Examining psychological problems and changes in the nervous system caused by cancer in patients with brain cancer and the effectiveness of using neuroleptics in their control

Pouya Ahmadian koudakan1, Houshang Hamidi Monfared2,

1-Doctor of Pharmacy (Pharm. D.), Shahid Beheshti University of Medical Sciences, Tehran, Iran
Email: Pouya_atlast@outlook.com
2.Bachelor's degree from Sharif University of Technology, Tehran, Iran
Email: hamidia76@yahoo.com

Abstract

The aim of the study is to study and compare neurological, psychological and cognitive changes caused by brain cancer in patients compared to healthy individuals and the effect of neuroleptic drugs in controlling them. This study is of a causal-comparative type. The statistical population of this study The statistical population of the study includes all patients with brain cancer hospitalized in hospitals in Tehran in 1403. The sampling method of this study was convenience. Thus, 50 people with brain cancer and 50 normal people were selected. To collect data, the Penn State Anxiety Questionnaire, the Perceived Stress Scale (Cohen et al.) and the short form of the Adult Socio-Emotional Loneliness Scale (De Thomas et al.) were used. The research data were analyzed by multivariate analysis of variance (MANOVA). The results showed that the average perceived positive stress in brain cancer patients is lower and the average perceived negative stress in these patients is higher than in normal individuals. Also, the average intensity of worry, uncontrollability of worry, and feeling of loneliness in brain cancer patients are higher than in normal individuals. As a result, it can be stated that perceived stress, worry, and feeling of loneliness are among the negatively influential variables in people with brain cancer and require the attention of families, officials, cancer patient associations, etc. to help increase the positive perception of stress, reduce negative stress, worry, and feeling of loneliness in these patients.

Keywords: Perceived stress, worry, feeling of loneliness, brain cancer.

Introduction

Brain cancer is a highly heterogeneous disease that is caused by the interaction of genetic risk factors and environmental factors, leading to the gradual accumulation of genetic and epigenetic alterations in brain cancer cells. Although epidemiological evidence highlights the presence of risk factors (such as age, obesity, alcohol consumption, and lifetime exposure to estrogen), a family history of brain cancer is the strongest risk factor. (2,1) Approximately 20% of all brain cancers are familial in origin and are etiologically linked to a specific susceptibility gene for the disease. (3) Cancer is generally a genetic disease. In other words, all cancers, including brain cancers, are caused by gradual genetic changes in tissue cells and the accumulation of these mutations. These mutations cause cancer in several ways and overgrowth of that cell, which ultimately leads to cancer. Changes or mutations in DNA can cause normal brain cells to become cancerous. Some DNA changes are passed down from parents (inherited) and can increase the risk of developing brain cancer. Other lifestyle factors, such as what you eat, how much exercise you get, etc., can increase the risk of developing this cancer. But it is not yet clear exactly how some risk factors cause normal cells to become cancerous. Hormones appear to play an important role in many cases of brain cancer, but how this happens is still not fully understood. Although several genetic

factors have been identified as causing cancer, new factors are constantly being added to this list, and recently RNA genes have been added to this list. These include microRNA genes, genes encoding long RNAs, and ... (4).

The World Health Organization defines quality of life as an individual's perception of his or her position in life within the context of the culture and value systems in which he or she lives and in relation to his or her goals, expectations, and standards. The main problems that affect the quality of life of patients are the psychological and psychological effects of the disease, diagnostic and therapeutic measures, stress, pain, depression, and the consequences of the disease on family, marital, and social relationships, as well as the economic burden caused by it. (5,6)

The findings show that patients with brain cancer suffered from psychological symptoms such as depression, anxiety, perceived stress, and feelings of helplessness (6). Part of this syndrome is due to awareness of cancer and cognitive feedback, and the other part is due to the side effects of common medical treatments such as mastectomy, chemotherapy, surgery, radiotherapy, such as losing hair and a part of the body that symbolizes being a woman and a mother (7). Among the psychological symptoms, the level of despair and stress that a person perceives creates a specific mental condition in which the person feels trapped, helpless, and disinterested in life. In this case, the person becomes extremely inactive and disabled and does not have the power to adapt to changing life conditions and moves away from the natural flow of life day by day (8). When people are in such conditions, they pay less attention to their general health, social relationships, nutrition, and other personal issues. And this, in turn, prepares the ground for the development of cancer (9). Timely diagnosis of brain cancer will be very important because only in the early stages of the disease can a good result be achieved by performing surgery and adjuvant treatments. Since rapid and timely diagnosis of the disease and proper treatment result in a relative recovery of a large percentage of patients and consequently prevent the destruction of many families, special attention to this issue is a necessity of our society.

