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Quality of life and adverse reactions caused by chemotherapy in breast cancer: an integrative review

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Abstract: The aim was to identify the current state of knowledge relevant to the adverse effects of chemotherapy in patients with breast cancer that affect quality of life (QOL). It is an integrative review in databases: CINAHL, SCOPUS, Web of science, PUBMED and SCIELO. 50 articles that met the inclusion criteria were analyzed, with most evidence level IV, which featured three groups: group 1, adverse reactions caused by chemotherapy, most commonly reported: nausea, vomiting, constipation, fatigue, insomnia, alopecia, waves heat, asthenia, cognitive dysfunction and amenorrhea; Group 2 interventions to improve QOL, reported according to specific adverse reactions; and group 3, factors that influence QOL with most related to the combination of administered chemotherapy. Adverse reactions should be evaluated in a multidisciplinary way and should be considered in decision-making, beyond individual vulnerability tests and information obtained from the evaluation QOL.

Keywords – *Chemotherapy, Quality of Life, Integrative review, Toxicities.*

I. INTRODUCTION

Cancer is focusing on the population overwhelmingly, of all types the breast is most often diagnosed in women [1]. It is estimated that each year, occurred more than 1,050,000 new cases of breast cancer throughout the world [2]. 57,960 new cases of breast cancer are expected in Brazil in 2016 [1].

The diagnosis of breast cancer carries a negative stigma, regardless of the disease prognosis. Despite the success of effective anticancer treatment, they can live with other problems related to: psychosocial impact of treatment; chances of relapse; association with other comorbidities such as cardiovascular disease, diabetes, osteoporosis [3].

The most common forms of treatments include surgery, chemotherapy, radiation therapy and hormonal therapy. More than one way can be used in a complementary manner. Despite the frequent success of the therapy, many adverse events (AE) are observed, leading to the decline functional [2].

Adverse events caused by chemotherapy drugs are related to their lack of specificity for tumor cells and cytotoxic effects on normal cells. These events predominate in cells that are in constant division, such as the hematopoietic tissue, the germinal tissue of hair follicles and gastrointestinal coating [3].

Despite increase survival, chemotherapy and hormonal therapies influence negatively the quality of life (QoL) due to these EAs [3].

Quality of life indicates a subjective and multidimensional concept, composed of multiple domains, often including physical, social, emotional, mental and funcionais [4]. There has been great interest over the last decades to assess and measure the impact of diseases and their treatment in quality of life patients [5], especially in chronic diseases and long-lasting as cancer. It is believed that the assessment of QoL in cancer patients can improve treatment and even the prognoses [5].

The measurement of QoL of a patient can thus be used in clinical practice for making decisions, in this context, provide accurate, realistic and understandable information about treatment, adverse events and necessary health care. This is an essential factor to build and strength the skills of the patients in coping with their current situation and to improve its QoL [6].

Given the above, this research aims to analyze the scientific evidence about the adverse events of chemotherapy in patients with breast cancer that affect the quality of life through literature analysis.

It is hoped that this study contribute to the construction of the oncology nursing knowledge about the QoL of those who undergo aggressive cancer treatments, specifically chemotherapy and seek to know mechanisms to minimize reactions to treatment and improve thus, the quality of their lives.

II. METHOD

The theoretical and methodological framework of the Evidence-Based Practice (EBP) were adopted, opting for an integrative literature review. The use of the search results is one of the pillars of evidence-based practice where nurses use as an aid to decision making in practice assistance [7]. The method used in the study is an integrative literature review. For this, they are covered six stages[8]:

1. Issue identification or formulation of the guiding question: For the present study, we formulated the following question: "What are the current scientific evidence on the adverse events of chemotherapy in patients with breast cancer that affect quality of life?" Databases selected: CINAHL (Cumulative Index to Nursing and Allied Health Literature), MEDLINE (Medical Literature Analysis and Retrieval System online), Scopus and Web of science and electronic libraries PUBMED and SCIELO. The choices of these databases are due to the fact that the broad scope of the same and libraries, for meet the inclusion criteria of articles.

