Correlation between stress, cortisol levels and coping strategies in cancer patients undergoing treatment

Correlación entre estrés, niveles de cortisol y estrategias de afrontamiento en pacientes con cáncer sometidos a tratamiento

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ABSTRACT:

Introduction: Cancer is one of the leading causes of morbidity and mortality worldwide, according to the World Health Organization (WHO), in 2012 14 million new cases and 8.2 million deaths. (WHO, 2019). Patients in treatment, surgery, chemotherapy and radiation therapy have been shown to have high levels of cortisol that influence their quality of life.

Objective: to identify the relationship between stress, cortisol level and coping strategies in cancer patients undergoing treatment.

Material and methods: Cross-sectional, descriptive and correlational study conducted June to December 2018. In 65 male and female patients under treatment.

Results: 68.2% were women 31.8% men, between 17 and 76 years. With diagnoses Ca breast (30.3%), prostate cancer (18.3), colon (15.2), lung (13.6), cervical (12.1% gastric (9.1%) skin cancer (1.5%). Statistics: 35.3% reported cortisol at normal levels and 64.5% high levels; stress averaged 13.9 (DE s 4.64). On the level of cortisol and the type of treatment, significant differences were observed (X2 x 1,546, p .04), i.e. the patient who has a mixed treatment cortisol is higher.

Conclusions: It is important to reevaluate the strategies focused on the problem, analyze implications and propose studies in the context in which they operate, in the future develop an intervention including nursing activities in chemotherapy and radiotherapy, supporting effective coping strategies. minimizing threats focused on the problem, it is important to have a deeper comprehensive approach.
RESUMEN:
Introducción: El cáncer es una de las principales causas de morbilidad y mortalidad en el mundo, según la Organización Mundial de la Salud (OMS), en 2012 14 millones de casos nuevos y 8,2 millones de muertes. Se demostró que los pacientes en tratamiento, cirugía, quimioterapia y radioterapia tienen niveles altos de cortisol que influye en su calidad de vida.
Objetivo: Identificar la relación entre el estrés, a nivel de cortisol y las estrategias de afrontamiento en pacientes con cáncer sometidos a tratamiento.
Material y métodos: Estudio transversal, descriptivo y correlacional realizado junio a diciembre del 2019.
Resultados epidemiológicos: 68.2% mujeres 31.8 % hombres, entre 17 y 76 años, con diagnósticos de: Ca mama (30.3%), de próstata (18.3), colon (15.2), pulmón (13.6), cervical (12.1% gástrico (9.1%) cáncer de piel (1.5%). Estadísticos: El 35,3% informaron cortisol a niveles normales y 64.5% niveles altos; el estrés obtuvo un promedio de 13.9 (DE = 4.64). Sobre el nivel de cortisol y el tipo de tratamiento, se observaron diferencias significativas (X² = 1,546, p = .04), es decir, el paciente que tienen un tratamiento mixto el cortisol es más alto.
Conclusiones: Es importante reevaluar las estrategias centradas en el problema, analizar implicaciones y proponer estudios en el contexto en que se desenvuelven, en futuro desarrollar una intervención incluyendo actividades de enfermería en la quimioterapia y radioterapia, apoyando estrategias de afrontamiento efectivas. En este sentido y derivado de la minimización de amenazas centradas en el problema, es importante tener un enfoque integral más profundo.

Palabras clave: Estrés, cáncer, estrategias, cortisol, pacientes.

INTRODUCTION

Cancer is one of the leading causes of morbidity and mortality worldwide, according to the World Health Organization (WHO), in 2012 14 million new cases and 8.2 million deaths related to cancer were reported (WHO). The most frequently diagnosed types of cancers in men were, lung, prostate, colon and rectum, stomach and liver, while in women it was breast, colon, rectum, lung, cervix and stomach cancer. It should be noted that most cases are diagnosed in advanced stages, which decreases the chances of cure, this by the adoption of new ways of life (sedentary and stressful) urbanization and a higher life expectancy.

Cancer is a vital non-normative fact that causes emotional stress, the types of treatments such as surgery, chemotherapy, radiotherapy produce devastating physical, psychological and emotional side effects, due to the psychosocial adjustment that involves a change in lifestyle to adapt to the changes produced by the cancer experience to the complexity of the situation it has been reported that 78% cancer patients diagnosed and 96% of those who receive some type of treatment have symptoms of stress, These symptoms, from the patient's point of view, are explained as feeling tired, weak, exhaustion, and heaviness, among others.