Considering that comprehensive and accurate research on these cases has rarely been conducted in our country, it seems necessary to carefully examine the correlates of this disease in society (11, 12).

Although the cause of cancer is considered to be multiple cellular mutations, most mutations are the result of interactions with the environment (10), and therefore more than half of them are preventable (13).

Most people who develop cancer experience a period of psychological stress that reduces their daily functioning. These psychological problems are clinically so severe that even patients abandon chemotherapy because of these problems (14). Given the importance of the issue of cancer and its high prevalence, it is necessary to identify the factors affecting it and control this phenomenon. The results of these studies can lead to increased awareness of factors that exacerbate the disease and reduce the vulnerability of people with cancer by providing more information about methods of controlling and treating this disease and by implementing appropriate strategies.

In a review study, they concluded that external factors such as stress, depression, and social support have a significant impact on immune system components that affect the onset or course of cancer. According to Att, the relationship between psychological factors and cancer is very complex and includes several biological, psychological, and social systems. In addition to the valuable findings of neurobiology and neurobiochemistry, attention to cultural environmental factors, interpersonal aspects in terms of behavior, cognition, and emotion are fully felt. There is a close relationship between psychological states and

cancer. According to recent research, stress is known to be one of the most important factors in the occurrence of cancer in humans. Psychological pressures, anxiety, and stress exacerbate the occurrence of cancer in humans by affecting the body's immune system. Every person experiences stress throughout their lives, and it seems that this is an integral part of life and cannot be avoided. Stress is a physiological response to biological stressors (surgical trauma and infection) and psychological stressors such as worry, fear, and social tensions. (13).

Perceived stress refers to a person's overall perception and interpretation of their susceptibility to stressors. Different people perceive and interpret the same stressor in different ways, and various factors can play a role in the formation of perceived stress and the person's interpretation of the level of stress(14). In fact, people with breast cancer have high stress. In addition to stress, these people also have anxiety. From a cognitive perspective, anxiety is referred to as a chain of thoughts and mental images that have a negative and to some extent uncontrollable emotional theme. Some psychologists also consider anxiety to be a type of avoidance emotional response that reduces emotional distress in the short term, gains control, and prevents the manifestation of more intense negative emotions(15).

However, contrary to this protective function, when people have chronic problems such as cancer, anxiety can reduce coping strategies in the long term and increase anxiety, depression, and other psychological problems, which naturally increases the problems of chronic patients such as cancer(16).

In a study conducted to investigate the relationship between brain cancer and life stress and the personality of individuals as a trigger for the occurrence of this cancer, they showed that the number of high-risk events (stressful and worrying) in the group of patients with breast cancer was significantly higher than in the healthy group ($p<0.005$), and this rate was 2.4 times higher than in healthy individuals. Also, the severity of these events was significantly higher in the patient group than in the healthy group ($p<0.001$) (17).

Therefore, there is a relationship between life events, high-risk life events, and the severity of each of them with the occurrence of brain cancer. Also, people with cancer have little contact with those around them and acquaintances due to the nature of their illness, and this factor can cause them to feel lonely. In fact, loneliness can be considered a noticeable inadequacy and weakness in interpersonal relationships, which is defined as the difference between the desired level and the existing level of social relationships of individuals, and the greater this difference, the greater the feeling of loneliness (18).

Some studies have pointed out the relationship between loneliness and the occurrence of cardiovascular problems, inflammation in the body, and memory impairment. Loneliness has several negative effects. For example, researchers have observed changes in some genes of the immune system of lonely people. Some key and important genes that play a role in antiviral reactions and antibody production undergo changes in the body of these people, which will weaken the immune system's function against viral attacks (19).