In SCIELO library were used Descriptors in Health Sciences (DeCS) "Breast cancer", "chemotherapy", "toxicity" and "quality of life" and to PUBMED, MEDLINE, CINAHL, Scopus and WEB oF SCIENCE used to the terms of the Medical Subject Headings (Mesh) "breast cancer", "drug therapy", "adverse events", "quality of life" and "toxicity".

The search took place in May 2014 and were included primary articles that answer the main question of the study and deleted comments and summaries. Regarding the identification of evidence of the articles selected level, it adopted the classification as Stetler et al [9].

Initially, all studies (n = 154) were exported to EndNote Web software, where the duplications between the bases were observed (n = 6). Subsequently, the titles and abstracts were read and assessed for inclusion criteria and guiding question. At this time, it was found that 21 articles addressed treatment with hormone for breast cancer, 19 drugs for breast cancer treatment, 16 toxicities of breast cancer treatment without addressing the quality of life, 12 others tumors, two models of evaluation of quality of life, totaling 70 exclusions. Secondly, 99 titles were separated for reading in full. Of these, 49 did not answer the main question, so 50 articles were analyzed.

2. Establishment of study selection:

The following inclusion criteria were established: clinical studies available in full between 2009 and 2014, in Portuguese, English and Spanish, with the primary objective of analyzing the scientific evidence about adverse events of chemotherapy in patients with breast cancer that interfere with QoL.

The exclusion criteria were defined: items that had been found in a previous search; escape from the subject studied; studies about adverse events caused by radiation therapy; language; items out of the selected period, those that did not involve human beings.

3. Studies rating:

The descriptors chosen for the searches were combined in each database. The articles were classified and the results were summarized and classified in groups, considering the revision of the goal.

4. Evaluation of the studies included in the review:

At this stage, an instrument designed and validated for analyse and extract the articles was adopted [10], which includes the identification of articles, the methodological aspects of the study and the characteristics of the searched QoL.

5. Discussion and interpretation of results:

It sought to establish the points of convergence and divergence between the articles, regardless of the type of research undertaken. We conducted a detailed analysis of the articles, aimed at achieving the objectives of this study.

6. Synthesis of knowledge evidenced in analyzed articles:

It was decided to present the results to the summary of the review of knowledge, by thematic groups and tables.

III. RESULTS

The collection of articles is shown in Table 1, including the number of items found, repeated and selected according to each database.

Table 1 - Number of articles obtained from the composition of the sample. Ribeirão Preto - SP, from 2009 to 2014.

Database	Articles found	Articles deleted	Articles selected	Articles duplicated	Total articles analyzed
CINAHL	33	10	15	04	05
SCOPUS	15	15	15	01	00
SCIELO	11	02	09	00	07
PubMed	90	49	55	01	38
Web of Science	05	05	05	00	00
Total	**154**	**81**	**99**	**06**	**50**

After reading and analyzing the studies, the following information groups were highlighted. Group 1 - Adverse events caused by chemotherapy, Group 2 - interventions that improve the QoL and Group 3 - Factors that influence QoL. Articles in the sample are described in Table 2.

Table 2 - Description of sample items: number of the study, reference design / level of evidence / number of patients, adverse events caused by chemotherapy, interventions that improve QoL and factors that influence QoL.

