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Better compliance with the guidelines on hand-foot syndrome in patients treated with capecitabine in colorectal and breast cancer as a result of nursing education

Zastosowanie się do wytycznych postępowania z zespołem ręka-stopa u pacjentów leczonych kapecytabiną z powodu raka jelita grubego, odbyticy i piersi jako wynik edukacji prowadzonej przez pielęgniarki

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Aim: The aim of this paper is to test nursing educational intervention as a method of managing with hand-foot syndrome in patients treated with capecitabine in an Eastern European setting. **Design and Methods:** 43 females and 49 males with colorectal and breast cancer and were treated with capecitabine monotherapy or polychemotherapy with completion of at least one cycle were enrolled for this trial in the Department of Oncology University Hospital in Krakow, between January 2011 and December 2014. **Results:** Patients who were in contact with their oncology nurses and followed the recommendations had a fiftyfold lower risk of developing hand-foot syndrome G2 or G3. **Conclusions:** Our data confirmed the role of oncology nurses in patient education process during the home-based therapies in Poland.

Cel: Celem niniejszego artykułu jest sprawdzenie edukowania przez pielęgniarki jako metody interwencyjnej w postępowaniu z zespołem ręka-stopa u pacjentów leczonych kapecytabiną w obszarze Europy Wschodniej. **Materiał i metoda:** 43 kobiety i 49 mężczyzn chorych na raka jelita grubego, odbyticy i piersi leczonych kapecytabiną w monoterapii lub polichemioterapii z zakończonym przynajmniej jednym cyklem chemioterapii zostało włączonych do badania w Oddziale Klicznym Onkologii Szpitala Uniwersyteckiego w Krakowie w okresie od stycznia 2011 do grudnia 2014 roku. **Wyniki:** Pacjenci, którzy byli w kontakcie z pielęgniarką onkologiczną i postępowali zgodnie z jej zaleceniami mieli 50-krotnie mniejsze ryzyko wystąpienia zespołu ręka-stopa w stopniu zaawansowania G2 lub G3. **Wnioski:** Nasze wyniki potwierdzają rolę pielęgniarki onkologicznej w procesie edukacji pacjenta w trakcie leczenia onkologicznego w warunkach domowych w Polsce.

Introduction

It is a well-known fact that both oncologists and oncology nurses have to continue education to boarden and update their specialist knowledge of new systemic treatment and treatment-related side effects [1,2]. It is so crucial especially for active home-based therapies with capecitabine, vinorelbine oral, sunitinib, etc. This kind of treatment requires a new type of patient education including prevention and management of toxicities. Oncology teams must inform their patients about the dosage, indications, contraindications, adverse events and methods preventing side effects of the anticancer medicines [1]. Active-home therapy requires the preparation of the patient information kit, including prescription guidelines, diary cards and support kits, etc. about therapy and related- side effects [2-4].

Capecitabine is an anticancer drug administered in patients with colorectal and

breast cancer. Taken orally capecitabine reduces a number of the hospitalizations due to replacement of 5Fu prolonged infusions, overcoming a risk of cytotoxic drug extravasation, and in consequence, tissue damage [5]. Unfortunately, 40% of patients or even more required modified therapy due to serious toxicity [6]. Palmar-plantar erythrodysesthesia (PPE) or hand-foot syndrome (HFS) and diarrhoea are the most common toxic effects of capecitabine [7,8]. The initial symptoms of PPE are dysesthesia and erythema localized on the palms of the hands, fingers and soles of the feet. Pain, dryness, desquamation, ulceration and oedema are more advanced symptoms and occur mainly on the palms of the hands [8,9]. It is the most common dose-limiting toxicity and the reason for the interruption of chemotherapy administration or a prolonged dose reduction. Therefore, it is very important to continuously control levels of toxicity in

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patients treated with capecitabine.

In Poland, oncologists are concurrently oncology educators. Performing these duties by the oncology nurse instead of the oncologist is our own experience concerning compliance with Gresset's et al. guidelines on PPE in patients treated with capecitabine, including nursing education and intervention is presented in this paper [10].

Design And Methods

The aim of this study was to estimate how nursing educational intervention is in compliance with the guidelines of hand-foot syndrome prevention in patients with colorectal and breast cancer. A total of 92 patients (43 females and 49 males) were enrolled for this trial in the Department of Oncology University Hospital in Krakow, Poland, between January 2011 and December 2014. The inclusion criteria for the study were as follows:

1. histological confirmation of breast or colorectal or small bowel cancer,
2. undergoing capecitabine monotherapy or polychemotherapy with completion of at least one cycle,
3. minimum age of 18 years,
4. Eastern Cooperative Oncology Group (ECOG) performance status of 2 or less,
5. signed informed consent.