In general, considering the increasing spread of cancer and the importance of psychological factors such as stress, anxiety, depression, etc. in causing and worsening the condition of these patients, as well as examining and comparing other influential factors such as loneliness, which has been linked to some diseases such as cardiovascular problems, inflammation in the body, memory impairment, etc. (20), this study will also be in this regard and will seek to answer this fundamental question: Is there a difference between perceived stress, worry, and feelings of loneliness in brain cancer patients and normal people?

Cancer cells are formed regularly in the body every day, but they are collected from the body according to a certain order. Facing stress and life problems can disrupt this order. Paying attention to the intensity and form of stress that an individual endures and the person's personality rank and position is effective in its relationship and effect with cancer. Some researchers believe that severe stress can be effective in the occurrence of cancer, and another group believes that long-term and chronic stress affects the development of this type of disease, but a review of research results shows that stress in both forms affects the likelihood of cancer. It has not yet been proven that stress increases or decreases the risk of brain cancer, but most studies are moving towards proving an increased risk. (21)

The idea that cancer may be related to emotional and nervous stress was first suggested around 200 AD when a scientist named Galen suggested that melancholic women were more likely to develop brain cancer. In 1759, a surgeon named Guy also suggested that life events could be a factor in cancer (22-28). Some studies have not only shown a link between brain cancer and emotional factors and stressful life events, but have also suggested an increased risk in younger women (28-32).

Everyone is occasionally attacked by cancer cells, which in most cases destroys the body's immune system. But in extreme anxiety, the hypothalamus, the body's thermostat, activates. The hypothalamus triggers a fight-or-flight response, which allows cancer cells to multiply. Doctors have documented evidence that a suppressed immune system allows cancer cells to grow. In one particular case, doctors operated on a damaged kidney and replaced it with a healthy one. The patient was given drugs that suppressed his immune system. A few days later, a tumor grew on the patient's chest. Further examination revealed that the patient's new kidney was full of malignant cells. The cancer cells had spread from the kidney to the lungs. The doctor immediately stopped the drugs that were suppressing the body's immune system, and within a few days, there was no sign of cancer in the patient. Doctors justified that the new kidney probably had cancer cells in it and the use of anti-immune drugs was stopped. The new kidney was destroyed, but the cancer cells no longer existed.

Research Method

The research method is of a causal-comparative (post-event) type, according to its objectives and hypotheses. The statistical population of the research includes all patients with brain cancer hospitalized in hospitals in Tehran in 1403.: The sampling method of this research is available. In this way, 50 people with brain cancer and 50 normal people who are relative counterparts of people with cancer (in terms of age, education, area of residence, income, etc.) were selected. In addition, the minimum sample for causal-comparative methods is 15 people (Delavar, 2006), which in this study, 50 people were selected in each group to increase external validity.

A questionnaire was used to collect information in this study. After obtaining the necessary permits, first, they visited hospitals in Tehran and selected a statistical sample from among patients with brain cancer and, for comparison, from healthy individuals in the same hospitals (in a way that they were comparable to the affected group in terms of age, education, etc.), and the objectives of the study were explained to them. Then, the research questionnaires (Penn State Anxiety Questionnaire, Short Form of the Adult Social-Emotional Loneliness Scale (SELSA_S), and Perceived Stress Scale) were provided to them to complete. Finally, the questionnaires of both groups were collected and the data were analyzed using SPSS statistical software.

Analysis and presentation of the results

In this section, the results of the descriptive findings are presented in the form of frequency and percentage tables as well as graphs of the variables under study. Also, central and dispersion indices have been extracted for quantitative variables. Next, in the inferential findings section, the hypotheses are explained. Multivariate analysis of variance (MANOVA) test was used to analyze the hypotheses.

A) Demographic characteristics

Table 1: Level of education among the study groups

Total	Bachelor's degree and above	Postgraduate diploma	Diploma	Undergraduate	Group	
50	8	15	17	10	Abundance	Healthy
%100/0	%0.16	%0.30	%0.34	%0.20	Percentage	
50	2	4	15	29	Abundance	Cancer patients
%100/0	%0.4	%0.8	%0.30	%0.58	Percentage	

As can be seen in Table (1), the highest frequency of education in the healthy group is related to and in the cancer patient group is related to education below a high school diploma.