Nº do estudo/ Referência	Delineamento/nível de evidênica/numero de pacientes	Reações adversas provocadas pela QT	Intervenções que melhoram a QV	Fatores que influenciam na QV
01. Moros et al. Rev. méd. Chile. Jun. 2010;138(6):715-722.	Descriptive, exploratory, randomized, Level II, n = 17	Pain, insomnia, fatigue, anxiety	Entertainment program, dynamic, aerobic exercise individualized	Age, Body mass index, stage, surgery, chemotherapy and treatment cycle
02. Gozzo et al. Rev. gaúch. enferm. set. 2013;34(3):110-116.	Prospective study, Level II, n = 79	Nausea and vomiting	Evaluate the woman throughout the treatment in all aspects	Protocol chemotherapy and amount of cycles
03. Sabino et al. Rev. bras. cir. plást. out.-dez. 2012;27(4):556-561.	Descriptive, exploratory study, Level IV, n = 36	Disturbances in self-image, self-esteem, feeling of being attractive, sexual activity	Physical activity, psychological and educational support.	Breast reconstruction, age, marital status, income, postoperative time, education
04. Jorge et al. Rev. latinoam. enferm. Sept.-Oct. 2010;18(5):849-855.	Descriptive, cross Level IV, n = 50	Physical domain (pain, tiredness, nausea and vomiting, anorexia)	Investigate and propose effective control actions	Chemotherapy regimen and amount of cycles
05. Verde et al. Rev. nutr. Nov-dez. 2009;22(6):795-807.	Experimental, descriptive and exploratory, Level II, n = 25	Physical domain, food aversion	Individualized feeding adequacy	Age, educational level
06. Nicolussi, Sawada. Rev. gaúch. enferm. dez. 2011;32(4):759-766.	Descriptive, exploratory, Level IV, n = 35	Emotional function, pain, insomnia, fatigue	Prevent and control side effects, adhere to treatments complementary	Socio-demographic conditions, clinical and therapeutic
07. Evangelista. Tese (doutorado). São Paulo; s.n; 2012. 97 p.	Descriptive, exploratory, Level IV, n = 354	Emotional function, role play.	Individualized interventions as culture, symptom control, social and emotional support	Self-confidence and sense of well-being
08. Bastani e Kiadaliri. Med Oncol. 2011; 28:S70–S74.	Descriptive, exploratory cohort, Level IV, n = 100	Physical domains, role playing, emotional, cognitive and social	Consider adverse events on QoL assessment during the decision making for the treatment	Protocol: FAC and TAC, long after completion of treatment, clinical and demographic
09. Ann et al. Psycho-Oncology. 2009;18:634–646.	Experimental, clinical, randomized, Level II, n = 219	Sleep quality and fatigue	Relaxation, control for consistent sleep	Chronic insomnia, comorbidities

10. Biswal et al. Integrative Cancer Therapies. 2012: 1–11.	Almost experimental, clinical trial, non-randomized, Level III, n = 100	Fatigue	Exercises, educational counseling, sleep therapy, complementary therapy	Anemia, tumor volume, staging and physical activity
11. Anitra et al. New Zealand Medicine Journal. 2014; 127(1388).	Descriptive case study, Level IV, n = 1	Fatigue, pain, loss of appetite, nausea / vomiting, insomnia.	Vitamin C intravenous	Staging, age, anemia, surgeries
12.Cueva et al. Invest New Drugs. 2012; 30:688–694.	Almost experimental, clinical trial, non-randomized, Level III, n = 10	Asthenia, insomnia, palpitation	Methylphenidate 20mg / day	Chemotherapy, staging, tumor type
13.Ruiter et al. Human Brain Mapping. 2012; 33:2971–2983.	Experimental, clinical, randomized, Level II, n = 32	Cognitive function	Neuropsychological tests	Adjuvant chemotherapy high doses, hormones, neurotoxic agents
14.Debes et al. Breast Cancer Res Treat (2010) 121:91–100.	Descriptive, exploratory, Level IV, n = 328	Physical and cognitive function	Neuropsychological tests revealed no differences in cognitive function	CEF Protocol is not associated with changes in cognitive function
15.Ferguson et al. Psychooncology. 2012; 21(2):176-186.	Descriptive, exploratory, Level IV, n = 40	Cognitive function	Training memory and attention	Using MAAT little improves cognitive function
16.Hatam et al. Arch Gynecol Obstet. 2011;284:215–220.	Descriptive, exploratory, Level IV, n = 100	Amenorrhea, anemia, febrile neutropenia, hyper pigmentation, neurological toxicity, edema	Use of G-CSF, education to patients, support group with shrink	TAC and FAC Protocol
17.Joffe et al. Menopause: The Journal of The North American Menopause Society. 2010;17(5): 908-916.	Experimental, randomized, placebo-controlled, Level II, n = 38	Hot flashes, sleep disruption, adherence to endocrine therapies	Zolpidem, specific additional treatment for sleep	Endocrine therapy for breast cancer
18.Kontos et al. Climacteric. 2010;13:4–21.	Literature review, case study, Level IV, n = 1346	Heat waves	Stellate ganglion block, hormone replacement therapy, complementary therapies	Chemotherapy and time after antineoplastic treatment
19.Van Waart et al. BMC Cancer. 2010;10:673.	Descriptive, randomized, controlled, multicenter, Level IV, n = 360	Fatigue, cardiorespiratory function, muscle strength	Physical activity program during chemotherapy	Chemotherapy, clinical and sociodemographic
20.Sherrill et al. Current Medical Research & Opinion. 2010;26(4):767–775.	Phase 3, randomized, placebo controlled, Level II, n = 579	Dermatologic events, diarrhea, mucositis	Adjustments in doses of chemotherapy	Chemotherapy protocol, age, metastasis
21.Shimozuma et al. Support Care Cancer. 2012; 20:3355–3364.	Phase 3, randomized, Level IV, n = 300	Peripheral Neuropathy	Prevention with frequent evaluation, management of chemotherapy dose	Chemotherapy Protocol (monotherapy taxane x AC + taxane)
22.Stubblefield et al. Cancer. April 15, 2012; 2250-2260.	Review, descriptive, Level IV, n = not applicable	Peripheral neuropathy	Model of physical rehabilitation, assess risk and monitor symptoms	Rehabilitation, pain, sensory symptoms, chemotherapy,

