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THE EFFECTS OF SUGGESTIVE COMMUNICATION ON THE PHYSICAL STATE OF THE PATIENT IN CRITICAL MEDICAL SITUATIONS

DECREASING THE SIDE-EFFECTS ENCOUNTERED BY BREAST CANCER PATIENTS DURING CHEMOTHERAPY WITH ADJUVANT HYPNOTHERAPY

DOCTORAL (PhD) DISSERTATION

THESIS

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„The words of the physician, enlightening, guiding,
and even as hypno-suggestive
are a sovereign human „instrument" in the art of healing."
(Völgyesi 1964, 1.o.)

1. Introduction

As an anesthesiologist and a hypnotherapist I have applied hypnosis successfully on several occasions during surgery. As my knowledge expanded I realized that several suggestions may be spoken to the patients in the preoperative period; in fact due to the cognitive state of the patients during surgery I don't need to apply formal hypnotherapy. I started paying more attention to my words and my behavior and to what sort of messages they may convey. I also started to gradually alter them so they would do more good than harm. I also discovered that speaking these suggestions was enjoyable for me as well, as it would soothe my anxiety. The interesting images, favorite places, and source-of-strength experiences that patients related often brought a joyful change to my daily routine. I absorbed myself in the world of suggestions, and my positive experience encouraged me a share my observations with others. At the same time I was asked to participate in a scientific study focusing on adjuvant hypnotherapy for cancer patients undergoing chemotherapy. As chemotherapy suites resemble the prepping areas of surgical theaters, patients tend to experience similar feelings of fear and being focused on pain in both situations. I felt I could utilize the knowledge I have gained. Reviewing this knowledge as part of a larger system allows me to apply my experience with better efficacy.

2. Theoretical background

All doctor-patient interactions may be considered critical where the focus of the patient is completely centered on the very real or feared loss of physical integrity. This may cause anxiety, fear-of-death experiences or even an existential crisis, in turn making any communication difficult. Implementing therapeutic procedures and plans however requires patient cooperation. Undergoing surgery, physical trauma, having a heart attack, being diagnosed with a tumor, having chemotherapy or even giving birth may be considered a critical doctor-patient interaction. A sudden change in physical state, i.e. sudden symptoms, pain, unnatural positions of the limbs (i.e. following a fracture or a dislocation) occupy the attention of the patient completely, excluding everything else. Focusing attention means

narrowing the function of the mind. Emotional recognition of an emergency leads to the release of stress hormones which not only stimulate the body but also activate neurophysiological changes that alter the patient's state of mind. Among other things there is an increase in the need for social support, and the ability to accept and execute suggestions is heightened. This mental state is also characterized by a significantly increased response to suggestion, namely suggestibility. Aside from isolation other negative impacts may heighten this state which may manifest itself as post-traumatic stress disorder (O'Connor et al. 2011, Arnaboldi 2014). The goal of positive suggestive communication is to evoke the patient's sources of strength, to renew a sense of capability, to dislodge the patient from the role of victim caused by stress, and to establish the patient as a member of the healing team (Bejenke 2011, Bejenke és Bloch Szentágothai 1998, Jakubovits 2006, Varga 2001, 2011b).

Psychological and physical factors interact in a complex way. There is the topic of psychoneuroimmunology. Neurotransmitters and hormones may affect the hypothalamic–pituitary–adrenal axis through the autonomic nervous system, which in turn regulates peripheral inflammatory processes. However, hormones, neurotransmitters, cytocines, and other molecules, peptides also have a direct effect on immune, tumor cells, glands, and nervous system. Several studies unanimously state that depression, social isolation, distress and traumatic life events adversely affect morbidity and mortality rates in cancer patients. (Bellinger 2008, Dégi 2008, Döbrőssy 2011, Kang 2009, 2012, Kiecolt-Glaser 2010, Lutgendorf 2011, Messina 2011, O'Connor 2011, Sabry 2013). Depression in women caused a significant increase in neutrophil granulocyte counts resulting in the production of carcinogenic superoxide free radicals (Irie et al. 2003, 2005). Women who suffered from high anxiety and affective disorders relating to their breast cancer had higher neutrophil granulocyte and lower lymphocyte counts These women had a stronger sense of their own symptoms (they had high „symptomatic perception"-also their focus of attention was narrower) and had worse quality of life (Kang et al 2009, 2012).

