Telephone counseling: identification of symptoms in patients with lymphoma undergoing antineoplastic chemotherapy

Aconselhamento telefônico: identificação de sintomas em pacientes com linfoma em quimioterapia antineoplásica

Consulta telefônica: identificação de sintomas en pacientes con linfoma en quimioterapia antineoplásica

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Abstract

Objective: To identify through telephone counselling the signs and symptoms presented by patients with Hodgkin’s Lymphoma undergoing chemotherapy with the protocol composed by doxorubicin, bleomycin, vinblastina and dacarbazina (ABVD) and to compare severity scores of the signs and symptoms presented in the cycles of the protocol.

Methods: Descriptive, prospective, quantitative study. Seven patients received telephone counselling in 24 scheduled and unscheduled calls, corresponding to 6 ABVD chemotherapy cycles. The MD Anderson Symptom Inventory and the Common Terminology Criteria for Adverse Events were used for scoring the symptoms, along with a conduct protocol. A descriptive and analytical analysis was conducted.

Results: Two hundred and eighty-six telephone calls generated 1,870 symptomatic complaints. In scheduled calls, the most prevalent complaints were fatigue, distress, lack of appetite, vomiting and nausea. As for the interference in daily life activities, the items related to general activities, work, difficulty walking, and mood changes were reported more frequently. In unscheduled calls, lack of appetite and irregular menstruation were the most recurring complaints. The analysis of the progression of symptoms showed an increase in nausea and vomiting (p<0.02), decrease in fatigue and shortness of breath (p<0.02), improvement in sleep (p<0.02) and decrease of stress (p<0.02).

Conclusion: Fatigue, nausea, vomiting and alterations in work activities were frequently reported. There was progression of nausea and vomiting but regression of fatigue and stress. Telephone consultation allowed a rapid communication and management of an expressive number of symptoms.

Keywords

Oncological nursing; Distance counseling; Health education; Hodgkin’s disease; Linfoma; Tratamiento farmacológico; Antineoplásicos

Descritores

Enfermagem oncológica; Aconselhamento à distância; Educação em saúde; Doença de Hodgkin; Linfoma; Drug therapy; Antineoplastic agents

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Enfermería oncológica; Asesoramiento a distancia; Educación en salud; Enfermedad de Hodgkin; Linfoma; Tratamiento farmacológico; Antineoplásicos

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Manuscript

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Introduction

Hodgkin’s lymphoma (HL) is a hematologic malignant neoplasm with a global prevalence of 0.6% and a national rate of 0.5% of cases per 100,000 inhabitants. Despite its relatively low incidence, HL represents 15% of all cancers in young adults (15-40 years old). Fortunately, the mortality rate was reduced by more than 60% since the early 1970s, due to the advances in antineoplastic treatment. This raised progression-free survival to 85.7%, regardless of the stage of the disease. The high success rate is also related to effective medication adherence.

There has been an increase in the use of antineoplastic chemotherapy (AC) and new cell targeted drugs, which specifically fight cancerous cells, have been included in the protocols. However, in Brazil, the new drugs are not authorized for first-line treatment in the public healthcare network (Unified Health System) and the chemotherapy protocol is composed of the drugs doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD chemotherapy), administered intravenously on day one (D1) and day fifteen (D15), in a cycle that is repeated 4 to 6 times.

These are systemic cytotoxic drugs, which, despite their excellent remission outcomes, also affect several systems, such as the hematopoietic, the integumentary, the gastrointestinal and the cardiac systems. Some toxicities are frequent and are associated to worst therapeutic adherence, requiring constant evaluation and monitoring.

The ABVD protocol is administered in an outpatient regimen and the patients are advised to keep their activities of daily living and their study and/or work activities as close as possible to normality. The education provided to the patients must prepare them for therapeutic adherence (cytotoxic chemotherapy, other daily medications, exams and medical appointments) and for monitoring and managing signs and symptoms. Adequate adherence to the therapeutic regimen is a key factor for achieving disease remission. Delays or dose reduction of ABVD may compromise dose intensity and the achievement of disease remission, as the Reed-Sternberg cells are chemo-sensitive but also genetically unstable with a tendency to develop early secondary resistance.

In this scenario, an effective communication between patient and healthcare team is essential to identify risk situations, manage signs and symptoms, provide emotional support and guarantee adherence to the therapeutic protocol. Among the possibilities, nurse-run telephone consultations are an affordable and economically viable alternative, considering the expansion of mobile phone coverage among citizens of large metropolises and the already proven positive outcomes in the detection and early management of signs and symptoms, which may lead to reduction or shortening of hospital admissions.