				layout, physical activity
23.Takei et al. Breast Cancer Res Treat. 2012;133:227–236.	Descriptive, exploratory, randomized, multicenter, Level IV, n = 242	Arthralgia, fatigue, excessive heat, weight gain, vaginal dryness	Change in endocrine therapy	Endocrine therapy, duration of therapy
24.Van den Hurk et al. Psycho-Oncology. 2010;19:701–709.	Descriptive, exploratory, prospective, multicenter, Level II, n = 204	Alopecia, altered self-esteem, body image	Cooling the scalp, alopecia handling	Antineoplastic agent
25.Yang et al. Journal of Advanced Nursing. 2011; 67(1):158–168.	Descriptive, exploratory, controlled, randomized, Level IV, n = 40	State of humor, psychophysiological function	Walk program, management of the treatment of symptoms	Staging, comorbidity, treatment adherence, motivation
26.Yoo et al. Cancer Chemother Pharmacol. 2013; 72:565–575.	Descriptive, exploratory, prospective, observational, Level IV, n = 312	Amenorrhea induced chemotherapy, menstrual irregularity	Evaluate use / choice of chemotherapy	Age hormone therapy, tamoxifen and taxane
27.Wefel et al. Cancer. July 15, 2010;3348-3356.	Descriptive, exploratory, prospective, longitudinal, randomized, Level IV, n = 42	Cognitive dysfunction, learning and memory	Neuropsychological assessment, identification of risk groups	Dose and chemotherapy agents, level of education, age
28.Jim et al. Cancer. Apr 15, 2009;115(8):1776-1783.	Descriptive, exploratory, Level IV, n = 187	Neuropsychological function, cognitive	Neuropsychological evaluation	Chemotherapy, hormonetherapy
29.Nuzzo et al. BMC Cancer. 2011;11:75.	Descriptive, exploratory, randomized, Phase 3, Level IV, n = 139	Neutropenia, stomatitis	Assess QoL and toxicities	Protocolo of chemotherapy
30.Biglia et al. J Sex Med. 2010;7(5):1891-900.	Descriptive, exploratory, Level IV, n = 35	Sexual function, anxiety, hot flashes, memory and concentration	Cognitive tests, multidisciplinary evaluation	Chemotherapy, hormone, age
31.Berger et al. Oncology Nursing Forum. Sept 2009;36(5),563-570.	Descriptive, exploratory, longitudinal, randomized, controlled, Level IV, n = 196	Fatigue, mental and physical function	Evaluate fatigue, physical and mental function, tools for measuring toxicities	Chemotheray regime, dose
32.Masmoud et al. La Revue de Santé de la Méditerranée orientale. 2009;15(2):362-368.	Descriptive, exploratory, Level IV, n = 23	Physical, cognitive, social function	Improve the infrastructure of care centers to cancer education	Education, structure, early detection, socioeconomic condition
33.Heather-Jane et al. Oncologist. 2013;18(7): 812-8.	Descriptive, exploratory, Level IV, n = 3222	Physical Function	Assess risks and benefits of each treatment	Tolerability, chemotherapy
34.Andrykowski et al. J Pain Symptom Manage. 2009, March;37(3):341–351.	Descriptive, exploratory, prospective, longitudinal, Level IV, n = 102	Fatigue	Evaluate fatigue, response to treatment	Causes of fatigue, adjuvant therapy
35.Cheung et al. Critical Reviews in Oncology /	Descriptive, systematic review, Level IV, n = 1820	Neuro-cognitive loss	Assess cognitive function, clinical evidence	Treatment regimen, dose, duration of