During the course of surgical excision of ovarian cancerous tumors Lutgendorf et al. (2011) were able to measure the activity of one of the most important defensive lymphocyte elements against tumors, the natural killer cells (NK). The activity of natural killer cells in the peripheral blood and near the tumor site was most significantly affected by social support. Adequate social support increased the activity of these cells. Behavioral risk factors such as stress and depression are associated with higher levels of adrenaline, and in these cases macrophages support the growth of the tumor were found in the microenvironment of the

tumor. Over 200 more genetic alterations were found in the tumor tissues of ovarian cancer patients with higher levels of depression and lower levels of social support compared to the group with higher social support and lower depression rates. Several of these 200 genes play a significant role in tumor progression.

Therefore we assume that an environment of supportive positive suggestion not only creates a beneficial social environment, but also has a positive effect on the white blood cell counts. Several studies confirm these claims (Eremin et al. 2009, Fancourt et al. 2014, Garland et al. 2009, MacDonald 2013, Qu et al 2013).

Hypnosis is a great instrument in evoking positive change in an altered state of mind. The goal of modern hypnotherapy is to emphasize healthy adaptive individual functions centered around the personality of the patient (Bányai É. 2006).

Hypnosis in adults and children is usually applied and investigated in relation to anxiety, pain, vomiting, quality of life, moods, function of the immune system and hot flushes. (Bányai 2014, Cramer 2014, Jakubovits 2010,2011, Jakubovits és mtsai 2010, Kravits 2013, Montgomery et al. 2010, 2011, 2013). Cramer et al. (2014) published a review on the efficacy of hypnosis in breast cancer patients. It was determined, that every cited publication was from the USA, and no data was found on breast cancer patients who participated in hypnosis during the course of chemotherapy. There is a need for more detailed description of the methods of hypnosis, the circumstances of therapy, patient symptoms, standardization, and for the studies to be blind. The following study makes up for these deficiencies.

2. Methods

The multidisciplinary, controlled, randomized, prospective clinical trial by Éva Bányai is to test the hypothesis that when chemotherapy is complemented with adjuvant hypnotherapy it has a positive effect on the psychological and physical well-being and the survival of moderate-to-high risk HER2 negative breast cancer patients. This large-scale study, which includes several professionals, hospitals as a medical doctor, my role in the team was to present the **effects of hypnosis on physical conditions (nausea/vomiting) and immune function.** With the results of this scientific study I would like to draw the attention of the Hungarian medical profession to the fact that utilizing the effects of suggestive methods is a simple and cost-effective way to complement tumor therapy.

Hypotheses

1. Adjuvant hypnotherapy has a positive effect on **nausea/vomiting** presenting in the chemotherapy suite as a **side-effect** of treatment during the administration of the 1st Paclitaxel course.

   a. Patients in the hypnotherapy group will experience **nausea** less often, and will **vomit** more seldom in the chemotherapy suite while receiving the 1st course of Paclitaxel compared to the control group.

   b. Patients with greater hypnotic suggestibility will experience **nausea** less often, and will **vomit** more seldom in the chemotherapy suite while receiving the 1st course of Paclitaxel compared to patients less prone to respond to hypnosis.

2. Adjuvant hypnotherapy has a positive effect on the **immune function** of these patients

   a. **White blood cell count**, and absolute **neutrophil, monocyte** and **lymphocyte counts** decreases to values under reference levels to a lesser degree in the hypnosis group compared to that found in the control group.

   b. More stable white blood cell counts have a positive effect on the **course of treatment**: treatment is more seldom omitted due to inflammation/and or neutropenia, and less medication is needed to induce bone marrow function in the hypnosis group compared to the control group.

Patient and Methods

Quantitative, three-arm, randomized, half-blind study conducted in 4 breast cancer centers, under the direction of Professor Éva Bányai (ELTE Department of Affective Psychological Department). The site of research are: National Institute of Oncology -Budapest (Professor István Láng), Oncoradiological Department of Markusovszky University Teaching Hospital - Szombathely (Professor András Csejtey) and Department of Clinical Oncology, University of Debrecen –Debrecen (Professor Zsolt Horváth, university docent, director of department). [1] [2]

As a hypnotherapist and a doctor it was my role in this study to plan the course of the study (i.e. planning questionnaires, information pamphlets, individual patient forms), provide the basis for the text of the suggestions (we later finalized the script together), to perform

[1] Ethics serial number of this study is 15530-0/2010-1018EKU (670/PI/10.)

[2] Research for this paper was supported by a grant of the Hungarian Research Fund (OTKA K-109-187) under the direction of Professor Éva Bányai

data mining, plan the database, enter the data into the database, analyze the data, and on occasion to meet with the patiens, or inform the patients regarding the study.We are currently at the midpoint of our planned study regarding both time and patient munbers (50 planned), so analysis of the data is preliminary.