The counseling provided in the nursing consultation is one of the activities of the nurse. It consists of a dialogic care aimed at helping a patient to resolve a problem. The nurse must have knowledge and skills to provide an accurate diagnosis and support the patient and the family in solving the problem, as well as the ability to establish a sensible and effective communication. To increase efficiency and effectiveness, the telephone consultation requires a protocol supported by theoretical references and scientific evidence, as well as training to properly conduct it, since it is a distant relation, which hinders objectivity and effective communication and limits the use of all senses for an accurate evaluation.

This study is justified by the need to increase the production of knowledge about the frequency and behavior of the signs and symptoms related to the ABVD chemotherapy protocol in the Brazilian population, supporting the planning and implementation of nursing activities that can generate greater control of the therapeutic regimen. It is important to associate the nurse-run telephone consultations with the monitoring of signs and symptoms, considering the multiplicity and severity of these symptoms and the possibility of therapeutic failure, characterized by non-adherence to treatment, evasion, delays or interruptions due to worsening of clinical status.

Thus, the questions that guided the present study were: Which signs and symptoms are pres-
ent in patients with HL undergoing ABVD chemotherapy and receiving telephone consultations? What are the intensities and oscillations of the signs and symptoms in each chemotherapy cycle? The objectives were: to identify through telephone consultations the signs and symptoms presented by patients with Hodgkin’s Lymphoma undergoing ABVD chemotherapy and to compare severity scores of the signs and symptoms presented in the cycles of the protocol.

**Methods**

**Design, setting, population and ethical procedure of the study**

Descriptive, prospective, quantitative study. The study was conducted at the Lymphoma Outpatient Clinic of the Hospital São Paulo, Federal University of São Paulo, São Paulo State, Brazil. The non-probabilistic sample was composed by consecutive patients, according to the inclusion criteria: diagnosis of HL, being over 18 years old and predicted to start and end the ABVD chemotherapy regimen between November 2015 and February 2017. The exclusion criteria were: patients with previous chemotherapy treatment, in any regimen; not having access to a landline or mobile telephone.

The project was submitted and approved by the Research Ethics Committee of UNIFESP, and the data was collected after signing of the consent term.

**Study protocol**

Patients received the telephone number, provided their own and were oriented about the calls they would receive on D-1, D2, D14 and D16 of each cycle. The calls made on D-1 and D14 were aimed at reminding the patient about the chemotherapy session on the next day and evaluating anticipatory emesis. The calls made on D2 and D16, which were the scheduled calls, were aimed at evaluating the signs and symptoms presented. In cases where clinical assistance was necessary, other calls were made on the same day and subsequent days, which were the non-scheduled calls. The telephone counselling was conducted by the nurses in the study, both of them specialists in oncology nursing.

Three instruments were used for data collection: a) A socio-demographic and clinical questionnaire, with: age, gender, race, family income, level of education, work situation, oncologic history, cancer staging; b) An instrument to register the telephone calls, containing date, reports of signs and symptoms, interventions, outcomes; c) Guidelines for the standardization of interventions, according to the Oncology Nursing Society’s guidelines, available in Putting Evidence into Practice (PEP);(11) d) A symptom grading scale. The MD Anderson Symptom Inventory (MDASI-core) quantifies the severity of symptoms, including signs with the same nomenclature, in an analogic scale from 0 (not present) to 10 (worst possible perception). The MDASI-core, originally in English, was developed to facilitate the evaluation of signs and symptoms presented by oncologic patients, and its version in Portuguese has been validated.(12)

The MDASI-core has two parts: severity of symptoms, with 13 items, and symptoms that interfere in activities of daily living (ADLs), with 6 items. Given the possibility of patients reporting signs and symptoms not present in the MDASI-core, we also used the Common Terminology Criteria for Adverse Events CTCAE v4.0, developed by the National Cancer Institute (NCI, USA), which grades the symptoms from 1 (mild symptom) to 5 (death).(13) The design of the study is outlined in figure 1.