Hematology. July 2012; 83(Issue 1): 99-111.				chemotherapy
36.Berger et al. Journal of Clinical Oncology. dec 2009; 27(35):6033-6040.	Descriptive, exploratory, experimental, randomized, Level II, n = 219	Fatigue, sleep quality	Behavioral therapy and sleep, feed control	Anxiety, education, heatwaves, food
37.Andrykowski et al. Cancer. dec 15, 2010:5740-5748.	Descriptive, exploratory, Level IV, n = 304	Fatigue	Monitor fatigue, perform physical activity	Obesity, treatment regimen, physical activity
38.Corey-Lisle et al. Cancer. jan 15, 2012:461-468.	Experimental, international, randomized, multicenter, Level II, n = 752	Does not specify overall QoL	Analysis of the risk-benefit of therapy, combined therapy	Treatment regimen, tumor response
39.van Nes et al. Breast Cancer Res Treat. 2012;134:267-276.	Descriptive, randomized, multicenter, open-label, phase 3, Level IV, n = 742	Insomnia, sexual disorders	Attention to prescribe endocrine treatment	Regime and adherence to treatment
40.Svensson et al. Breast Cancer Res Treat. 2010 Oct;123(3):785-93.	Descriptive, exploratory, TEX trial, randomized, controlled, Level IV, n = 287	Physical function, sexual, pain, fatigue, insomnia and diarrhea	Guidelines to patients	Treatment regimen, performance status, response rate, safety and survival
41.Ganz. Journal of the National Cancer Institute Monographs. 2010;41:218-222.	Descriptive Review - Editorial, Level VI, n = does not apply	Psychological function	Analyze perceptions	Histological type
42.Kornblith et al. J Clin Oncol. 2011 Mar 10;29(8):1022-8.	Descriptive, exploratory, telephone interview, Level IV, n = 350	Social function, psychological, fatigue, nausea and vomiting, constipation, diarrhea, syndrome foot hand	Decrease QoL is the price paid with the use of standard treatment, and increase survival	Treatment regimen, dose, time of use
43.Lee et al. British Journal of Cancer. 2010; 102:1341-1347.	Descriptive, exploratory interview, as the benefits of treatment, Level IV, n = 378	Physical function, appetite	Assess QoL as clinical routine	Treatment regimen, dose, cycles
44.Iiristo et al. Acta Oncologica. 2011; 50: 338–343.	Descriptive, exploratory questionnaire sent by mail, 8 times for 1 year Level IV, n = 446	Physical function, infection, myalgia, bone pain	Evaluate chemotherapy, make individual management treatment regimen	Treatment regime, dose
45.Hermelink et al. Psycho-Oncology. 2010;328: 1322-1328.	Descriptive, exploratory, prospective, randomized, Level IV, n = 101	Cognitive dysfunction, neuropsychological, depression, anxiety	Consider neuropsychological function to determine the treatment dose,	Treatment regimen, personality, affectivity
46.Ochayon, L et al. Oncology Nursing Forum. September 2010; 37(5).	Descriptive, exploratory, Correlational, Level IV, n = 132	Change in mood and irritability	Educational emotional support, physical activity, instruments for measuring symptoms	Hormonal therapy, physical activity