The stress defined by Selye, is a general adaptation syndrome in which a complex mechanism of the neuroendocrine system is activated to prepare the body for fight or flight behavior. Stress induces diseases that depend on substances such as catecholamines, cortisol and deterioration of the immune system; all these mediators have an impact on the spread and metastasis of cancer and the mechanisms of DNA repair.
Cancer patients have a perception of stress. The prevalence of stress in cancer patients is reported to be above 30% \(^{8}\). Despite its impact on the daily functioning, stress in cancer patients is often overlooked and under-treated \(^{9}\).

Cancer and treatment are important sources of stress. Major theoretical definitions of stress emphasize perception as an important component responsible for the experience of stress, According to Lazarus and Folkman \(^{10}\).

Primary appraisals of demand, difficulty, and/or uncertainty when weighed against secondary appraisals of coping resources and abilities may result in further perceptions of stress as a challenge to be met and overcome (resources outweigh demands) or as a threat to be endured (demands outweigh resources). Perceptions of a stressful event’s duration (chronic vs. acute), severity, controllability, and predictability can also influence responses to the stressor \(^{11}\). Stress results from the perceived potential loss of resources. As a result, perceptions of current resources and the potential to gain resources are involved in perceiving an event as stressful.

Cancer diagnosis/treatment has been conceptualized as a stressor \(^{12}\); however, this perception of stress is subjective is necessary to perform objective tests that assess stress. Cortisol is known as the stress hormone; it is the principal glucocorticoid secreted by the suprarenal cortex and is liberated to the blood stream in situations of stress; it affects many physiological functions, including vital anti-inflammatory and immunosuppressive actions, as well as metabolism and homeostasis in order to exert their effects on the peripheral tissue in response to stress \(^{13}\).

Consequently, a basal cortisol concentration (5 to 25 micrograms / dL) is required, but may rise immediately in response to physical or mental stress and stressors, usually returning to baseline levels later \(^{14}\). The measurement of cortisol in the blood can act as an indicator of the effects of stress, independently of the self-report scales. The hypersecretion of cortisol has been observed as a physiological pathway related to the effects of chronic stress; that is to say, with results that are harmful to health due to the reduction of immunological efficacy \(^{15}\).

As such, cortisol has been suggested as a valuable tool in clinical and research settings to provide additional physiological data regarding the presence of chronic stress and the severity of that stress \(^{16}\).

Previous literature has shown that patients with cancer in treatment, mainly with surgery (not biopsy), chemotherapy and radiotherapy have high cortisol levels that can influence their quality of life. Thus, it is important to examine cortisol levels with biochemical measurements in patients with cancer that are undergoing treatment, which allows the evaluation of the presence of this hormone \(^{17}\).

The patients at the time of being diagnosed with cancer, patients implement coping strategies that helped them manage stressful situations and adapt to changes according to Lazarus and Folkman, coping strategies are tools or resources that the subject develops to deal with specific external or Coping is the way in which the individual internal demands \(^{10}\). Manages the stress and can act as an important mediator between stressful situations and health \(^{18}\). The coping strategies in people with cancer refer to the adaptation process in which cognitive and behavioral processes are used with those who try to change the situation; as well as adjust their emotions, orienting themselves to make sense of the disease, dealing with impotence.
and uncertainty, difficulties in achieving life goals and physical and psychological changes (19).

The literature indicates that the use of coping strategies may be related to other variables, such as age (20), gender (21), marital status and schooling (22). Some studies have shown that the use of coping strategies to deal with stress in patients, positively influences how they face their disease, whether terminal or not, and affects the development of chronic stress and cortisol levels (23).

However, the evidence is scarce among the variables of cortisol level in blood to assess chronic stress in people with cancer and in treatment. Therefore, the purpose of the present study was to know the stress levels, what coping strategies were used and how this affected the cortisol levels in cancer patients undergoing treatment in a public hospital.

**OBJECTIVE**

Identify the relationship between stress, cortisol level and coping strategies in cancer patients to treatment in a public hospital.

**METHOD**

**Design**

A transversal, descriptive and correlational study was carried out during the period from June to December 2019. 65 patients who were in chemotherapy treatment during the follow-up period by the Oncology service (Chemotherapy) were included.