Participants

Inclusion criteria for patients were: general well being (ECOG performance status (PS) ≤ 1), female gender, being over the age of 18, having undergone mastectomy and axillar block dissection for breast tumors (stage N0T1c to stage N(1-3) T2, G1-3, HER2 negative) and having been prescribed chemotherapy following surgery, known hormone receptor status of the tumor, obtainable preliminary laboratory and radiological findings. The patients speak Hungarian and agreed to a psychological evaluation during chemotherapy.

Patients were first asked by the treating physician to participate in the study after chosen by the breast committee based on stratification criteria. This was followed by a discussion with a psychologist. The intervention group included patients who agreed to listening to music or hypnotic suggestion in the chemotherapy suite. Patients who did not wish to listen to music or participate in hypnosis were included in the control group. These patients only filled out a psychological evaluation form at th end of the interview. In the other hospitals (in Szombathely and Debrecen), where hypnosis was not available patients were asked whether they would be willing to participate in a music/hypnosis study. This was necessary to avoid the feeling of social isolation. In the intervention group hypnability was assessed following the interview and the psychological evaluation test. After this, those not in the control group were tested to gauge their degree of hypnability. Patient information was gathered into envelopes based on menopausal and hormonal status and hypnability. Patients were randomized into music/hypnosis groups by choosing from these envelopes. Patients in the intervention group listened to either music or hypnosis during treatment and at the full blood count tests. The first baseline blood test was performed prior to the first course of chemotherapy.

Treatment Conditions

Patients received 4 Adriamycin/Cyclophosphamid (AC) and 12 Paclitaxel (PAC) chemotherapy treatments according to standard international protocols. The oncologists handled all chemotherapy-related events according to standard hospital guidelines.

Standard hypnosis texts or music was recorded on MP3 players, and patients listened through headphones during every course of chemotherapy and when they sat for their blood tests, all in all on 21 occasions. Hypnotherapy starts with indirect induction, which is followed by a therapeutic suggestion that incorporates active-alert hypnotic elements by Eva Banyai to increase immune system function (Bányai 1976,1998). We used indirect and direct suggestions to facilitate the activity of the immune system and the psychological and bodily resources. There were two main types of suggestions: The first one was cognitive reframing, the second one was an emotional approach: we used i.e. metaphors (Varga 2004).The therapeutic suggestion were constructed by the psychological team.

Outcome Measures

Observers conducted Visual Analog Scoring of the emotional and physical state of the patients before every course of treatment. Vocal recordings were made of these assesments. They sat by the patients during treatment noting their reactions, marking nausea and vomiting. They also kept track of the topics patients raised in the course of spontaneous conversation, and the events of intervention and treatment were recorded in writing and on vocal recordings. Psychological interviews and blood test to determine Natural Killer Cell Activity were conducted before AC and before PAC treatment and on the week following the end of chemotherapy. This data is still being analyzed.

Measurement points and variables

We measured full blood count before starting chemotherapy, before each cycle and at the next week of end of chemotherapy, following 24 weeks, all in all on 17 occasions. Hematological data was pulled from hospitals databases.

We registered the occurrence of nausea and vomiting in the treatment room, during the course of every treatment. We focused on the 1st Paclitaxel cycle in particular, because this is the only data that is currently available.

3. Results

So far 25 patients took part in the adjuvant hypnosis group, we had 22 patients in the music group and 22 in the control group. 43 patients received the full course of chemotherapy, 20 had side-effects so adverse that they had to terminate their treatment early (peripheral neuropathy, anaphylaxis, cardiotoxicity). 6 patients were excluded from the study: 3 patients gave up chemotherapy, 2 refused hypnosis, 1 patient wished to be treated in a

different hospital. We lost 1 patient in the hypnosis group, 1 in the music group and 3 in the control group to metastatic cancer. In every group 1 patient had metastases.

From a demographic point of view, or regarding pre-treatment full blood count values patients did not differ.

Regarding nausea and vomiting

The *incidence* of nausea and vomiting were compared between the hypnosis, music and control groups with Chi square test. The average percentage of nausea and vomiting was significant lower in the hypnosis group than in the the control group. In the hypnosis group there was only one patient who vomited, and it occurred before she started listening to the hypnotic suggestions. During the suggestions and the Paclitaxel drip, she felt relaxed, and felt well after the treatment.