47.Webber et al. The Oncologist. 2011;16:1333–1344.	Descriptive questionnaire 6 and 12 months after treatment, prospective, cohort study, Level IV, n = 130	Decrease in sexual interest, impaired sexual function	Identification and physical concomitant treatment of mood changes	Menopausal status
48.Rey et al. The Breast Journal. 2012;18(5): 406–414.	Descriptive, exploratory cohort, ELLIPSE 40, Level IV, n = 452	Cognitive impairment	Dispensing tranquilizers	Age, psycho-social vulnerability
49.Lemieux et al. Journal National Cancer Institute. February 2, 2011;103 (Issue 3)	Case study, systematic review of randomized clinical trials, Level IV, n = 190	Biomedical and no biomedical datas	Consider QoL in clinical decision	Mode of treatment, metastasis
50.Ryhanen et al. Journal of Clinical Nursing. 2013; 22: 1016–1025.	Descriptive, exploratory, randomized, controlled, Level IV, n = 90	Depression, fatigue	Biomedical and no biomedical interventions	QoL of patients did not influence the decision and clinical intervention of health professionals

To measure QoL, the most used instruments were: 20 (35.2%) EORTC QLQ-C30, 06 (10.5%) BR23 and 06 (10.5%) FACT-B. 04 articles (7%) have used various questionnaires to measure QoL. The PSQI, POMS, Piper fatigue scale, HADS, CES-D and BDI were used in 03 articles each. WHOQOL-bref, STAIS, SF36, MENQL, FSI, FCS, FACT-G and FACT-ES were used in two each. And other Mc Coy instruments female sexuality questionnaire, BAECKE, BIS, BMI, Body attitude test, CARES, CVLT, ES, FBSI, FQL, FSI-TT, GHQ-30, Greene climateric scale, HADS, Hopkins Symptoms Checklist 25, IMQ, IPAQ, LASA, MAQ, MASQ, MBA, MFI, NART, PANAS, PFS, PMOS, PNQ, QOL-CS, SCFS-6, Seven drug physical activity recall, SF36, SOFA, SPHERE, Taiwanese version of the MD symptom inventory, Treatment satisfaction and VAS in just one article each.

IV. DISCUSSION

This review showed that adverse drug events are common causes of morbidity and mortality, despite the extensive process of regulating the efficacy and safety [13]. In all areas, these reactions are responsible for 7% of all hospital admissions, occur in 10 -20% of patients, and result in increased hospital stay [14].

Regarding the country of the authors, it has shown great interest in the topic in several countries. 86% were in English, and 14% in Portuguese and Spanish. These data relate to the databases in which the articles were found, where the majority was PubMed and SCIELO requiring articles in English.

In relation to the author, the data showed that the issue still prevails among doctors and nurses, who are the professionals who care for these patients directly experiencing the cancer patient problems. It is evident also, the predominance of scientific production linked to universities or university hospitals. According to study Meneghel et al [15], the production of knowledge is concentrated in the universities, that have qualified staff and resources to the development of research.

Most research is descriptive exploratory design, with evidence level IV (78% of studies), showing that there is a lack of randomized controlled trials in this area of knowledge, so there are better levels of evidence for clinical practice. However, one can not fail to stress the importance of observational studies, which has the advantage of controlled and randomized clinical studies the lowest cost, faster, larger sample size easily and are mainly used to identify the risk factors and prognostic indicators and situations in which randomized controlled trials would be impossible or unethical [16].

Regarding aspects of QoL, it emphasizes the importance of the authors define what they mean by QoL, and this definition should be consistent with the type of instrument used and the theoretical framework of QoL that supports the construction of the instrument and the discussion of article, since the absence of an explicit theoretical framework to guide the development of research in quality of life, has limited use and generalizations of QoL assessment in clinical trials in cancer patients [17].

The most widely used instruments to assess QoL of cancer patients undergoing chemotherapy in the articles included in this review were similar to those found in other studies [18].

Group 1 showed the adverse events caused by chemotherapy, where the most reported complaints and symptoms were nausea, vomiting, constipation, fatigue, insomnia, alopecia, hot flashes, asthenia, cognitive dysfunction and amenorrhea.

