the patient, rather than the other way about”. This was also mentioned by Härter et al. (29) who reported that medical illnesses may affect the neurotransmitter systems or neuroanatomic sites associated directly with production of anxiety. They have stated that in addition to the stressful life events which may produce anxiety, internal stimuli may also change the homeostasis and lead to anxiety, as well. It is also reported that the stage of disease can have a strong effect on how patients feel, and cancer-related concerns influence important biochemical mediators (2,5,9,55).

In conclusion, despite the common perception that psychological factors may play a role in cancerogenesis, our results did not reveal a significant difference in anxiety levels and agreed with many reports which failed to find any such association. Considering the increasing incidence of cancer among the society and the high number of reports revealing the association between psychological status and chronic diseases, this finding may require further prospective studies to determine the effects of stress and/or anxiety on development of oral malignancies. Ad-

ditionally, establishment of potential factors which are more frequently observed in oral cancer patients would be helpful not only to ascertain the accurate etiological agents, but also to set efficient screening, prevention and public education programmes, as well.

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