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A comparative study of prophylactic antiemetic treatment in cancer patients receiving radiotherapy

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Summary

Purpose: *Gastrointestinal side effects can often complicate radiotherapy (RT) in cancer patients. This work presents results of a retrospective open label study aiming to evaluate the optimum prophylactic treatment for nausea and vomiting in patients receiving fractionated radical or palliative RT.*

Methods: *576 cancer patients were allocated in 5 treatment groups: 120 patients received tropisetron, 129 tropisetron plus dexamethasone, 101 metochlopramide, 119 dexamethasone, and 107 received metochlopramide plus dexamethasone. To determine the optimum antiemetic prophylactic treatment, nausea and vomiting were evaluated at baseline, 24 and 72 h after the initiation of RT, and at the end of every week during RT. Adverse effects, Eastern Cooperative Oncology Group (ECOG) performance status (PS), and the intensity of nausea and vomiting were recorded.*

Results: *Statistically significant differences in incidence and intensity of nausea and vomiting were found among the 5 antiemetic treatment groups from the 1st till the 5th week of the RT. Tropisetron + dexamethasone group had significantly reduced odds for nausea and vomiting, and significantly less severe nausea and vomiting than any other treatment group. Factors significantly associated with increased ECOG PS were palliative RT, dose fraction >3Gy, field size >200 cm^2, and treatment with metochlopramide, metochlopramide+dexamethasone and dexamethasone.*

Conclusion: *Patients receiving prophylactic antiemetic treatment with tropisetron+dexamethasone completed RT with lower intensity of nausea and vomiting and lower ECOG PS scores compared to groups that received other antiemetic treatments.*

Key words: cancer, emesis, prophylactic antiemetic, radiotherapy

Introduction

Surgery, RT and chemotherapy are the main modalities of cancer treatment, with RT and surgery, in contrast to chemotherapy, being essentially local treatments employed for local disease control. The therapeutic benefit is however influenced by the degree of side effects [1,2]. Gastrointestinal side effects can complicate radical or palliative RT with nausea and vomiting being the most distressing side effects for the patient, negatively impacting the quality of life (QoL) [3,4].

Evidence from a study with 1387 patients from 5 countries receiving fractionated RT between thorax and pelvis, with a mild to moderate risk for emesis, showed that approximately 40% of the patients with no antiemetic prophylaxis experienced emesis or nausea [5]. In their study, Kirkbridge et al. focused on patients receiving fractionated RT to the upper abdomen combined with oral intake of either dexamethasone (2 mg × 3/day) or placebo during the first week of RT. Complete protection from Radiation Induced Nausea Vomiting (RINV) was significantly better in the dexamethasone group with acceptable RINV but with no overall positive effect on global QoL [6]. The Italian Group for Antiemetic Research in Radiotherapy (IGARR) in a double-blind randomized clinical trial in patients undergoing fractionated RT to the upper abdomen compared prophylactic ondansetron plus dexamethasone vs. placebo. Vomiting was reported in 30% and 40% and

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nausea in 57% and 67% of cases, respectively. The 10% of control in the group treated with ondansetron plus dexamethasone was not statistically significant [7].

The irradiated site remains the most important prognostic factor used in clinical practice for defining the risk profile of the patients [7-9]. The emetogenic risk of RT is divided into 4 levels: high, moderate, low and minimal, with patients submitted to abdominal RT being at major risk of nausea and vomiting compared to those receiving treatment to the thorax, brain, head, neck and pelvis. The clinical pattern related to vomiting includes the latent period, the acute phase disturbances, and the recovery phase [10].

The purpose of the present study was to determine the optimal prophylactic treatment for nausea and vomiting in cancer patients receiving fractionated radical or palliative RT.

Methods

All patients included in this retrospective study received prophylactic antiemetic treatment. Inclusion criteria were: age ≥18 years; diagnosis of malignant disease undergoing fractionated RT (palliative or radical) at moderate or highly emetogenic areas. Exclusion criteria were: administration of rescue antiemetic treatment; concomitant chemotherapy or concomitant treatment with phenobarbital, rifampicin or phenylbutazone; bowel obstruction, hepatic or renal failure, electrolyte disorders, hypersensitivity to antiemetic treatment, prior history of high risk emetogenic RT or primary or secondary brain neoplasm causing signs or symptoms of increased intracranial pressure.

