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ACUPUNCTURE IN ANXIETY LEVELS OF WOMEN WITH BREAST CANCER: A RANDOMIZED PRAGMATIC STUDY

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ABSTRACT

Breast cancer has multi-dimensional aspects, representing the first mortality cause by neoplasia among women, and frequently triggering off conditions of anxiety, depression and fear. The objective of this study was to assess the effects of acupuncture in the treatment of anxiety in women with a diagnosis of breast cancer. This is a randomized clinical trial composed by 46 women with breast cancer, 22 in the experimental group, and 24 in the control group. The dependent variables were trait and state of anxiety, and the independent variable was intervention with acupuncture at the preoperative period of mastectomy. The State - Trait Anxiety Inventory (STAI) was used, and the following points: Nei Guan (PC6), Shenmen (HT7), Hegu (LI4), Zusanli (E36), Sanyinjiao (SP6), Taichong (LR3), Yintang, Baihui (DU 20), Jiuwei (REN 15), Shanzhong (Ren 17). After six acupuncture sessions, the average of the State of Anxiety in the experimental group was reduced in a significant way, while in the control group, there was an increase in symptoms. A significant reduction in the systolic pressure was observed in the experimental group, before and after needle sessions at the 1st and 3rd sessions, while cardiac frequency presented significand reduction in all sessions. It was evidenced that intervention with acupuncture was efficient for the treatment of anxiety in women with the diagnosis of breast cancer.

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INTRODUCTION

Breast cancer represented in 2018 11.6% of all cancers, with an estimated risk of 55.2/ 100,000, an absolute number of 2.1 milion (Bray, 2018). Brazil is the second kind in prevalence, representing 29.7% of neoplasias and the first cause of mortality. A national estimate for the 2020-2022 triennium is 66,280, representing an incidence rate of 61.61 new cases per 100,000 women (Brasil, 2020). Often, women present anxiety symptoms in response to the diagnosis, treatment, and the development of the disease, sometimes intense anxiety, and other times accompanied by other potentially hazardous emotions to their integrity. Fear, dread, apprehension, imminent danger, and tension are a few of the expressions of anxiety, a universal emotion, but which frequently manifests in a hyperbolic way to the circumstances of life (Gentil, 1997).

This feeling may be transitory (known as a state of anxiety) or more stable, depending on its characteristics (anxiety traits). Enjoyable and positive occasions may also generate anxiety, especially when there is an expectation period, butaround 25 to 35% of women with breast cancer will develop anxiety or depression in some treatment stage, 33% of whom will present depression, anxiety, or both in the first year after diagnosis, and 50% within the first five years (Burgess, 2005). Anxiety, depression, and insomnia are among the most frequent reasons for the search for Integrative and Complementary Medicine (ICM) (Pilkington, 2007). According to another study[7], in the USA, 42.7% of anxious adults have relied on these approaches. In Brazil, in 2016, more than 2 million Integrative and Complementary Practices (ICP) procedures were done in primary care, and of those, 770,000 were Traditional Chinese Medicine (CTM), including Acupuncture. Around 1,708 municipalities offer this type of service, most of them at primary care (78%), followed by specialized and hospital care (18% and 4% respectively) (Brasil, 2017). Considering

the importance of the inclusion of ICM approaches in the confrontation of breast cancer, which has a significant impact on the life of women and their families, and which still lacks clinical research, this study had the objective of assessing the effects of acupuncture in the treatment of anxiety in women with the diagnosis of breast cancer.

METHODS

The study is a randomized clinical trial, which we carried out at the Ylza Bianco Outpatient Clinic at Hospital Santa Rita de Cassia/Associacao Feminina de Educacao e Combateao Cancer, HSRC/Afecc), in the city of Vitoria, State of Espirito Santo, Brazil. The sample was composed of 46 women diagnosed with breast cancer, 22 in the experimental group and 24 in the control group. The groups, both receiving psychological support, were established randomly, through a previous draw done by computer software. We included women over 21 years old referred to surgical treatment; we excluded pregnant women, metastatic, had severe psychiatric disorders, and extensive skin lesions. We also excluded volunteers who wished to discontinue acupuncture and those who failed two consecutive sessions or those with a medical recommendation. The primary outcomes were trait and state of anxiety. We evaluated the following variables for the characterization of the intervention and control groups: age range, marital status, schooling, knowledge, expectations and previous treatments with acupuncture, income, presence of social support, religion/belief, tumor stage, the presence of co-morbidities, drugs in use, tobacco use, alcoholic beverages consumption, age of menarche and menopause, hormones use, family history of breast cancer or ovary cancer. We evaluated Anxiety Trait and State using the State-Trait Anxiety Inventory (STAI) developed by Spielberger, Gorsuch, and Lushene (1970) (Spielberger, 1970) and translated and adapted for Brazil by Biaggio and Natalicio (1979) (Biaggio, 1979). It is considered as Trait (STAI-T) the pre-existing anxiety in an individual, and State (STAI-S) the anxiety present at any specific moment in life. We analyzed the frequency of anxiety trait among the options: nearly always (4), frequently (3), sometimes (2) rarely (1); while the anxiety state had the available options: no (1); a little (2); a lot (3), totally (4). The scores of these items vary between 20 and 80 points and can indicate low anxiety levels (20 to 40), medium (41 to 60), and high (61 to 80). We evaluated for the analysis of the tools each symptom's scores. The inventories were applied by a previously trained person, blinded for the therapeutic procedures, at two different moments. The first inventory was applied before any intervention and immediately after receiving the breast cancer diagnosis news. After three weeks, we applied the second inventory before mastectomy.