The study was conducted with omitting the randomisation. All patients who started capecitabine in the period of time (between 2011 and 2014) were educated by the oncology nurse. Nursing consultation was defined as a detailed explanation about the rationale for the use of capecitabine as well as other details of the treatment regimen such as dosage, timing of doses during the day and in relation to food intake, and managing missed doses. This consultation included the prevention, recognition and management of treatment-related adverse events.

Capecitabine in monotherapy was administered at 2500 mg/m²/day in two daily doses for two weeks, followed by one week of rest. In the case of polychemotherapy, capecitabine dose was decreased at 2000 mg/m²/day in two daily doses for two weeks with one week of rest.

This treatment was repeated every 21 days for 8 cycles (24 weeks) until disease recurrence/progression. In the case of severe toxicity or the patient's consent to withdrawal the treatment was also terminated. Every patient was clinically evaluated for adverse events (especially hand-foot syndrome) by oncologist every three weeks. Hand-foot syndrome, as well as other side effects were graded according to CTCAE v 4.0 (Common Terminology Criteria for Adverse Events). Definitions of plantar-palmar erythrodysesthesia syndrome grades are shown in table I. Physical examination and blood lab tests were conducted before starting each cycle of therapy. Patients' characteristics are presented in table II. Oncology nurses underwent training concerning the potential side effects of capecitabine and the management with the toxicity before starting this trial. At the pre-treatment consultation every patient was educated by the oncology nurse using a booklet with information about capecitabine.

Table I

Palmar-plantar erythrodysesthesia syndrome grade according to CTCAE v 4.0 criteria.

Stopniowanie nasilenia zespołu dłoniowo-grzbietowej erytrodysestezji według kryteriów CTCAE wersja 4.0.

grade	definition
G1	minimal skin changes or dermatitis (e.g., erythema, edema, or hyperkeratosis) without pain
G2	skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain; limiting instrumental activities daily living
G3	severe skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain; limiting self care activities of daily living

Table II

Patients' characteristics.

Charakterystyka pacjentów.

Characteristics	Patients number = 92 (%)
diagnosis: breast cancer rectal cancer colon cancer small bowel cancer	 22 (24) 10 (11) 59 (64) 1 (1)
gender: females males	 43 (47) 49 (53)
place of residence: town village	 52 (57) 40 (43)
education: primary technical college university	 15 (16) 18 (20) 42 (46) 17 (18)
aim of treatment: adjuvant treatment palliative treatment	 26 (28) 66 (72)
type of treatment: monochemotherapy polychemotherapy	 28 (30) 64 (70)
compliance: lack of cooperation with patient no contact with patient, but patient put the changes on his own patient had contact, but did not follow the recommendations patient had contact and followed the recommendations	 9 (10) 15 (16) 37 (40) 31 (34)
Nursing consultation	48 (52)
HFS in 1st cycle, grade: 1	 4 (4)
HFS in 2nd cycle, grade: 1 2 3 1-3	 27 (29) 7 (8) 2 (2) 36 (39)
HFS in 3rd cycle, grade: 1 2 3 1-3	 27 (29) 36 (39) 2 (2) 65 (71)
HFS in 4th cycle, grade: 1 2 3 1-3	 15 (16) 26 (28) 9 (10) 50 (54)
HFS in 5th cycle, grade: 1 2 3 1-3	 12 (13) 16 (17) 13 (14) 45 (49)
HFS in 6th cycle, grade: 1 2 3 1-3	 9 (10) 8 (9) 5 (5) 22 (24)
HFS in 7th cycle, grade: 1 2 3 1-3	 3 (3) 2 (2) 2 (2) 7 (8)
HFS within 8th cycles, grade: 1 2 3 1-3	 17 (18) 45 (49) 27 (29) 89 (97)
Dose reduction due to skin toxicity	22 (24)
Treatment completion due to skin toxicity	9 (10)

The patients received a log to record side effects they experienced. Moreover, they were warned to take special care of their affected areas and they obtained practical advice on preventative and management techniques for PPE. Every patient was provided with the oncology nurse's phone number. Patients were able to get advice whether to stop taking their medication, to reduce the capecitabine dose or to come earlier before the fixed date of the appointment.

A group defined as „the patients had contact and followed the recommendations” followed precisely the nursing consultations. „The patients had contact and did not follow the recommendations” meant that the patients told the doctor that they had ignored the nursing instructions.

Although treatment with capecitabine in colorectal and breast cancer patients is standard therapy in Poland, the study was approved by a local institutional ethical committee in order to conduct the oncology nurse education and interventions.

Qualitative variables are reported as the number and percentage of subjects in each category. A comparison between the groups was carried out using a chi-squared test. The multiple logistic regression was used to estimate odds ratios (OR) with 95% confidence intervals (95%CI). The results were considered statistically significant at P values of ≤ 0.05 .