**Instruments and Measurements**

The sampling was intentional for convenience by subject-type of pathology; from the area of oncological attention (chemotherapy) 65 people were selected and accepted to participate, after signing the informed consent, it should be noted that participation was voluntary, for patients with different types of cancer (breast cancer, prostate, uterine cervix and gastric cancer). The eligibility criteria were patients who were aged over 18 years, patients under 18; the tutor authorized their participation, had cancer, had received medical treatment, was fully conscious, did not have a mental illness, and agreed to participate in this study. The exclusion criteria were patients who were unconscious, had a mental illness, or refused to participate in this study.

The Stress Profile questionnaire developed by Nowack consisting of seven dimensions was used, for the present study some subscales of the Stress Profile were used (24). Stress, which is an assessment of the perception of some type of discomfort and distress in different areas such as health, work, family, personal finances, social obligations and environmental concerns; in the last three months. This scale consists of six items and has shown an alpha of 0.72. Coping strategies, divided into four different approaches: Positive appraisal is measured by five items that evaluate the use of positive thoughts that the person can use to reduce the stressful situation by referring to successful results of a similar situation and focusing on the positive of the current situation, Negative appraisal measures the tendency of the individual to have
thoughts of self-blame and to face the stressors with a negative perspective, concentrating on the mistakes made in a given situation. a) The negative appraisal scale has five items; Threat Minimization is measured by five items that value the tendency of the individual to mitigate the importance of a stressful circumstance, making fun of this situation or avoiding it, Problem-focused is the scale that calculates the disposition of the individual to carry out a specific plan for the satisfactory solution of the problem causing the stress, it consists of four items.

The psychometric properties of the instrument report reliability by halves of 0.89 and 0.91 in populations of different cultures and educational level. The homogeneity of the scales with test-retest reliability shows a range of 0.51 to 0.92 Cronbach alpha and the factorial analysis report them with low to moderate relation (0.41 to 0.75 eigen), which confirms that the constructs represented by these dimensions are the sufficiently independent to justify their interpretation separately (24).

The samples were taken by the nursing, these were performed at the time of placement of a peripheral venous catheter to avoid a second puncture. The blood samples were processed in clinical analysis laboratory to measure serum cortisol levels using the Cobas 6000 equipment (25). They were then provided with the instrument to identify the coping strategies developed by Nowack, this has been used by researchers to study various topics, reporting a Cronbach alpha coefficient between 0.70 and 0.83 (26,27).

**Ethical Considerations**

The Ethics and Research Committee of the institution approved the research. It was started by identifying the participants who were later invited to participate in the study; by accepting, the objectives of the study were explained to them in detail, in addition to explaining that this would not affect their level of care if they did not accept. They were asked to sign the informed consent and they were also explained that participation included taking a blood sample to measure cortisol levels. Ethical considerations. Based on the Helsinki Declaration in Category I for Retrospective Documentary Research Studies and the Regulations of the General Health Law on Health Research and in accordance with Article 17 is a study with minimal risk.

**Data Assessment**

Statistical analyses were performed with SPSS version 19.0. To determine the stress level, cortisol level, and coping strategies, descriptive statistics were used (means, standard deviations, frequencies, and percentage). Demographic characteristics and disease related variables were compared according to the participants and their features (p< .05). It was determined that the variables did not conform to a normal distribution; therefore, non-parametric statistics were used. Cortisol levels were compared between subgroups based on treatment-related variables using the the Kruskal–Wallis test. Correlations between variables, a p value of .05 or less was considered statistically significant. A Spearman correlation was performed to detect if cortisol levels and coping strategies in cancer patients with treatment have effect to develop stress. A p value of .05 or less was considered statistically significant.
RESULTS

Sociodemographics and cancer data

The study consisted of 65 participants, 68.2% were women and 38.2% men, and were between 17 to 76 years, with an average age of 52.2 (DE=14). With regards to their marital status, the highest percentage reported being married (65.2%), followed by the single (19.7%), widowed (9.1%) and divorced (6.1%). Regarding education, it was found that 10.6% do not have any type of formal study, 36.3% have primary, 30.3% secondary, 10.6% preparatory or technical career and 12.1% undergraduate studies. In occupation, 47% reported being housewives, 25.8% employed, and 10.6% pensioned, and 9.1% did not work, the rest reported various occupations. In reference to the type of cancer, the highest percentage was reported for breast (30.3%), prostate cancer (18.3), colon (15.2), lung (13.6), cervical (12.1%), gastric (9.1%), and skin cancer (1.5%).