We run tests after pre-surgery and after the acupuncture treatment. We included women with a histopathological breast cancer diagnosis that met established criteria. We approached them after the visit with the oncological surgeon. The ones who agreed to participate received instructions about the research procedures and signed the Informed Consent Form. After that, we collected the medical history and submitted them to a physical examination. To avoid bias in the interpretation of data, a Field Journal was given to all women at the first visit, with instructions given by the investigator for each to daily record, or to ask someone to record detailed descriptions of the activities developed in daily life, as well as eventual complaints, abnormalities, and any free notes. We collected these data at the last visit. After data registration, we released the women in the control group with follow-up visit schedules after three weeks to repeat the procedures. The women in the intervention group were submitted to acupuncture twice a week for three weeks, in a total of 6 sessions. We established the number of sessions according to the average time between breast cancer diagnosis and mastectomy at the service and the interest in evaluating whether that number will bring benefits. Tumor staging was defined using the clinical records based on the TNM system proposed by the Union for International Cancer Control[11].We followed STRICTA[12], and we used a classical approach, with manual stimulation, the expectance of "de qi" in the following points: *NeiGuan* (PC6), *Shenmen* (HT7), *Hegu* (LI4), *Zusanl*i (E36), *Sanyinjiao* (SP6), *Taichung* (LR3), *Yintan*g (extra), *Baihui* (DU20), *Jiuwei* (REN15), *Shanzhong* (Ren 17). We used 16 metallic, inox, disposable needles registered at ANVISA (Brazilian regulatory agency), size 0.20x30mm, in the respective depths recommended by Deadman *et al*. The retention time was that 30 minutes. A specialist in acupuncture with 18 years of experience, ARVN, MD, carried out the assistance.We managed to control some physiological parameters before and after each acupuncture session: Systemic Arterial Pressure (SAP) and heart rate (HR) using a digital automatic arm monitor, Omron brand. The evaluation and procedures days were interspaced, avoiding experimental and control group women to meet to avoid the *Hawthorne* effect. We carried out a descriptive analysis of the data. We used the Chi-squared test or *Fisher* exact test to compare clinical and demographic data, habits, and knowledge about acupuncture. We used the independence *Student* t-test to compare PAS EFC groups, and we tested anxiety using Paired *t-test* to compare moments before and after a visit inside the group. We tested clinical markers using the non-parametric test of *Wilcoxon*. The significance level adopted was 5%, and the statistical package used for the analysis was IBM SPSS 20. The Center of Studies of the Santa Rita de Cassia Hospital/AFECC and by the Committee of Ethics in Research of the Health Sciences Center of the Federal University of Espirito Santo approved the research protocol. The study was registered at Plataforma Brasil under the number 41753142.

RESULTS

The sample was composed of 46 participants, 22 women in the experimental group, and 24 in the control group. Table 1 presents the comparison of socio-demographic and clinical data of the groups through absolute and percentage values.