Results

Median age was 62.8 years \pm 10.5 years (range: 31-85 years). Colon cancer was diagnosed in 64% of patients. More than half of the patients lived in towns and had a college or university education. Gender, education and place of residence of the patients were not related to skin toxicity. Hand-foot syndrome G3 occurred more frequently in older patients (mean age: 67.3 \pm 9.1 versus 60.9 \pm 10.5 years; $p=0.007$). Dose reduction was associated with older age of the patients (mean age: 68.4 \pm 9.5 versus 61.1 \pm 10.2 years; $p=0.004$). Results are presented in table III. Hand-foot syndrome G3 occurred in 27 patients. Twenty two out of 27 patients required dose reduction. In this subgroup, 17 out of 22 patients had no nursing consultation and 5 patients had a nursing consultation ($p=0.099$). Those patients who were in contact with their oncology nurses and followed the recommendations had fiftyfold lower risk of developing hand-foot syndrome G2 or G3 as compared to the patients who did not cooperate. Odds ratio (OR) for these two groups is 0.02. All data are collected in tables IV and V. In the whole group (N=92) the results for the multivariate logistic regression for dependent variate dose reduction are presented in table VI. The patient who had contact with oncology nurses and followed the recommendations did not require dose modification/reduction.

Discussion

A well-educated oncology nurse or an oncologist is able to explain to the patient the potential adverse events and the possibilities of preventing them [1,3,4,6-9,11-13]. Home-based therapy imposes on patient

Table III
Comparison between two nominal variates (chi-squared test).
Porównanie dwóch zmiennych (chi-kwadrat test).

dependent variate	„explaining” variate:	p
completion treatment due to skin toxicity (N=9)	aim of treatment: palliative treatment (N=9, 14% out of 66 palliative treated) adjuvant treatment (N=0, 0% out of 26)	0.043
	compliance: lack of cooperation with patient (N=3, 33% out of 9) no contact with patient, but patient put the changes on his own (N=4, 27% out of 15) patient had contact, but did not follow the recommendations (N=2, 5% out of 37) patient had contact and followed the recommendations (N=0, 0% out of 31)	0.002
dose reduction due to skin toxicity (N=22)	diagnosis: breast cancer (N=7, 32% out of 22) rectal cancer (N=5, 50% out of 10) colon cancer and small bowel cancer (N=10, 17% out of 60)	0.044
	kind of treatment: monotherapy (N=11, 39% out of 28) polytherapy (N=11, 17% out of 64)	0.022
	compliance: lack of cooperation with patient (N=4, 44% out of 9) no contact with patient, but patient put the changes on his own (N=9, 60% out of 15) patient had contact, but did not follow the recommendations (N=9, 24% out of 37) patient had contact and followed the recommendations (N=0, 0% out of 31)	<0.001
	nursing consultation: NO (N=17, 39% out of 44) YES (N=5, 10% out of 48)	0.002
HFS >G1 within treatment (N=72)	aim of treatment: palliative treatment (N=56, 85% out of 66) adjuvant treatment (N=16, 62% out of 26)	0.015
	compliance: lack of cooperation with patient (N=9, 100% out of 9) no contact with patient, but patient put the changes on his own (N=14, 93% out of 15) patient had contact, but did not follow the recommendations (N=35, 95% out of 37) patient had contact and followed the recommendations (N=14, 45% out of 31)	<0.001
HFS G3 within treatment (N=27)	aim of treatment: palliative treatment (N=24, 36% out of 66) adjuvant treatment (N=3, 12% out of 26)	0.019
	type of treatment: monotherapy (N=14, 50% out of 28) polytherapy (N=13, 20% out of 64)	0.004
	compliance: lack of cooperation with patient (N=6, 67% out of 9) no contact with patient, but patient put the changes on his own (N=9, 60% out of 15) patient had contact, but did not follow the recommendations (N=11, 29% out of 37) patient had contact and followed the recommendations (N=1, 3% out of 31)	<0.001
	nursing consultation: NO (N=19, 43% out of 44) YES (N=8, 17% out of 48)	0.005

involvement and compliance with the systemic treatment and management in the case of side effects. Compliance, which is also called adherence is defined as „the degree or extent conformity to the recommendations about day-to-day treatment by the provider with respect to the timing, dosage, and frequency” [14]. It is especially important for this kind of therapy because it determines the dose-intensity of the treatment, and in consequence, treatment efficacy and toxicity [15]. Good compliance correlates with the good quality of life in patients treated with capecitabine [16]. Also according to our data the patients who were in contact with their oncological nurse and followed her consultations did not require dose reduction. Contact with the oncology nurse influenced compliance. The patient must be aware that temporary interruptions or dose modifications ordered by physicians do not reduce the overall efficacy of capecitabine [9,11,17]. Furthermore, the patient should have good

educational skills because he is included in a treatment team and his activity may be critical for the final outcome [2,11,18]. Constant communication between the patient and the hospital oncology team (oncology nurse and oncologist) has a key role in the cooperation [2,11,17,19]. Our study is consistent with the opinion of other authors.