Regarding *hypnability* we found that patients who experienced nausea during the 1st Paclitaxel course had a hypnability point that was significantly higher based on t-test results. This was not trues concerning vomiting. More sensitive patients are probably more sensitive to outside stimuli (i.e. seeing someone vomit in the next chair). We observed the positive effects as well, as hypnosis patients did not vomit during the hypnotic intervention.

Regarding immune cells

White blood cell counts from the three groups were compared with ANOVA and independent t-tests. Results from the hypnosis and the music groups were higher than results from the control group. Many differences were significant between the hypnosis and the control group, and less differences were significant between the music and the control group. As the tendency of cell count changes were similar in the hypnosis and the music group, I combined their results (intervention group), and compared them to results from the control group. Results from the intervention group were more significant differences between the intervention and the control group. Basophil cell counts were highest in the music group, even higher than in the hypnosis group. At the moment we cannot give an explanation for this phenomenon. In the hypnosis group no one experienced anaphylaxis, but it did occur in the music and the control groups.

We calculated average results using the data from each group regarding each measurement point, and we compared results between groups. ANOVA showed significant differences regarding every type of cell. According to the post hoc analysis monocyte cell counts were found to differ only in the hypnosis versus the control group, and the basophil cell count only in the music versus control group, the other cell counts were found to differ in the control versus hypnosis and control versus music group. Control group cell count numbers were always lower, compared to the intervention groups.

The postponed

We expected a higher rate of postponement in the control group, yet these events were equal in every group. Treatment needed to be postponed in approximately one third of the patients.

The need for **Granulocyte Colony-Stimulating Factor** in the control group showed significant differences with Chi–square analysis compared to the intervention groups. We calculated the cost of the stimulating factor treatment, at the lowest available price. This cost was around 73 Euros/person in the control group, as opposed to the hypnosis or music group where costs were around 14/ Euros/person. The costs of hypnotherapy ahould also be consiedred when evaluating cost-effectivity.

Summary

- Data on nausea and vomiting during the 1st Paclitaxel treatment course supported our hypothesis that hypnosis reduces the side-effects of chemotherapy, which correlates with hypnability. This finding supports previous data from the literature.

  One of the disadvantages in evaluating the results is that there is no data available regardingt the other measuring points.

- Regarding white blood cell count, the intervention groups demonstrate significantly more favorable values than the control groups. The ratio of postponement due to neutropenia or inflammation was similar to that found in the control group. Nevertheless in the hypnosis group less granulocyte cell stimulating factor was needed than in the control group. It supported our hypothesis that hypnosis reduces the side-effects of chemotherapy.

One of the disadvantages in evaluating the results is that were unable to gather data on every immun function we planned, as measurements are still underway.

6. Discussion, conclusions

The data shows that information from the environment may affect patients in an altered cognitive state in one of two ways: negative and positive effects come from social and familial environments, from other patients, from the medical staff most important to the patient, the treating physician and the nurses. The adjuvant positive suggestions that were introduced as an integral part of the therapy resulted in significant physical changes. These changes may be seen as the summation of positive and negative effects, determined grossly by the personality of the patient, including personal life experiences, expectations, way of thinking and inner strength reserves. Even though several factors played a role, bodily changes were measurable.

Among many other factors, our research has its limitations that harden the interpretations of our results. One limitation is that the verbatim recording of the personal experiences and nausea data of the control group is not yet all available, so instead of 16 times, the hypothesis concerning nausea could have only been tested in 1 occasion when the raters knew the type of the group in which the patient belonged to. The evaluation of the blood count is aggravated by the fact that the data were produced in several laboratories, side-effects were not treated with a standardized protocol, and it happened several times that patients belonging to different groups were present at the same time in the treatment room, therefore they could make an impact on each other. Besides of the limitations, and small sample size, the changes in the physical conditions could have been measured, however the results should be treated carefully, and should be supported by further research.

The technique may be applied by every member of the healing team according to individual competence. Those who do not wish to perform hypnosis or lack the proper training may develop their skills through suggestive communication training programs. Patients may master autohypnosis, providing them the opportunity to practice these skills independently (Bányai 2003, 2006, 2008a,2014). Not only the method, but the suggestion itself may be personalized, which may increase the efficacy of hypnosis. This may be easier if we explore patient expectations of chemotherapy beforehand. It would be ideal, if this were

performed by the treating physician. This way we could expand upon the thoughts of our predecessors: „...the most commonly used „medication" in medicine is the doctor himself: in other words it is not only the pills that count, but how they are administered..." (Bálint 1956/1990, 4.o.).

Long-term effects, analysis of further physiological parameters, and comparing physiological parameters with psychological factors will clarify yet uncertain points.

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