Table 2: Mean and standard deviation of age among the study groups

Standard deviation	Average	Group
5/43662	31/7400	Healthy
9/35995	46/6000	Patient

As can be seen in Table (2), the mean (and standard deviation) age of healthy individuals is 32.84 (and 5.54) and among patients is 45.59 (and 9.46).

B) Descriptive findings

Table 3- Mean and standard deviation of positive and negative perceived stress in the study groups

Standard deviation	Average	Group	Variable
4/68409	18/0800	Healthy	Stress Perception Done Negative
3/63692	19/9800	Patient	
3/78400	21/7600	Healthy	Stress Perception Done Positive
4/82946	16/1400	Patient	

According to the results of Table 3, the mean (and standard deviation) of negative perceived stress in healthy individuals is 17.08 (and 4.59) and in cancer patients is 18.98 (and 3.53) and the mean (and

standard deviation) of positive perceived stress in healthy individuals is 20.76 (and 3.38) and in cancer patients is 15.14 (and 4.72).

Table 4- Mean and standard deviation of anxiety intensity and uncontrollability of anxiety in the study groups

Standard deviation	Average	Group	Variable
3/26124	12/9200	Healthy	Uncontrollable worry
2/11271	15/3000	Patient	
13/03406	34/0800	Healthy	Severity of concern
4/95983	46/1200	Patient	

According to the results of Table 4, the mean (and standard deviation) of anxiety uncontrollability in healthy individuals is 11.93 (and 3.17) and in cancer patients is 14.32 (and 2.01) and the mean (and standard deviation) of anxiety intensity in healthy individuals is 33.09 (and 13.03) and in cancer patients is 12.46 (and 4.95).

Table 5- Mean and standard deviation of loneliness in the study groups

Standard deviation	Average	Group	Variable
8/17265	30/0600	Healthy	Feeling lonely
8/68499	43/8600	Patient	

According to the results of Table 5, the mean (and standard deviation) of loneliness in healthy individuals is 30.06 (and 8.17) and in cancer patients is 43.86 (and 8.68).

C) Inferential statistics

Hypothesis 1: There is a difference between positive perceived stress in brain cancer patients and normal individuals.

According to the results of Table (6), the significance level of the test for equality of variances (P>0.05) shows that the variances are equal.

Table 6- Results of Levine's test to determine equality of variances

Significance level	Degree of freedom 2	Degree of freedom 1	F
0/146	97	1	1/878

Table 7- Results of the multivariate analysis of variance (MANOVA) test

Eta squared	Significance level	F	Mean squares	Degree of freedom	Sum of squares	Source of changes
0/951	000/0	1905/442	32220/250	1	3220/250	Model

0/323	000/0	46/696	789/610	1	789/610	Group
			16/910	98	1657/140	Error
				100	34667/000	Total

According to the results of Table (7), and considering the F value (46.69) and also considering that the significance level of the test error for the 0.99 confidence level is less than 0.01, it can be said that the first hypothesis is confirmed and there is a difference between positive perceived stress in patients with brain cancer and normal individuals, and the mean of positive perceived stress in patients with brain cancer is lower than normal individuals.

Second hypothesis: There is a difference between negative perceived stress in patients with brain cancer and normal individuals.

Table 8- Results of the Levine test to determine equality of variances

Significance level	Degree of freedom 2	Degree of freedom 1	F
155/0	98	1	1/482

According to the results of Table (8), the significance level of the test for equality of variances (P>0.05) shows that the variances are equal.

Table 9- Results of the multivariate analysis of variance (MANOVA) test

Eta squared	Significance level	F	Mean squares	Degree of freedom	Sum of squares	Source of changes
0/852	000/0	1939/411	33508/090	1	33508/090	Model
062/0	022/0	5/384	91/250	1	90/350	Group
			15/762	98	1652/660	Error
				100	35241/000	Total

According to the results of Table (10), the significance level of the test error for equality of variances (P>0.05) shows that the variances are equal.

Table 10- Results of the Levine test to determine the equality of variances

Significance level	Degree of freedom 2	Degree of freedom 1	F
077/0	98	1	2/369

According to the results of Table (10), the significance level of the test for equality of variances (P>0.05) shows that the variances are equal.