**Data analysis**

The relative proportions of socio-demographic and clinical variables were calculated to characterize the sample. Means were calculated to describe the intensity of the variation of symptoms in the different intervals between telephone calls (D-1, D2, D14 e D16). The non-parametric Wilcoxon test was used to compare the means of the symptoms before and after treatment (D-1 versus D2 and D14 versus D16) and, consequently, identify changes in the clinical status. Values of $p \leq 0.05$ were considered statistically significant. All statistical proce-
dures were conducted with the software Statistical Package for the Social Sciences (SPSS for Windows) version 19.0.

**Results**

Data from the present investigation were generated by 286 telephone calls with seven patients diagnosed with HL and submitted to 6 cycles of ABVD. Most of the participants were female (85.7%), white (57.1%), had 12 or more years of education, an average monthly family income of 1.7 minimum wages (approximately US $ 297/month), mean age of 29.8 years (SD 7.33), and a family history of oncology. Clinically, 71.5% of the patients were in an advanced stage and most had B symptoms and bulky mass, according to Ann Arbor staging with Cotswolds modifications.\(^{(14)}\) Absolute and percentage data are shown in table 1.

In the pre- and post-ABVD periods (D-1 and D16), 286 telephone calls were registered, of which 168 were scheduled and 118 were unscheduled, i.e. were made by the nurse (41.5%) for additional clinical evaluation or by the patients themselves (69; 58.5%).

All patients complied with the proposed chemotherapy regimen. There were no evasions nor delays in the days established for D1 or D15 in any of the cycles, from C1 to C6. In the 286 telephone calls, referral to the emergency room (ER) occurred 3 times, by evaluation of possible infection (n: 1) and metrorrhagia (n: 2). Throughout the patients’ telephone follow-up period, 1,870 symptomatic manifestations were reported. In the statistical analysis of the 19 signs/symptoms of the MDASI-core in 4 moments/cycles, 456 mean severities were calculated, and only the signs/symptoms with values higher than 5.0 were presented. During scheduled calls, the most prevalent complaints were fatigue, distress, lack of appetite, vomiting and nausea. Regarding the interference of symptoms on ADLs, the highest items were general activity, work and walking, followed by relations with other people,
Lack of appetite and pain

Lack of appetite was more present in the 4th cycle, when it reached the score of 8.86; between cycles, the mean was 5.29. There was a marked progression in the 4th cycle, in the period between before and after cytotoxic chemotherapy. These differences were statistically significant (p=0.02) (Figure 3).

Pain was reported by three patients, all with a bulky mediastinal mass. The maximum score reported was 7. Note that the incidence of pain is in cycle 1, with scores decreasing between D-1 and D16, until it reached zero (Figure 3).

Shortness of breath and fatigue

Shortness of breath was a constant complaint in the first and second cycles, with a mean of 5.7, decreas-

mood and enjoyment of life. In unscheduled calls, the most frequent complaints were lack of appetite and irregular menstruation. These data are displayed on table 2.

Subsequently, the results of each symptom with score greater than or equal to 5 are presented according to the scores (from 0 to 10), per chemotherapeutic cycle and comparing scores from C1 to C6, using linear logarithmic scales. To optimize information, two symptoms were grouped in each demonstrative figure.

**Nausea and vomiting**

These were the symptoms with highest severity, mainly in the fourth cycle, when they reached values of 9.1 and 9.4, respectively. Figure 2 show a marked progression of nausea and vomiting before and after chemotherapy. In cycle 1, nausea increased from 0 (D-1) to 6.9 (D2) and from 0.4 (D14) to 3.6 (D16). The differences in these means in the six cycles were statistically significant (p ≤ 0.02). Anticipatory nausea and vomiting were present only in the first cycle with means between 0.14 and 0.29.

**Lack of appetite and pain**

Lack of appetite was more present in the 4th cycle, when it reached the score of 8.86; between cycles, the mean was 5.29. There was a marked progression in the 4th cycle, in the period between before and after cytotoxic chemotherapy. These differences were statistically significant (p=0.02) (Figure 3). Pain was reported by three patients, all with a bulky mediastinal mass. The maximum score reported was 7. Note that the incidence of pain is in cycle 1, with scores decreasing between D-1 and D16, until it reached zero (Figure 3).