In our trial the patients - who did not follow the recommendations and had hand-foot syndrome G3 - more often had a technical education and lived in a town. These data were statistically significant. „A kind of philosophy” or „a kind of thinking” of this patients group may be the main reason for this correlation. Such observation has not been elicited yet, but it requires further studies on the bigger groups of patients.

Our patients had difficulties in grading the PPE symptoms and coordinating the grade with the appropriate acting. Therefore, the oncology nurses should have more frequent and easy contact with their patients.

Table IV
Hand-foot syndrome > G1.
Zespół ręka-stopa > G1.

Variate		
	OR (95% CI)	p
compliance: lack of cooperation/patient was not in contact*	1	-
patient had contact, but did not follow the recommendations	0.50 (0.03-7.32)	0.6
patient had contact and followed the recommendations	0.020 (0.0005-0.19)	0.002
nursing consultation	4.03 (0.71-22.80)	0.1
female	1.66 (0.26-10.55)	0.6
education: primary	1	-
technical	0.26 (0.01-5.40)	0.4
college	0.18 (0.01-2.40)	0.2
university	0.22 (0.01-4.17)	0.3
age	0.93 (0.85-1.01)	0.09
aim of treatment: palliative treatment	1	-
adjuvant treatment	0.43 (0.07-2.46)	0.3
place of residence: village	1	-
town	0.86 (0.16-4.61)	0.9
diagnosis: colorectal cancer	1	-
breast cancer	0.60 (0.06-5.57)	0.6

* Two groups are counted together (because they were not enough numerous, 9 and 15 patients, respectively).

Table VI
Results of multivariate logistic regression in the whole group (N=92) (irrespective of HFS grade).

Wyniki wieloczynnikowej regresji logistycznej w całkowitej grupie pacjentów (N=92) (bez względu na nasilenie zespołu ręka-stopa).

Variate		
	OR (95% CI)	p
compliance: lack of cooperation/patient was not in contact	1	-
patient had contact, but did not follow the recommendations/ patient had contact and followed the recommendations *	0.06 (0.01-0.34)	0.001
nursing consultation	0.20 (0.04-0.98)	0.043
female	0.21 (0.03-1.48)	0.1
education: primary	1	-
technical	0.10 (0.009-1.24)	0.069
college	0.57 (0.08-3.99)	0.6
university	1.31 (0.10-16.68)	0.8
age	1.14 (1.03-1.26)	0.012
aim of treatment: palliative treatment	1	-
adjuvant treatment	0.26 (0.04-1.80)	0.2
place of residence: village	1	-
town	9.03 (1.55-52.59)	0.013
diagnosis: colorectal cancer	1	-
breast cancer	5.44 (0.53-55.47)	0.1

* None of the patients who followed the recommendations did not require dose reduction (but only one patient out of this group had hand-foot syndrome G3).

The main limitation of the study is a small number of the participants because it was conducted in a single centre. According

to our knowledge, it is the first publication on compliance with capecitabine from an Eastern European country with a healthcare

Table V
Hand- foot syndrome G3.
Zespół ręka- stopa G3.

Variate		
	OR (95% CI)	p
compliance: lack of cooperation/patient was not in contact	1	-
patient had contact, but did not follow the recommendations	0.041 (0.005-0.34)	0.003
patient had contact and followed the recommendations	0.007 (0.0004-0.15)	0.001
nursing consultation	0.40 (0.07-2.27)	0.3
female	0.20 (0.02-1.72)	0.1
education: primary	1	-
technical	0.05 (0.004-0.73)	0.026
college	0.72 (0.09-5.85)	0.8
university	1.72 (0.11-26.47)	0.7
age	1.12 (0.99-1.26)	0.059
aim of treatment: palliative treatment	1	-
adjuvant treatment	0.13 (0.02-1.09)	0.057
place of residence: village	1	-
town	16.27 (2.34-113.1)	0.004
diagnosis: colorectal cancer	1	-
breast cancer	4.66 (0.38-57.32)	0.2

system based on the insurance model.

Nowadays role of the oncology nurses in the patients education process during the home-based therapies is being established. Awareness that a well-educated nurse gives better support for her patients is increasing. On the other hand, well-informed patients may present better compliance with the anticancer treatment, which may further influence on the quality of life and survival.

Conclusion

Our data confirmed the role of oncology nurses in the patients education process during the home-based therapies in Poland.

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