Table 11- Results of the multivariate analysis of variance (MANOVA) test

Eta squared	Significance level	F	Mean squares	Degree of freedom	Sum of squares	Source of changes
0/952	000/0	1583/258	153881/000	1	152881/000	Model
0/287	000/0	37/507	3624/040	1	3624/040	Group
			96/622	98	9568/960	Error
				100	175974/000	Total

According to the results of Table (11), and considering the F value (38.50) and also considering that the significance level of the test error for the 0.99 confidence level is less than 0.01, it can be said that the third hypothesis is confirmed and there is a difference between the severity of worry in brain cancer patients and normal people, and the average severity of worry in brain cancer patients is higher than normal people.

Fourth hypothesis: There is a difference between the uncontrollability of worry in brain cancer patients and normal people.

Table 12- Results of the Levine test for determining the equality of variances

Significance level	Degree of freedom 2	Degree of freedom 1	F
073/0	98	1	1/855

According to the results of Table (12), the significance level of the test for equality of variances (P>0.05) shows that the variances are equal.

Table 13- Results of the multivariate analysis of variance (MANOVA) test

Eta squared	Significance level	F	Mean squares	Degree of freedom	Sum of squares	Source of changes
0/972	000/0	2457/538	17187/210	1	17287/210	Model
0/181	000/0	20/266	141/610	1	151/610	Group
			7/022	98	688/180	Error
				100	18117/000	Total

According to the results of Table (13) and considering the F value (20.26) and also considering that the significance level of the test error for the 0.99 confidence level is less than 0.01, it can be said that the fourth hypothesis is confirmed and there is a difference between the uncontrollability of worry in brain

cancer patients and normal people and the average uncontrollability of worry in brain cancer patients is higher than normal people.

Fifth hypothesis: There is a difference between cancer patients who use neuroleptics and those who do not use them.

Table 14- Results of Levine's test to determine the equality of variances

Significance level	Degree of freedom 2	Degree of freedom 1	F
0/141	98	1	2/420

According to the results of Table (14), the significance level of the test error for the equality of variances (P>0.05) shows that the variances are equal.

Table 15- Results of the multivariate analysis of variance (MANOVA) test

Eta squared	Significance level	F	Mean squares	Degree of freedom	Sum of squares	Source of changes
0/951	000/0	1931/009	137604/160	1	137604/160	Model
0/406	000/0	66/972	4761/000	1	4861/000	Group
			71/111	98	6978/840	Error
				100	149334/000	Total

According to the results of Table (15) and considering the F value (66.972) and also considering that the significance level of the test error for the 0.99 confidence level is less than 0.01, it can be said that the fifth hypothesis is confirmed and there is a difference between the feeling of loneliness in patients with brain cancer and normal people and the average feeling of loneliness in patients with brain cancer is higher than in normal people.

Discussion and Conclusion

The present study was conducted with the aim of comparing perceived stress, worry and loneliness in patients with brain cancer and normal people. The results of the hypothesis analysis are as follows:

The first two hypotheses of this study examined the difference between positive and negative perceived stress between patients with brain cancer and normal people. The results obtained showed that there is a difference between positive and negative perceived stress in patients with brain cancer and normal people. So that the average perceived positive stress in brain cancer patients is lower than normal people and the average perceived negative stress in brain cancer patients is higher than normal people. Therefore, both research hypotheses were confirmed. These results were consistent with the findings of research (5, 8, 16, 22).

In a study, they showed that the number of high-risk events (stressful and worrying) in the group of patients with breast cancer was significantly higher than the healthy group ($p<0.005$), and this rate was 2.4 times that of healthy people (27). In another study, they showed that there was a significant relationship between the history of physical or mental illness of the spouse or child, the number of adverse events (stressful and worrying events) and the child's unemployment with brain cancer. They also reported in the study that high levels of anxiety and stressful events are associated with physical diseases (cancer) (21).