These effects may be related to the type of treatment applied. In research conducted in the study 02 with 79 women who participated in the study, 93% had nausea and vomiting 87%, at least once during treatment, data higher than those found in the literature. The results of a prospective study involving a group of 200 patients found that the combination of symptoms, loss of appetite, nausea and vomiting, had a negative impact on QoL, more than nausea, vomiting and loss of appetite individually [19]. Although the results of this study point to a QoL that remain during chemotherapy, most studies shows significantly bad interference of chemotherapy on QoL of women with breast cancer [19].

Fatigue can be expressed in physical, emotional and mental levels [20]. Causes of fatigue related to cancer treatment should be seen as multifactorial and associated with lack of both physical fitness and emotional [20].

In a study by Davidson et al. [21], about a third of breast cancer survivors women reported chronic fatigue associated with insomnia, depression, loss of the function and quality of life. Study Dimeo et al. [22] demonstrated that the fatigue reaches to affect at least 30% of the surviving patients, which can affect the quality of life more than pain.

It is believed that the decrease in physical activity worsen the adverse events, leading patients to experience a recurring negative effect further exacerbates the feeling of fatigue. Forced reduction of physical activity levels develops a pathological condition that associated with other adverse events such as loss of appetite, may enhance the physical wear and, consequently, the loss of total muscle strength. This loss of muscle strength is a further blow to the cancer patient's efforts to perform simple daily tasks, compromising significantly their quality of life [22].

Regarding asthenia, 12 study researched 288 women with breast cancer treated with adjuvant chemotherapy, and reported pre asthenia and post-treatment in 10 and 20%, respectively.

The decline in cognitive function such as memory, attention and executive, has been reported among the various adverse effects of adjuvant therapy, found in the study [13]. The study 13, brings evidence of effects on the white part and gray brain after use high doses of adjuvant chemotherapy, with subsequent impact on cognitive function. However, the study 14 neuropsychological tests revealed no differences in cognitive function among patients with breast cancer after chemotherapy.

The study 27 showed that the decline in cognitive function has been associated with systemic dose chemotherapy, during and after complete treatment cycles. These findings are due to the development of research on animals showing changes in brain structure and function, acute and delayed form, associated to common chemotherapeutic agents as 5-FU.

Heat waves also change the QoL due interruptions during sleep repeatedly throughout the night. May persist for day and night and can result in lethargy, moodiness and decreased well-being [23]. Sleep disorders occur in 23-49% of breast cancer survivors for 5 years after diagnosis, and can have several causes including endocrine therapy (tamoxifen and aromatase inhibitors) [24].

Peripheral neuropathy was related to taxanes administration, which also affects QoL, its incidence is around 60% [25]. It is an important cause of dose reduction or interruption / discontinuation of treatment [25].

Alopecia is related to body image, causing impact on self esteem and self image and can lead to emotional distress. Among the effects of chemotherapy, the study 27 women reported among the greatest fears, the presence of metastasis, followed by alopecia and full mastectomy.

Sexual activity, quality of the relationship with the partner and desire were harmed in the research 30 after adjuvant chemotherapy and after surgery. Difficulties in comprehension were reported of women's conditions by the partner.

In group 2, regarding interventions that improve the QoL, increased the number of surviving breast cancer, reinforces the need to investigate the long-term impact of the disease itself and the adverse events of anticancer treatments available. In this context, the increased survival and decreased risk of relapse are faced with the effects of experience as nausea, vomiting and changes in dietary patterns, which can compromise the quality of life of patients [26].

Regarding the management of asthenia, it has been suggested the use of methylphenidate with good tolerance and improves the effects on quality of life, in addition to stimulating factor use of granulocyte colonies (G-CSF) and dexamethasone for 2 days according to a study 12.

The study 15 used the MAAT (Memory and Attention Training Adaptation), designed to assist technical and teaching strategies to reduce the negative impact on the function and quality of life in relation to cognitive problems. Demonstrated user satisfaction and improved quality of life and related to memory performance.

Clinical evidence is insufficient, according to a systematic review 35, whose studies evaluate the relationship between the types, dose intensity of chemotherapy and cognitive impairment regimes. More research is needed to examine these factors.