From January 1999 to April 2004, 1800 patients underwent RT in high and moderate emetogenic areas using 6MV linear accelerator, in the Radiotherapy Department of Areteion University Hospital in Athens, Greece. A total of 576 patients fulfilled the above mentioned criteria and were eligible for study inclusion.

Patients were divided into 5 groups, depending on the prophylactic antiemetic treatment administered. The first group included 120 patients that had received tropisetron 5 mg/daily p.o. (Trop group); the second included 129 patients that had received tropisetron 5 mg/daily plus dexamethasone 2 mg/daily, both p.o. (Trop+Dex group); the third included 101 patients that had received metochlopramide 20 mg/daily p.o. (Met group); the fourth included 119 patients that had received dexamethasone 2 mg/daily p.o. (Dex group) and the fifth included 107 patients that had received metochlopramide 20 mg /daily p.o. plus dexamethasone 2 mg / daily, both p.o. (Met+Dex group).

Each patient's medical history was recorded at baseline together with the findings of physical examination, including ECOG PS. All prophylactic antiemetic medications were administered one hour before each RT session. Data were collected on diary cards for all visits. To determine the efficacy of the antiemetic treatment two parameters were evaluated: nausea and vomiting.

The primary efficacy variable was the proportion of patients achieving control (complete control =no vomiting or nausea; partial control= 1- 4 events of vomiting and/or 1-12 h of nausea on any of the RT days; no control= 5 or more events of vomiting and/or more than 12 h of nausea on any of the days of treatment). The secondary efficacy variable included the incidence of nausea and vomiting. Intensity of nausea was graded on a 5-point scale (CTC, version 3.0) as follows: grade 0 = no nausea; grade 1 = loss of appetite without alteration in eating habits; grade 2 = oral intake decreased without significant weight loss, dehydration or malnutrition (i.v. fluids indicated < 24 h); grade 3= inadequate oral caloric or fluid intake (i.v. fluids, feeding tube, or total parenteral nutrition [TPN] indicated ≥24 h); grade 4= life–threatening condition; and grade 5 = death.

The intensity of vomiting was graded on the following 5-point scale (CTC, version 3.0): grade 0= no episode; grade 1 = 1 episode in 24 h; grade 2 = 2-5 episodes in 24 h (i.v. fluids indicated < 24 h); grade 3= ≥6 episodes in 24 h (i.v. fluids indicated); grade 4= life – threatening condition; and grade 5= death.

Patients recorded nausea, vomiting and other adverse effects such as constipation, diarrhea, headache, anorexia, fatigue, and extrapyramidal symptoms in a diary card. All adverse effects were coded from the Official Reference of Common Toxicity Criteria (CTC, version 3.0) Patient characteristics and RT intent (palliative or radical) and schedule were recorded to identify risk factors for radiation induced emesis (RIE). Nausea and vomiting were monitored at 24 and 72 h, and at the end of every week during RT. Palliative RT lasted 1-3 weeks, while radical RT lasted 1-6 weeks.

RT-related factors such as therapeutic intent (radical, palliative), site treated, dose per fraction (standard < 3 Gy vs. high ≥ 3 Gy), total dose, and field size (measured in cm^2 considering the largest field when more than one was used: small ≤ 200 cm^2, medium 201-400 cm^2), were studied in relation with their impact to emesis.

Statistical analysis

To assess the effect of potential risk factors on the incidence of nausea and vomiting, a univariate random effects logistic regression model was used. This model takes into account the longitudinal nature of the data. Factors found to be significant in the univariate model

were then used in a multivariate model.

For the intensity of nausea and vomiting, a random effects ordinal logistic regression model was used. This model was used in the incidence analytical procedure in order to identify the independent risk factors for the intensity of both nausea and vomiting. Univariate and multivariate random effects ordinal logistic regression was used for ECOG PS.

The statistical analysis was carried out in Stata v. 6 (College Station, TX, USA).