The findings show that patients with brain cancer suffer from psychological symptoms such as depression, anxiety, perceived stress, and feelings of helplessness (8). Most people who develop cancer experience a period of psychological stress that reduces their daily functioning. These psychological problems are clinically so severe that even patients quit chemotherapy because of these problems (13). There is a close relationship between psychological states and cancer. According to recent research, stress is known to be one of the most important factors in the occurrence of cancer in humans (24). Psychological stress, worry, and stress exacerbate the occurrence of cancer in humans by affecting the body's immune system. Despite all the issues related to stress and its dangerous consequences, it can be said that more important than the stressful factors in life is the way to deal with it. People with cancer have a negative evaluation of stress due to high worry and anxiety, as well as the role of their disease in stress, and they always perceive stress negatively. However, unlike negatively perceived stress, people who see stress as an opportunity for challenge and appropriate planning (positively perceived stress) and try to manage their plans instead of worrying, cause appropriate behaviors and physiological responses, whereas the presence of cancer prevents such perception, and this is the factor that causes people with cancer to receive low scores in positively perceived stress.

The third and fourth hypotheses of the study were that there is a difference between worry and its component (severity and uncontrollability of worry) in brain cancer patients and normal individuals. The results obtained in this regard showed that there is a difference between the severity of worry and uncontrollability of worry in brain cancer patients and normal individuals, and the average of both of these components is higher in brain cancer patients than in normal individuals, and both research hypotheses were confirmed. This finding was consistent with the results of studies (15, 22). In a study, they showed that there is a significant difference between worry factors and breast cancer patients in two groups of patients and normal individuals (12). Also, in a study, they reported a significant relationship between brain cancer and emotional factors as well as worrying life events (16). In another study, they concluded that external factors such as stress, long-term worry, depression, and social support have a significant effect on components of the immune system that affect the onset or course of cancer (18).

Regarding the inference of this finding, it can be stated that physical complications along with psychological disorders cause stressful thought habits and increase the anxiety caused by the disease with the passage of time and the progression of the disease (20). Sick individuals consider stress and anxiety as a life-threatening situation and disorder and always put their anxiety in a cycle of repetition and increase. According to the metacognitive theory, the anxiety cycle occurs when negative beliefs about anxiety become active in the individual. Negative beliefs (lack of control and high intensity of anxiety) include beliefs that anxiety can lead to a worsening of the physical condition (presence of cancer) and the occurrence of adverse psychological or social consequences. When negative beliefs become active, the individual negatively evaluates anxiety, that is, he/she experiences anxiety about anxiety (high intensity

and lack of control) that the existence of an incurable or incurable disease such as cancer causes this process to increase even more.

The final hypothesis of the study was that there is a difference between cancer patients who use neuroleptics and those who do not. Based on the results obtained, there is a difference between cancer patients who use neuroleptics and those who do not. And the average feeling of loneliness in patients who use drugs is higher than those who do not use them, and this research hypothesis was confirmed. The result obtained was consistent with the findings of (18, 20).

In a study, it was shown that depressed people with cancer have little relationship with neuroleptics due to the nature of their disease, this factor can cause them to feel lonely (21).

Summary of the results of the study

The present study aimed to investigate and compare the neurological, psychological and cognitive changes caused by brain cancer in patients compared to healthy people and the effect of neuroleptics on their control. The results showed that there is a difference between positive and negative perceived stress, worry and loneliness in patients with brain cancer and normal people. So that the average perceived positive stress in brain cancer patients is less than normal people and the average perceived negative stress in brain cancer patients is more than normal people. Also, the average intensity of worry and uncontrollability of worry in brain cancer patients is more than normal people. In addition, based on the results, the average depression and loneliness in brain cancer patients who do not use depression medications is higher than those who use medication. As a result, it can be stated that perceived stress, worry and loneliness are among the negative variables affecting people with brain cancer and require the attention of families, officials, cancer patient associations, etc. to help increase the positive perception of stress, reduce negative stress, worry and loneliness in these patients.

Research Limitations

1. Lack of control over the severity and duration of the disease is one of the limitations of the present study. Because its impact on the level of anxiety and stress of patients varies based on the severity and severity of the disease.

2. Limitation in the scope of the research sample, because with 50 people (in each group for comparison), we will hardly be able to generalize the results.

3. Since this study was conducted on sick women in Tehran and could be affected by specific cultural and regional characteristics, this study has limitations in generalizing the results to other regions.

4. Because a questionnaire was used to collect data in this study and, like other self-report studies, there may be a possibility of bias in the results, the generalization of the research results is limited.

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