**Shortness of breath and fatigue**

Shortness of breath was a constant complaint in the first and second cycles, with a mean of 5.7, decreas-
ing to 0 after the 2nd cycle (p = 0.02). The patients with bulky mass had the highest scores. Fatigue was the only symptom that was present before C1 and lasted until the last cycle. In the first cycle, the mean of the symptom was 8.58, and it had values higher than 6 until C6. Despite the high scores, there was improvement between C1 and C6 (P = 0.03) (Figure 4).
Distress and mood alterations
Complaints of distress oscillated, with a peak of 9.29 on C4. D16 from C6 was the only moment of the evaluation that all patients reported absence of distress. The linear logarithmic graph correlated C1 (D-1 with a mean of 5.3) and C6 (with a score of 0 on D16) and generated a statistically significant result (p=0.02). Mood alterations were more frequent on C4 and oscillated on the other cycles. On C2 and C5, both on D16, the scores were close to zero. The comparison between C1 and C2 showed a statistically significant difference (p=0.02) (Figure 5).

Alterations in work activities, including domestic work
General activities presented higher values since C1 (mean of 6.57 on D-1), which progressed during treatment, reaching a mean score of 9.0 (p=0.03) on D16 of C6. Note that on C4 there was a sudden increase from 7.71 to 9.43. Regarding alterations in work activities, including domestic work, since C1 the mean was higher than 6.71, and it was even higher on the subsequent cycles, reaching 10.0 on D16 of C6, with a 85.7% rate of abstention from work (Figure 6).

The symptoms reported by the patients for which the Common Terminology Criteria for Adverse Events (CTCAE v4.0) was used were presented in a descriptive way.

Irregular menstruation and sexual activity
The female participants were in reproductive age, and 83.4% of them presented interruption of the menstrual cycle after the second cycle of the ABVD protocol. One patient (16.6%) reported metrorrhagia and was immediately referred to the emergency unit (ER). Regarding sexual activity, 100% of the patients had doubts, such as: whether they could have sexual activity during treatment and if they could engage in sexual activity without a condom.

Figure 4: Shortness of breath and fatigue according to the MDASI-core, on D-1; D2; D14 e D16, in 6 cycles of ABVD

Figure 5: Distress MDASI-core

Figure 6: Mood alterations MDASI-core
Mucositis
In the second and third months there were calls reporting mucositis in 20% of the sample, with scores between 1 and 2 (NCAE-CTC 4.0 Scale). Nursing interventions and dental follow-up occurred and the problem was solved after the 4th cycle.
Immediate vomiting – during ABVD administration
It was reported from the 1st to the 6th cycle in 30% of the sample, who had 3 to 5 episodes of vomiting during infusion, Score: 2 (NCAE-CTC 4.0 Scale).

Flu-Like syndrome
Due to the signs and symptoms reported, the patients were referred to the ER for differential diagnosis of infection, which was discarded.

Reaction in the intravenous site
Of the 7 patients, five (71.4%) started ABVD therapy in a peripheral vein. Chemical phlebitis represented 5.56% of all symptoms, categorized by CTCAE v4.0 as “injection site reaction” Score: 2. From C2-D16, 100% of patients were receiving ABVD via TI-CVC (totally implanted central venous catheter).

Discussion
HL is equally distributed between genders, despite the predominance of women in the present sample. This may be related to the favorable rates of therapeutic adherence, the verbalization of signs and symptoms and the propensity to seek help and follow guidelines, since there were no delays in the protocol nor evasions. A study has already shown that seeking care and adopting adaptive behaviors favorable to treatment are attitudes more common among women.\(^{(16)}\)

The expressive number of symptomatic complaints during telephone consultations might be related to the advanced stage of the disease (stages III and IV), which also explains the high scores of several symptoms. Unfortunately, diagnoses at advanced stages of cancer are common in Brazil, which is a result of the lack of structure and process in oncologic care in the SUS. Another analytic perspective for the advanced and polysymptomatic disease is the low health literacy of the Brazilian population, which is related not only to the level of education, but also to the ability to adopt health protective behaviors and to identify symptoms related to cancer and to other chronic or not chronic diseases.\(^{(17)}\)

Clinical treatment for cancer is known to produce several symptoms. The prevention and management of these symptoms are extremely important for maintaining the quality of life of the patients and for the continuity of the therapeutic regimen.\(^{(9)}\) A high emetogenic potential is observed in the composition of the ABVD protocol. In the present investigation this potential was present and elevated from C1 to C6, and it was the main factor for abstention from work during treatment, followed by the symptom of nausea/vomiting.