Results

The incidence rate of nausea was 311/576 (54%), while that of vomiting was 232/576 (40%). Two hundred and sixteen out of 576 patients (37.5%) were complete responders, i.e. had neither nausea nor vomiting.

The incidence of vomiting was related with the following risk factors: field size of RT, metastatic lesion and treatment intent. Concerning vomiting, the following risk factors were statistically significant: metastatic lesion, dose fraction, RT field size, site treated and treatment group (Table 1).

Multivariate analysis was performed aiming to identify whether any of the above risk factors were independently associated with the incidence of nausea and vomiting (Table 2). It was found that metastatic lesion and treatment with Trop+Dex, Met, Met+Dex and Dex were independently associated with the incidence of nausea. Specifically, patients with metastasis were almost 4 times more likely to have nausea than those without adjusted odds ratio (AOR): 3.76; 95% CI: 2.93 - 4.83; p

Table 1. Incidence of nausea and vomiting by risk factors

Risk factors	*Nausea*		*Univariate odds ratio (95% CI)*	*p-value*	*Vomiting*		*Univariate odds ratio (95% CI)*	*p-value*
	No n=265 (%)	*Yes n=311 (%)*			*No n=344 (%)*	*Yes n=232 (%)*		
Age (years)								
< 60	114 (43)	124 (40)	1.0		148 (43)	90 (39)	1.0	
≥ 60	151 (57)	187 (60)	1.14 (0.82-1.58)	0.44	196 (57)	142 (61)	1.19 (0.85-1.67)	0.31
Gender								
Male	134 (51)	163 (52)	1.0		170 (49)	127 (55)	1.0	
Female	131 (49)	148 (48)	0.93 (0.67-1.29)	0.66	174 (51)	105 (45)	0.81 (0.58-1.13)	0.21
Metastasis								
No	153 (58)	147 (47)	1.0		97 (57)	103 (44)	1.0	
Yes	112 (42)	164 (53)	1.52 (1.09-2.12)	0.012	147 (43)	129 (56)	1.68 (1.19-2.35)	0.002
Radiotherapy								
Radical	123 (46)	126 (41)	1.0		159 (46)	90 (39)	1.0	
Palliative	142 (54)	185 (59)	1.27 (0.91-1.77)	0.15	185 (54)	142 (61)	1.35 (0.96-1.90)	0.08
Dose fraction (Gy)								
< 3	145 (55)	152 (49)	1.0		191 (56)	106 (46)	1.0	
≥ 3	120 (45)	159 (51)	1.26 (0.91-1.75)	0.16	153 (44)	126 (54)	1.48 (1.06-2.07)	0.021
Field size (cm^2)								
< 200	234 (88)	253 (81)	1.0		303 (88)	184 (79)	1.0	
≥ 200	31 (12)	58 (19)	1.73 (1.08-2.77)	0.021	41 (12)	48 (21)	1.93 (1.22-3.03)	0.004
Site treated (radical)								
Stomach	28 (23)	40 (32)	1.0	0.06	41 (26)	27 (30)	1.0	0.03
Pancreas	38 (32)	23 (18)	0.42 (0.21-0.86)	0.02	47 (30)	14 (16)	0.45 (0.21-0.97)	0.04
Ovary	37 (31)	37 (29)	0.70 (0.36-1.36)	0.29	47 (30)	27 (30)	0.87 (0.44-1.72)	0.69
Lung	17 (14)	26 (21)	1.07 (0.49-2.33)	0.86	21 (13)	22 (44)	1.59 (0.74-3.44)	0.24
Site treated (palliative)								
Upper abdomen	52 (44)	53 (34)	1.0	0.09	68 (45)	37 (30)	1.0	0.021
Thorax	36 (31)	46 (29)	1.25 (0.70-2.24)	0.47	42 (28)	40 (32)	1.75 (0.97-3.15)	0.06
Brain	30 (25)	58 (37)	1.89 (1.05-3.40)	0.03	40 (27)	48 (38)	2.20 (1.23-3.94)	0.008
Side effects								
No	168 (64)	193 (62)	1.0	0.73	218 (64)	143 (62)	1.0	0.68
Yes	96 (36)	117 (38)	1.06 (0.75-1.49)	<0.01	125 (36)	88 (38)	1.07 (0.76-1.51)	<0.001
Treatment								
Trop	60 (23)	60 (19)	1.0		78 (23)	42 (18)	1.0	
Trop+Dex	85 (32)	44 (14)	0.52 (0.31-0.86)	0.011	107 (31)	22 (9)	0.38 (0.21-0.69)	0.001
Met	33 (12)	68 (22)	2.06 (1.19-3.56)	0.01	42 (12)	59 (25)	2.61 (1.51-4.50)	0.001
Met+Dex	44 (17)	63 (20)	1.43 (0.84-2.42)	0.18	52 (15)	55 (24)	1.96 (1.15-3.45)	0.013
Dex	43 (16)	76 (24)	1.76 (1.05-2.96)	0.03	65 (19)	54 (23)	1.54 (0.92-2.59)	0.10