Use of zolpidem, a hypnotic agent, improves sleep and quality of life of breast cancer survivors with hot flashes associated with sleep disorder, but treatments for sleep may be important to improve strategies to improve well-being (study 17) .

To alleviate hot flashes, studies encouraging use of a variety of drugs including clonidine, gabapentin, inhibitors of serotonin and norepinephrine selective. SGB (Stellate ganglion block) has emerged as a new technique to reduce this toxicity. Other alternatives include hormone replacement therapy (study 18). In study 39, the authors emphasize the option to use hormones only for patients in post menopause with breast cancer with hormone receptor positive.

Physical activity during treatment with chemotherapy, has been a promising strategy to minimize or prevent the short and long term adverse events. In a study 25 women reported fewer symptoms and severity and improved mood compared to the control group.

A retrospective study multicentric epidemiological cohort indicated use of intravenous vitamin C improved the quality of life, reducing fatigue in breast cancer during chemo / radiotherapy [21].

According to a study 43, there are no effective drugs approved to prevent or treat peripheral neuropathy induced taxane. Symptoms vary depending on the type of nerve (motor, sensory and autonomic) affected and the severity.

For alopecia, it was suggested in the study 24, the cooling technique of use of the scalp. It was effective in 52% of cases, contributed to the improvement of well-being and quality of life.

Authors of the study 30 reported the need for multidisciplinary support for patients with breast cancer after surgery in order to evaluate new interventions and improve sexuality and QoL.

The need for improved infrastructure, public education to promote early detection and improve patient care was reported in research 32, done by Masmoudi et al. Thus, you can perform well-designed studies on QoL, to evaluate performances and medical and psychosocial interventions.

In group 3, factors that influence QoL, found that the combination of chemotherapy is invariably associated with side effects, and usually chemotherapy drugs are administered in combination. The most common are regimes with cyclophosphamide, methotrexate and 5-fluorouracil; cyclophosphamide, adriamycin and 5-fluorouracil; Adriamycin and cyclophosphamide (AC); cyclophosphamide, epirubicin and 5-fluorouracil (FEC); AC followed by paclitaxel; paclitaxel, adriamycin and cyclophosphamide (TAC); or a variety of combinations of cytotoxic drugs (Study 10). In 38 studies, the type of chemotherapy and dose influenced the QoL of patients the side effects of nausea and vomiting, fatigue and other symptoms. We also found in several studies that socioeconomic factors such as age, marital status, education level and the clinical and stage of disease, type of surgery, comorbidities, anemia, survival time also interfere with the patient's QoL in chemotherapy. Several national and international studies have also demonstrated the influence of these factors on HRQoL of patients in chemotherapy [27,28]. In relation to cognitive function, the use of tamoxifen showed no influence or association with impaired memory, attention or execution papers [29]. In the study 27 of Wefel et al., declines in the areas of learning and memory, performing functions and processing speed, were more common. Not associated with humor, another clinical measure or demographic characteristics.

Tamoxifen and chemotherapy cause severe hot flashes, resulting in sleep disturbance, fatigue, anxiety, irritability, depression, and sexual dysfunction, thus reducing the quality of life [30].

Among the study's limitations, give it highlighted the presence of the diagnosis of breast cancer in women at different stages of treatment, differing chemotherapy regimens, and thus the results can not be generalized to the various stages of the disease, since the initial usually no symptoms related to the tumor to the most advanced.

There was lot of reported adverse events during treatment with chemotherapy, and wide range of fields observed in the questionnaires used to measure QoL. In addition, there was the use of some subjective instruments to assess QOL and adverse reactions, which may not have been sensitive enough to detect changes among respondents or other qualitative data.

V. CONCLUSION

With the results of this review, we conclude that the adverse chemotherapy reactions in patients with breast cancer should be assessed throughout treatment in all its aspects, not limited only to reviews and questions about the physical signs and symptoms, but also encompassing the psychosocial aspects.

It found that chemotherapy causes more damage in the areas of HRQoL. In this continuous and dynamic process, the assessment should be multidisciplinary and should be considered in decision making, in addition to thinking about the individual vulnerabilities and information and tests obtained from the evaluation of QOL.

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