ABVD chemotherapy is classified, in specialized literature, as having a risk greater than 90% for nausea and vomiting. Regarding the management of nausea and vomiting, the guidelines of the American Society of Clinical Oncology – ASCO (USA) recommend the combination of four drugs, one of which is neurokinin 1 (NK\(_1\) - Aprepitant), which unfortunately is not available at the studied institution.\(^{(18)}\)

Unbalanced nutrition is a risk among these patients due to the loss of appetite and persistent nausea and vomiting. According to the national consensus on oncology nutrition, protein-calorie malnutrition among cancer patients is related to the immunoinflammatory response that increases metabolism, generating a hypercatabolic state due to the acute trauma of the malignant neoplasia. Corroborating this, some patients complained of mucositis, which is considered one of the most common oral complications in cancer patients, resulting from the toxicity of many chemotherapies which can cause local and systemic infections, which should be early diagnosed and treated.\(^{(9,19)}\) It could be observed that, in general, gastrointestinal complaints remained frequent after chemotherapy, but had a progressive decrease until one day before the next session (D12 and D14).

The complaints of shortness of breath and pain were present in patients with bulky mediastinal mass, defined as tumor >10 cm. Both symptoms are associated with tumor growth capable of compressing intrathoracic structures. The chemosensitivity of the HL is the reason for disappearance of symptoms at the end of the second cycle.\(^{(2,6)}\)
Fatigue was the only symptom persistent throughout the treatment. Studies have shown that it may continue to be a complaint among HL survivors for years, regardless of duration of the disease and time since the end of treatment. An accurate evaluation of the patient with fatigue during and after treatment is necessary for the identification of other complications that may aggravate the condition, such as pulmonary toxicity and cardiotoxicity, caused by the drugs bleomycin and dacarbazine, present in the protocol. Thus, up to several years after the end of treatment, continuous surveillance should be conducted, with evaluation of less specific symptoms such as weariness, fatigue and functional limitations in daily activities, along with medical follow-up examinations.

Flu-like syndrome complaints and severe menstrual alterations such as metrorrhagia were referred to a primary care unit for a differential evaluation of other diseases related to immunosuppression and thrombocytopenia. Early identification of risks and referral to specialized care were essential for an efficient outcome, without compromising the therapeutic regimen.

Sexual activity generated doubts among all patients of the study, and the questions occurred after the second cycle of chemotherapy. This can be related to the establishment of an affective bond with the nurse, demonstrating the lack of dialogue on this basic human need by the interdisciplinary team before the start of chemotherapy. The difficulties demonstrated by health professionals and patients in establishing an appropriate dialogue about sexuality in cancer care have been evidenced by studies, which emphasize the urgent need to adopt interventions capable of suppressing communication failures, which include telephone consultations.

As for the psychosocial symptoms, high scores were observed in C1 and C4, coinciding or not with aggravations of physical symptoms. The immediate acceptance to participate in the telephone consultations, the easiness to obtain answers during the application of the instruments and the number of unscheduled calls made by the patients showed their appreciation of the opportunity for dialogue with the nurse. In the current paradigm, patients are invited to participate actively in the decision-making process and must be supported to do so, finding ways to express concerns, fears and uncertainties arising from diagnosis and treatment, as well as receiving adequate care.

The limitations of the study are related to the reduced sample size, due to the low prevalence of the diagnosis compared to other oncological diseases. Another limitation is the restriction of the objectives of the study to the prevalence and severity of symptoms. The results of the present investigation indicated that patients were poly-symptomatic during the period of chemotherapy for LH, using the ABVD protocol, and that several care demands can be properly guided by the nurse duly qualified to practice advanced nursing, demonstrating the possibility of expanding the research.

Conclusion

The most prevalent symptoms were fatigue, distress, lack of appetite, vomiting and nausea. It was possible to evaluate the oscillations of the severity of the symptoms during the 6 cycles of the ABVD protocol, and the symptoms that demonstrated statistically significant oscillations were: nausea and vomiting, when comparing symptoms of C1 to C6, one day before and one day after chemotherapy, and lack of appetite on C3 and C4. The interference of symptoms in activities of daily living were statistically significant in relation to distress and enjoyment of life, mainly compromised in periods of greater physical symptoms. The nurse-run telephone consultation was demonstrated to be an important strategy for an effective control of the therapeutic regimen, allowing an early identification and management of signs and symptoms, with actions concomitant with complaints.

Collaborations

Louzada KRS, Brevidelli MM, Baiocchi O and Domenico EBL contributed to the study design,
analysis and interpretation of data, article writing, critical review of the intellectual content and approval of the final version to be published.

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