For abbreviations see text

Table 2. Multivariate association among incidence of nausea, vomiting and risk factors

Risk factors	*Nausea*		*Vomiting*	
	Multivariate odds ratio (95% CI)	*p-value*	*Multivariate odds ratio (95% CI)*	*p-value*
Metastasis				
No	1.0		1.0	
Yes	3.76 (2.93-4.83)	< 0.001	2.96 (1.92-4.57)	< 0.001
Dose fraction (Gy)				
< 3			1.0	
≥ 3			1.40 (0.89-1.44)	0.12
Field size (cm^2)				
< 200	1.0		1.0	
≥ 200	1.10 (0.86-1.40)	0.44	1.14 (0.89-1.44)	0.27
Treatment		< 0.001		< 0.001
Trop	1.0		1.0	
Trop+Dex	0.58 (0.41-0.83)	0.003	0.66 (0.47-0.93)	0.02
Met	2.02 (1.39-2.94)	< 0.001	2.44 (1.67-3.56)	< 0.001
Met+Dex	1.42 (1.96-2.09)	0.07	1.88 (1.30-2.74)	0.001
Dex	1.77 (1.23-2.55)	0.002	1.89 (1.32-2.70)	< 0.001

For abbreviations see text

< 0.001). The risk factors independently associated with the incidence of vomiting were metastasis and treatment group. Patients with metastasis were almost 3 times more likely to suffer of vomiting than those without (AOR: 2.96; 95% CI: 1.92-4.57; p < 0.001).

A statistically significant difference was observed in the intensity of nausea and vomiting among the 5 treatment groups from the 1st to the 5th week of RT (Table 3). For the Trop group complete control of nausea and vomiting was observed in 60 (50%) and 78 patients (65%), respectively. For the Trop+Dex group complete control of nausea and vomiting was achieved in 85 (65.9%) and 107 patients (82.9%), respectively. Complete control of nausea and vomiting was recorded in 33 (32.7%) and 42 (41.5%) patients, respectively, in the Met group. In the Met+Dex group 44 patients (41%) achieved complete control of nausea and 52 (48.5%) complete control of vomiting. Finally, in the Dex group complete control of nausea and vomiting was found in 43 (36.1%) and 65 (54.6%) patients, respectively.

The univariate analysis concerning nausea and vomiting intensity and potential risk factors showed that the risk factor associated significantly with nausea and vomiting intensity was treatment group (Table 4). The mean profiles of ECOG PS for each treatment group are shown in Table 5.

Table 3. Intensity of nausea and vomiting by treatment group (mean ±SD)