Table 1. Comparison of demographic and clinical data of women with breast cancer in the Metropolitan Region of Vitoria/ES, according to the study group, 2015/2016

Characteristic	Experimental		Control		p-value
	n	%	n	%	
Age range					
Until 49 yrs.	6	27,3	5	20,8	0,480
50 - 59 yrs.	5	22,7	10	41,7	
60 - 69 yrs.	9	40,9	6	25,0	
Aged 70 and over	2	9,1	3	12,5	
Marital status					
Married/Stable union	11	50,0	17	70,8	0,126
Others	11	50,0	7	29,2	
Years of schooling					
≤ 8 years	6	27,3	12	50,0	
> 8 years – 9 years	6	27,3	7	29,2	0,270
> 9 – 9.5 years	9	40,9	4	16,7	
> 9.5 years	1	4,5	1	4,1	
Family income					
Until 2 minimum wages	17	77,3	20	83,3	0,441
More than 2 minimum wages	5	22,7	4	16,7	
Religion					
Catholic/Evangelic	20	90,9	20	83,3	0,376
None	2	9,1	4	16,7	
Support					
With support	18	81,8	19	79,2	0,559
Without support	4	18,2	5	20,8	
Menarche age					
Before 15 yrs.	17	77,3	21	87,5	0,300
After 15 yrs.	5	22,7	3	12,5	
Menopause age					
Until 50 years/Still ovulates	18	81,8	21	87,5	0,449
After 50 yrs.	4	18,2	3	12,5	
Hormone use					
No	8	36,4	15	62,5	0,070
Yes/She has already used	14	63,6	9	37,5	
Hormone type					
Anovulatory	10	71,4	6	66,7	0,582
Hormone replacement	4	28,6	3	33,3	
Family cancer history					
Yes	8	36,4	4	16,7	0,118
No	14	63,6	20	83,3	
Comorbidity					
Yes	18	81,8	18	75,0	0,422
No	4	18,2	6	25,0	
Staging					
Initial (0-II)	12	66,7	13	65,0	0,593
Late (III-IV)	6	33,3	7	35,0	

Table 2. Average and standard deviation of the anxiety level of women with breast cancer in the Metropolitan Region of Vitoria/ES, 2015/2016

Anxiety	Experimental	Control	p-value
Trait	49±11	46±9	0,284
State			
Before visit	53±15	46±9	0,064
After visit	38±7	48±10	0,000
p-value	0,000	0,145	-

Table 3. Cardiac monitoring of the Experimental Group of women with breast cancer in the Metropolitan Region of Vitoria/ES, 2015/2016

Parameter	Visits						
	1	2	3	4	5	6	p-value
Sistolic Pressure							
Before visit	146±29	140±23	141±30	134±20	132±20	140±22	0,031
After visit	135±28	132±21	132±29	131±22	130±20	136±25	0,751
p-value	0,028	0,055	0,007	0,413	0,427	0,220	
Diastolic Pressure							
Before visit	85±13	80±13	81±14	78±11	75±9	78± 10	0,012
After visit	83±20	76±12	77±13	77±12	76±9	77±13	0,268
p-value	0,563	0,113	0,009	0,645	0,490	0,529	

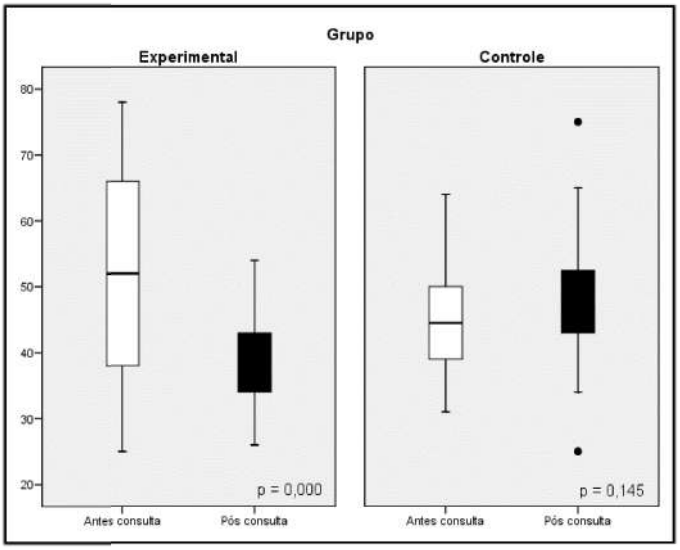

Figure 1. Anxiety level of women with breast cancer in the Metropolitan Region of Vitoria/ES, 2015/2016