Statistical data

According to the results, 35.3% of the participants reported normal cortisol levels and 64.5% high levels; stress obtained an average of 13.9 (SD = 4.64); Regarding the types of coping strategies, the ones that report higher means are the positive appraisal and the threat minimization.

Stress, cortisol levels and coping strategies Analysis on cortisol levels in patients. The Kruskal Wallis test was carried out, to compare the differences of the groups; no differences were observed in the cortisol level and the type of cancer also the estimates of the medians of the sample for the two groups indicate that for these groups they are all the same (X2 =1.476, p=.96), Regarding the cortisol level and the type of treatment, significant differences were observed (X2 = 1.546, p=.04), that is to say, the patients who have a mixed treatment (chemotherapy and radiotherapy or hormonal, among others), the cortisol level is significantly higher than in the other types of treatment. Stress did not show significant differences with the cortisol level and the types of coping.

In reference to the cortisol level and the types of coping, it was found that the problem focused was the coping mechanism that showed significant difference with reference to the level of cortisol, that is, problem-focused coping raises cortisol levels in oncology patients that are undergoing treatment. On the other hand, the correlations found with the Spearman coefficient show that there are statistically significant relationships between depression and cholera (rho-.822,p-.000), mean stress (rho-.825,p-.000), confusion (rho-.822,p-.000), mean stress (rho-.825,p-.000), confusion (rho-.822,p-.000), mean stress (rho-.825,p-.000), confusion (rho-.822,p-.000), mean stress (rho-.825,p-.000), confusion (rho-.822,p-.000), mean stress (rho-.825,p-.000), confusion (rho-.822,p-.000), mean stress (rho-.763,p-.000), a negative relationship with friendship (rho-.396,p-.001) and the vigor (rho-.468,p-.000) measured in the instruments applied (Table 1).
Other relationships found in the analyses were those of cancers with kindness reagents (0.258, p.039), confusion (-0.321, p.001), melancholy (0.435, p.000), fatigued (.286, p.022), aggressive (-0.350, p.005) and bad temper (-0.337, p.006), suggesting in such a way a possible relationship between the type of cancer and the aggressiveness that the person may present to others. (Table 2)

### Table 1: Correlation of depression in cancer patients

<table>
<thead>
<tr>
<th>Rho Spearman</th>
<th>Depression Correlation Coefficient</th>
<th>Medium Cholera</th>
<th>Tension</th>
<th>Confusion</th>
<th>Friendsh</th>
<th>Vigor</th>
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<tr>
<td>Sig. (bilateral)</td>
<td>.822** .825** .763** -.396** -.468**</td>
<td>.000 .000 .000 .001 .000</td>
<td>65</td>
<td>65</td>
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</tbody>
</table>

n=65
* Correlation is significant at level 0.05 (bilateral).
** Correlation is significant at level 0.01 (bilateral).

Nowack Test applied to cancer patients treated in a high-specialty medical unit in the period June to December 2019

### DISCUSSION

The object of the study was to find the relationship between stress, cortisol levels and coping strategies that oncological patients undergoing treatment use (chemotherapy, radiotherapy and hormonal treatment) and to know if the level of cortisol is consistent with the perception of stress. In relation to the type of cancer, those reported by the participants are the most prevalent worldwide (pulmonary, colorectal, gastric and breast), as reported by the WHO (1). This suggests that unhealthy lifestyles of people such as tobacco and alcohol consumption, poor diet and physical inactivity are the most influential factors.

With regards to the stress level regarding the relationship with cortisol levels, the relationship was expected to be positive because studies show that when perceived stress increases, cortisol secretion also increases, however, no significance was obtained, as reported by other studies that found no relationship between cortisol and variables such as stress (28).

According to the type of cancer, no significant difference was found with cortisol level, that is, the levels are similar in all types. However, authors have reported that in
various types of cancer such as prostate, mammary, since this difference may be due to the fact that in these studies some patients had metastases, it has also been found that patients with breast, ovarian, prostate, stomach cancer and colon present an alteration of the endocrine function, which is observed in changes in the amplitude, changes of phase, period, peaks and irregular channels of cortisol secretion. In patients with lung cancer, alteration in the cortisol level has also been reported. However, in this study the characteristic of the participants was that the time with the disease was similar and everyone was currently undergoing treatment. On the other hand, the type of treatment showed differences with cortisol levels, patients with mixed treatments (chemotherapy and radiotherapy) have higher cortisol levels; that could be explained to emotional reactions perceived in a negative way, such as sadness or anxiety with chemotherapy and radio therapy, these negative emotions coupled with physical effects prolong stress. Chronic stress and cortisol dysregulation can influence inflammation and immune function in a way that promotes fatigue, depression, and the risk of cancer recurrence. Cortisol is seen as a physiological marker of stress that allows assessment of the existence of chronic stress.