Time	*Nausea*					*Vomiting*				
	TD	*T*	*M*	*MD*	*D*	*TD*	*PT*	*M*	*MD*	*D*
Baseline	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0
n	129	120	101	107	118	129	119	101	107	119
24 hours	0±0	0.02±0.12	0.009±0.09	0±0	0.008±0.09	0±0	0.008±0.09	0±0	0±0	0±0
n	129	120	101	107	119	129	120	101	107	119
72 hours	0.08±0.3	0.12±0.38	0.15±0.52	0.05±0.23	0.08±0.35	0.03±0.2	0.13±0.5	0.08±0.33	0.02±0.1	0.07±0.3
n	129	120	100	107	119	129	120	100	107	119
1st week	0.40±0.8	0.40±0.7	1.17±1.1	0.84±0.93	0.82±0.99	0.31±0.8	0.41±0.9	1.24±1.4	0.85±1.2	0.78±1.3
n	128	120	99	107	119	128	120	100	107	119
2nd week	0.35±0.7	0.43±0.7	0.95±1.02	0.79±0.91	0.86±0.88	0.22±0.7	0.33±0.7	0.95±1.3	0.79±1.0	0.62±0.9
n	119	107	63	91	97	119	107	64	87	97
3rd week	0.14±0.46	0.6±0.9	0.66±0.76	0.82±0.9	0.71±0.7	0.10±0.5	0.24±0.8	0.7±1.01	0.85±1.1	0.58±0.8
n	60	30	40	41	66	65	61	30	40	41
4th week	0.09±0.4	0.41±0.6	0.5±0.7	0.69±0.82	0.73±0.76	0±0	0.09±0.3	0.5±0.7	0.6±0.7	0.6±0.8
n	51	44	24	36	37	51	44	24	36	37
5th week	0.19±0.4	0.56±0.68	0.46±0.65	0.66±0.79	0.73±0.77	0±0	0.18±0.4	0.33±0.5	0.58±0.7	0.6±0.8
n	47	37	24	36	37	47	37	24	36	37
6th week	0.15±0.4	0.8±0.76	0.66±0.81	0.75±0.88	0.28±0.48	0±0	0.36±0.7	0.5±0.54	1.0±0.9	0.28±0.48
n	13	25	6	8	7	13	25	6	8	7

TD: tropisetron+dexamethasone, T: tropisetron, M: metochlopramide, MD: metochoclopramide+dexamethasone; D: dexamethasone, n: number of patients, SD: standard deviation

Table 4. Intensity of nausea and vomiting by risk factor

Risk factors	*Nausea*		*Vomiting*	
	Univariate estimated coefficient (95% CI)	*p-value*	*Univariate estimated coefficient (95% CI)*	*p-value*
Age (years)		0.84		0.88
< 60	0.0		0.0	
≥ 60	0.02 (-0.21, 0.26)		0.02 (-0.27, 0.31)	
Gender		0.61		0.19
Male	0.0		0.0	
Female	-0.06 (-0.29, 0.17)		-0.18 (-0.47, 0.09)	
Metastasis		0.57		0.67
No	0.0		0.0	
Yes	0.06 (-0.16, 0.28)		0.06 (-0.21, 0.33)	
Therapy		0.45		0.38
Radical	0.0		0.0	
Palliative	-0.08 (-0.31, 0.14)		-0.12 (-0.39, 0.15)	
Dose fraction (Gy)		0.51		0.67
< 3	0.0		0.0	
≥ 3	-0.07 (-0.29, 0.15)		-0.06 (-0.33, 0.21)	
Field size (cm^2)		0.94		0.41
< 200	0.0		0.0	
≥ 200	0.01 (-0.26, 0.29)		0.13 (-0.18, 0.45)	
Site treated (radical)		0.14		0.08
Stomach	0.0		0.0	
Pancreas	-0.49 (-1.03, 0.05)	0.07	-0.33 (-1.02, 0.36)	0.35
Ovary	-0.03 (-0.48, 0.42)	0.88	0.08 (-0.49, 0.66)	0.77
Lung	0.20 (-0.29, 0.69)	0.42	0.54 (-0.05, 1.13)	0.07
Site treated (palliative)		0.66		0.31
Upper abdomen	0.0		0.0	
Thorax	0.13 (-0.25, 0.51)	0.51	0.26 (-0.19, 0.71)	0.26
Brain	0.15 (-0.19, 0.51)	0.38	0.32 (-0.10, 0.75)	0.14
Side effects		0.99		0.55
No	0.0		0.0	
Yes	0.001 (-0.23, 0.24)		0.09 (-0.20, 0.38)	
Treatment		<0.001		<0.001
Trop	0.0		0.0	
Trop+Dex	-0.58 (-0.97, -0.20)	0.003	-0.79 (-1.32, -0.27)	0.003
Met	0.34 (-0.0002, 0.69)	0.05	0.70 (0.28, 1.11)	0.001
Met+Dex	0.38 (0.02, 0.75)	0.04	0.84 (0.41, 1.26)	<0.001
Dex	0.42 (0.09, 0.75)	0.012	0.65 (0.24, 1.07)	0.002