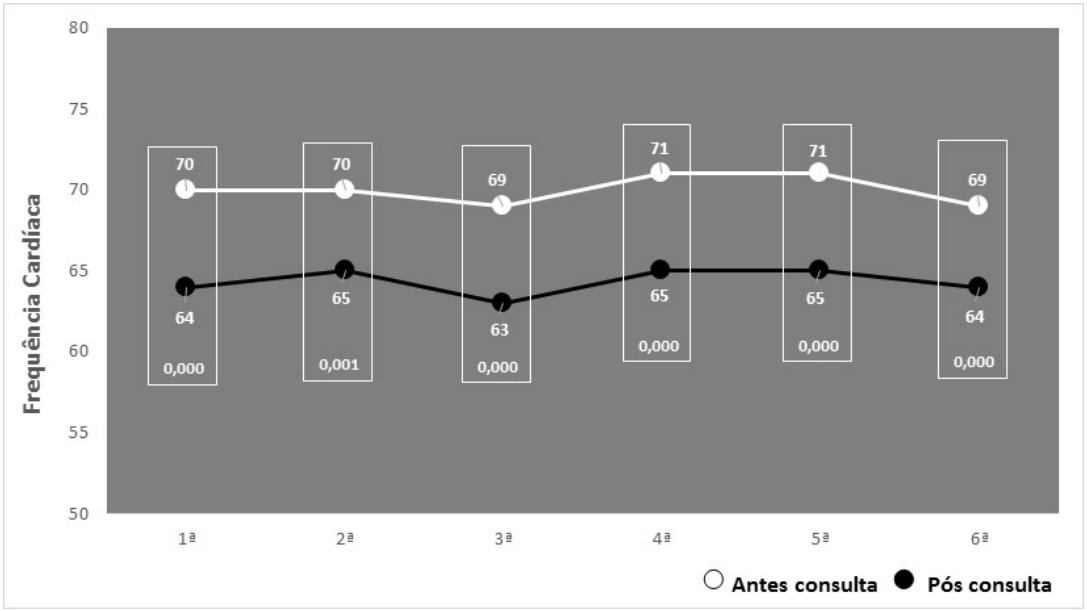

Figure 2. Cardiac Frequency - Experimental Group of women with breast cancer in the Metropolitan Region of Vitoria/ES, 2015/2016

Table 2 shows that women in the experimental and control groups presented a medium level of anxiety trait, with no significant statistical difference. Regarding the pre-visit anxiety state, there was also no significant difference between the averages in the groups, medium anxiety. However, we observed that after the intervention with acupuncture, the average of the experimental group was a reduction in the level of anxiety in a significant way ($p<0.000$), going to a low anxiety state, and reduction of the symptoms presented (53 to 38). In contrast, the control group increased anxiety symptoms (46-48), maintaining a medium anxiety level. Figure 1 shows a graphic with anxiety levels. Table 3 shows the significant median reduction of the Systemic Arterial Pressure (SAP) before interventions, considering the start and end of treatment ($p=0.031$). There was also a significant reduction of SAP before and after needle sessions at Sessions 1 and 3. A significant difference in the median diastolic pressure before the visit and throughout treatment was observed, as well as a significant reduction before and after Session 3. Cardiac frequency presented a significant reduction before and after all acupuncture sessions, as is showed in Figure 2.