Regarding the types of coping strategies and the cortisol level, problem-focused strategies reported a significant relationship, suggesting that people suffering from terminal illnesses have an important need to use strategies to deal with stressful events during their illness (pain, discomfort, fear of die, family or economic problems). Diseases are an important source of demands, cognitive and behavioral efforts to handle external and / or internal situations that exceed the resources of the individual. The problem-focused coping strategy consists of the use of resources directed towards oneself or towards the environment, obtaining information about the best way to modify the problematic situation, to then carry out the pertinent action. The coping strategies have been considered as an important mediating factor in relation to the adaptation to the disease. However, oncological patients undergoing treatment, when focusing their efforts on understanding and managing their disease, may present poor stress management or persistence of stress, without that this type of coping allows total adaptation, but is observed in the increase of cortisol, helping to maintain chronic stress among patients.

The high cortisol levels are influenced by the threat minimization and problem-focused coping strategies, the results are consistent with the classic behavioral response to a threatening condition to fight or flee. These types of coping strategies show the fight and flight response, this is important since the activation of the Hypothalamic–pituitary–adrenal axis (HPA) produces the secretion of cortisol to mobilize and make available the energy of the organism so that it can respond to the demands of the environment, specifically the cope with the cancer disease and the implications of treatment in all aspects of your life. These conditions can change the direction of the relationship of psychological variables with indicators of the organism in one direction or another. Miller and colleagues mention that when stress is persistent and uncontrollable the activity of the HPA axis decreases, but when the stress has some controllable elements, it is possible that the HPA axis is activated to give the necessary metabolic support for an active coping; this has been evidenced in experimental studies. Likewise, the cortisol is a hormone that acts as a neurotransmitter in the brain, in response to stressful situations and a low level of glucocorticoids in the blood, a high level of stress hormone, and all its physical and biological repercussions.
In reference to the relationship between stress and the coping strategies, the patients with high stress use positive and negative appraisal influence to face the situation, especially the treatment and everything derived from the same event; this can help improve psychological well-being and personal growth, this is similar to reported in the literature by other authors where, it is mentioned that the meaning of life and the Self-concept are reorganized based on the situation they face \(^{(19)}\). This type of stress is the one that the individual perceives; when people perceive stress, they use these types of coping strategies.

It is important to reassess problem-focused strategies, analyze its implications and propose studies that deepen the context, in which they are developed, so in the future we can develop an intervention or include nursing activities in the area of chemotherapy and radiotherapy that supports the use of effective coping strategies. Although it is considered as a strategy that generates a better adjustment to cancer, the patient may not give the necessary importance to the problem and thus raise cortisol levels.

This study demonstrates the variations between coping strategies and stress. In relation to coping strategies, threat minimization and problem-focused, it is important to make a deeper integral approach to generate different ways of managing it. It is recommended to carry out similar studies, with a comparative group and under different circumstances that generate stress.

**CONCLUSION**

As noted above in the 4 thematic axes on cancer patients, their response has been modified depending on some elements; such as the phase of the disease process in which they are found, the type of cancer they have, as well as the personal and family situation at the time of diagnosis and during treatment. As well, the experiences lived of the patient in acquaintances or relatives with this type of pathologies, moreover, when a similar situation has been had with a family member.

Though, it is important to comment on when the patient is diagnosed, this act produces an emotional impact on an individual level but also in the family environment, negative thoughts regularly appear, since cancer most of the time relates it to death.

After this moment comes denial, in this, there is a great difficulty of accepting the reality that is being lived, sought second medical opinions, or often repeat the studies in the face of distrust of the results.

Likewise, the support system that the patient has at the time of the diagnosis results has effect, this greatly helps adaptation during the initiation of treatment. Therefore, we can see that there are several factors that will make the response vary depending on each individual, since it arises as a result of the treatment process and result of this, however, it should be noted that the support acquired from the various sources can facilitate adaptation to the situation, or failing to show in some cases unadopted behaviors at the onset of the disease.

However, cancer treatment regardless of the mode of therapy chosen, will have an impact on the way of life of the patient and his or her family.
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