For abbreviations see text

Table 5. ECOG performance status by treatment group over time (mean±SD)

Time	*PT*	*TD*	*M*	*MD*	*D*
Baseline	1.27±0.74	1.35±0.68	1.58±0.69	1.77±0.5	1.53±0.53
n	120	129	101	107	118
24 hours	1.27±0.74	1.35±0.68	1.58±0.69	1.77±0.5	1.53±0.53
n	120	129	101	107	119
72 hours	1.27±0.74	1.35±0.68	1.57±0.68	1.77±0.5	1.54±0.54
n	120	129	100	107	119
1st week	1.27±0.74	1.36±0.68	1.59±0.67	1.78±0.5	1.58±0.62
n	120	128	100	107	119
2nd week	1.27±0.74	1.32±0.68	1.42±0.68	1.78±0.5	1.42±0.52
n	107	119	64	88	97
3rd week	1.00±0.74	0.95±0.62	1.03±0.62	1.62±0.5	1.02±0.53
n	60	65	29	40	41
4th week	0.72±0.55	0.86±0.5	0.96±0.55	1.62±0.5	0.97±0.2
n	43	51	24	36	37
5th week	0.81±0.5	0.89±0.48	0.96±0.55	1.58±0.55	1.0±0.0
n	37	46	24	36	37
6th week	0.88±0.4	0.77±0.6	1.33±0.51	1.62±0.52	1.0±0.0
n	25	13	6	8	7

For abbreviations see footnote of Table 3

The univariate analysis concerning ECOG PS and risk factors has shown that the risk factors significantly associated with increased ECOG PS were older age ($p < 0.001$), gender ($p<0.005$), metastasis ($p < 0.001$), palliative RT ($p < 0.001$), dose fraction ≥ 3 Gy ($p < 0.001$), and field size ≥ 200 cm^2 ($p < 0.001$) (Table 6).

The multivariate associations of those risk factors with ECOC PS are presented in Table 7. Field size ≥ 200 cm^2 and kind of antiemetic treatment were independently associated with ECOG PS. More specifically, field size ≥ 200 cm^2 was associated with a significantly higher ECOG PS compared with field size < 200 cm^2. Met and Met+Dex groups were independently associated with higher ECOG PS than Trop ($p < 0.001$ and 0.001, respectively).

Table 6. Univariate association between ECOG performance status and risk factors

Risk factors	*Univariate estimated coefficient (95%CI)*	*p-value*
Age (years)		
< 60	0.0	
≥ 60	0.85 (0.52-1.18)	< 0.001
Gender		
Male	0.0	
Female	-0.77 (-1.10, -0.44)	< 0.001
Metastasis		
No	0.0	
Yes	2.82 (2.41-3.23)	< 0.001
Radiotherapy		
Radical	0.0	
Palliative	3.32 (2.89-3.76)	< 0.001
Dose fraction (Gy)		
< 3	0.0	
≥ 3	2.66 (2.27-3.06)	< 0.001
Field size (cm^2)		
< 200	0.0	
≥ 200	3.47 (2.59-4.34)	< 0.001
Site treated (radical)		
Stomach	0.0	0.08
Pancreas	0.86 (0.18-1.54)	0.01
Ovary	0.23 (-0.36,-0.83)	0.45
Lung	0.40 (-0.56, 1.37)	0.41
Site treated (palliative)		
Upper abdomen	0.0	< 0.001
Thorax	-0.79 (-1.52, -0.06)	0.03
Brain	1.57 (0.55-2.58)	0.003
Side effects		
No	0.0	0.002
Yes	-0.54 (-0.87, -0.20)	
Treatment		
Trop	0.0	<0.001
Trop+Dex	0.23 (-0.28, 0.75)	0.37
Met	0.83 (0.25-1.41)	0.005
Met+Dex	1.77 (1.20-2.34)	< 0.001
Dex	0.60 (0.12-1.07)	0.01

For abbreviations see text

Table 7. Multivariate association between ECOG performance status and risk factors