DISCUSSION

There were no significant differences regarding any socio-demographic or clinical profile variable ($p>0.05$), which suggested homogeneity between the experimental and control groups, and hence comparison is possible. Women in both groups started the study with medium anxiety levels, as shown by Trait. However, in the analysis of the moment of the life of these women, characterized by State, it was observed that only the women in the experimental group presented a reduction in anxiety, with a significant difference ($p=0,0000$) between the groups (Figure 1), and this reduction occurred exactly after a very difficult moment of the treatment, just after the diagnosis of breast cancer and before mastectomy, suggesting that the intervention with acupuncture has influenced in the reduction of the anxiety levels (Mallory, 2015). Anxiety is one of the great challenges associated to cancer, and it is related to the fear of death[16]. Although the level of anxiety varies between one person and the other, it can raise the perception of pain, alter sleep pattern, cause nausea and vomits, and interfere in the quality of life. In the most severe cases, it can even abbreviate the subject's life. Acupuncture can be a useful tool to integrate the therapeutic arsenal in the combat of this disease, including a contribution in the recovery of surgery, because it reduced the anxiety in pre-surgical, considered a risk factor for nausea, vomits and pain (Acar, 2013). It was also observed a reduction in Systolic Arterial Pressure in two sessions and throughout the treatment, as well as a reduction in Cardiac Frequency after all each session. This data may suggest that the women in the experimental group were relaxed and that the intervention with acupuncture may reduce Systolic Arterial Pressure and the Cardiac Frequency in women with breast cancer. Agelink *et al. (2003)* studied the action of systemic points, similar to the ones used in this research, and identified a significant reduction in the cardiac frequency, suggesting a potential cardiovagal modulation with acupuncture. However, this data in this study is insufficient to establish a sure relation with the anxiety levels. Despite the inherent difficulties in the life circumstances of the participants in the moment of the investigation, it was observed great acceptance of the treatment with acupuncture. Several volunteers requested the continuation of the procedures, and other women have requested to return in the subsequent stages, such as during chemotherapy, with the rationale that acupuncture has improved their general state and their emotional aspects, such as anxiety, depression, sleep and pain. According to Swisher *et al.* (2002) the expectation of the use of acupuncture is related to a systemic improvement, confirmed throughout treatment as an improvement in the psychosocial wellbeing, including an increase in hope and optimism. These aspects are shared by Molassiotis*et al*.[20] and by Molly Mallory *et al*.[15], who also highlight the high levels of satisfaction with this type of treatment. During this study, most surgeons and mastologists of the service were contacted, but there weren't, however, any referral of women on the part of these professionals. The importance of establishing a dialog about the use of ICM with several different professionals that assist cancer, including oncologists, is highlighted, discussing the therapeutic objectives and the potential benefits and adverse effects of ICM. That is a very relevant fact, since the knowledge about the use of ICM in cancer is quite expressive. According to Swisher *et al*.[19], less than 25% of health professionals have some information about ICM, and on the other hand a high percentage of ICM use in women with breast cancer can have implications in the clinical management of the disease (Molassiotis, 2006). Among the adverse effects, small hematomas on the sites of the needle punctures were observed in 3 women. However, there were no reports of other more serious disorders, showing the safety of treatment, even in oncological patients. According to Hyojeong *et al*. (2006) adverse effects are not observed in the greater part of studies with the use of acupuncture for the reduction of pre-surgical anxiety. This means that even if there may be a few adverse effects presented, such as ecchymosed, increase in pain, syncope, among others, when carefully used according to the safety rules established, it is a safe method (Ernst, 2003). The presence of social support was referred by most volunteers, and it can exert a strong influence over well-being, foster health recovery, especially acting in the improvement of the emotional aspects that are shaken by the disease (Ambrósio, 2015). Although several women confirmed that they knew acupuncture, in general they referred only to have "heard of it". Even after the publication of the National and State Policies for Complementary and Integrative Practices (Brasil, 2006; Espírito Santo, 2013) respectively, and the investment of 45.2 billion BRL for the financing of integrative practices of medium and high complexity in 2016, its access is still limited. This fact is possibly related to the reduced number of acupuncturists and the availability of visits in the public health system, to the limited actions in the dissemination of the specialty, the lack of knowledge of other professionals, and to the lack of clinical studies, which could change a few knowledge gaps into clearer evidence. The results of this research suggest the viability of the use of this humanized treatment in an oncological reference center at the hospital level, aiming at minimizing the suffering of patients, improving interpersonal relationships and aggregating new therapeutic possibilities to the users of the public health system.

Our study presents some limitations. Control patients did not receive a sham acupuncture and received less attention than the acupuncture group and this could be considered a "placebo effect' as anxiety is known to be particularly responsive to it (Vogel, 1980). We did not consider the option of using a sham treatment. This term has not been clearly defined in relation to acupuncture (Moffet, 2009). Even no traditional points can present important effects (Lewith, 1983), using dummy points (White *et al*., 2000) or even cocktail sticks (Cherkin, 2009), can produce effects. The so-called sham procedure may have stronger psychological effects than a pharmacological placebo and even physiologic effects can be found (Kaptchuk, 2006). We designed our study on that of Vickers (Vickers, 2004) that he called a pragmatic study, i.e., a policy of "using acupuncture" versus "avoiding acupuncture", so we did not consider using a sham treatment. Our aim was to observe the result of acupuncture in anxiety under real-life conditions comparing with a group that has no receive this kind of treatment. For that we used the third category described by Hammerschlag[33]: *acupuncture plus standard care versus standard care only.* This seemed to us the best ethical option in that there is no attempt to deny standard treatment to all women. We could, in this way, reflect about the conditions of daily medical practice and maximize the external validity. In this way it should open the possibility of expanding the use of acupuncture in pre-surgery in oncological surgeries, including in the remaining stages of treatment, as well as in the approach in other types of cancer, always with the association and integration of care with the several medical specialties and the multi-professional team. We hope this work could foster the dissemination of acupuncture in health services and universities, contribute to research and consolidation of public policies.

CONCLUSION

This study has shown that the intervention with acupuncture, in our sample, reduced the levels of anxiety in women with breast cancer

diagnosis. With only six classic acupuncture sessions before total or partial mastectomy, a significant result can be obtained in the improvement of the anxiety levels. Moreover, after the intervention pre-serum levels and cardiac frequency reduction was observed among the volunteers, effects that still need to be studied more deeply.

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