Risk factors	*Multivariate estimated coefficient (95%CI)*	*p-value*
Age (years)		
< 60	0.0	
≥ 60	0.38 (-0.29, 1.06)	0.26
Gender		
Male	0.0	
Female	-0.19 (-0.87, 0.48)	0.57
Metastasis		
No	0.0	
Yes	-1.51 (-3.47, 0.44)	0.13
Radiotherapy*		
Dose fraction (Gy)		
< 3	0.0	
≥ 3	-0.49 (-1.94, 0.95)	0.50
Field size (cm^2)		
< 200	0.0	
≥ 200	1.01 (0.02-2.0)	0.04
Site treated (palliative)	Overall	0.15
Upper abdomen	0.0	
Thorax	-0.09 (-0.89, 0.70)	0.94
Brain	1.07 (-0.30, 2.46)	0.13
Side effects		
No	0.0	
Yes	0.14 (-0.63, 0.91)	0.72
Treatment	Overall	0.004
Trop	0.0	
Trop+Dex	0.62 (-0.54, 1.77)	0.29
Met	2.98 (1.57-4.38)	< 0.001
Met+Dex	2.12 (0.90-3.34)	0.001
Dex	0.84 (-0.22, 1.90)	0.12

*Dropped due to collinearity
For abbreviations see text

Discussion

The main goal of this study was to provide evidence about which prophylactic antiemetic treatment can be effective for patients irradiated with fractionated RT (palliative or radical). Prevention implies the assessment of emetogenic risk and use of optimal antiemetic therapy as a prophylaxis prior to radiation.

The most common antiemetics used for prevention of radiation-induced emesis are the benzamides (eg. metoclopramide). Trials have demonstrated good clinical efficacy of 5-HT3 receptor antagonists compared with placebo in patients undergoing fractionated emetogenic RT regimens to the upper abdomen [11-13]. Despite strong evidence for increased control of RINV with 5-HT3 receptor antagonists, these agents are not always administered to patients at risk of developing emesis [5,14]. Therefore, besides suffering, there is also the risk of treatment interruption as a conse-

quence of these symptoms. It has been estimated that a break in RT of just one day may reduce disease control rate by around 1.4%, while a break of one week results in a reduction in control rates of 10-12% [15,16].

In the 5 patient groups complete control of nausea and vomiting respectively, was as follows: 50% and 65% for the Trop group, 66% and 83% for the Trop+Dex group, 33% and 42% for the Met group, 41% and 49% for the Met+Dex group and 36% and 55% for the Dex group. It can be concluded that the Trop+Dex group was more effective in controlling nausea and vomiting compared to the other treatment groups.

According to univariate analysis, high risk for development of nausea was significantly correlated with field size >200 cm^2, presence of metastatic lesion and palliative RT. Concerning vomiting, statistically significant risk factors were metastatic lesion, dose fraction, field size, site treated with radical or palliative RT and kind of antiemetic treatment. Concerning the above risk factors, the ones that were independently associated with the development of nausea and vomiting were metastasis and kind of antiemetic treatment. Metastasis was independently associated with increased likelihood for nausea and vomiting (almost 4 and 3 times as much, respectively). Patients that had received any of Met, Met+Dex and Dex were significantly more likely to develop nausea and vomiting than those treated with Trop. Alternatively, Trop+Dex was independently associated with a significant reduction in the odds of nausea and vomiting.

As for the intensity of nausea in relation with the treatment group, Dex group was independently associated with more nausea than Trop group, while Trop+Dex group was independently associated with less nausea than Trop group. Trop+Dex group was also independently associated with less vomiting than Trop group, while any of the rest 3 antiemetic groups (Met, Met+Dex and Dex) were independently associated with more vomiting than Trop group.

The risk factors statistically significantly associated with increased ECOG PS were older age, metastatic lesion, palliative RT, dose fraction ≥3 Gy, field size > 200 cm^2, site treated, when therapy was palliative and any treatment group except Trop+Dex group.

In conclusion, the findings of this work show that patients treated prophylactically with tropisetron plus dexamethasone completed their RT with reduced nausea and vomiting and improved ECOG PS compared to patients that received other antiemetic treatments during their RT.

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