Elzahry et al., J Nucl Med Radiat Ther 2017, 8:6
DOI: 10.4172/2155-9619.1000349

Journal of
Nuclear Medicine & Radiation Therapy

Research Article Open Access

Assessment of Bone Pain Response in Cancer Patients Receiving Single Dose of Sm-153 EDTMP Therapy

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Abstract

Background: Painful metastatic bone dissemination is a common complication of solid malignant tumors that can lead to severe morbidity. There are different treatment strategies currently available for pain relief. Among those, we obtained clinical experience with Sm-153 EDTMP.

Objective: It was to evaluate the overall therapeutic response in 110 patients who underwent a single dose of Sm-153 EDTMP therapy and report if there is a significant correlation of metastatic bone pain response with gender, pathology of primary cancer, patient's age, extent of the metastatic bone dissemination.

Patients and methods: 110 cancer patients were included in this retrospective analysis, 63 (57.2%) males (age range; 52-89 years) and 47 (42.7%) females (age range: 35-84 y), their diagnosis were prostate and breast cancer, respectively. all patients performed conventional bone scintigraphy to prove the evidence of metastatic bone dissemination. Pain severity was assessed clinically and according to WHO Analgesia Scale.

Results: Out of 110 cancer patients received a therapeutic dose of 153 Sm- EDTMP for palliation of painful metastatic bone lesions, 93.6% (103/110) showed overall therapeutic response and 6.4% (7/110) showed no response at all. 61% (67/110) of patients were completely pain-free, 32.6% (36/110) were partially responded to therapy, that response shows insignificant relations with the patients gender, pathology of primary tumor, patients age as well as the extent of metastatic bone dissemination.

Conclusion: The results of this study showed that a single dose of Sm-153 EDTMP offers an effective treatment option in patients with painful metastatic bone disseminations irrespective to their gender, age, tumor pathology as well as to the bone lesions extent.

Keywords: Bone pain response; Cancer patients; Sm-153 EDTMP therapy

Introduction

Many patients with cancer develop symptomatic skeletal metastases at an advanced stage of their disease, they often complicated with pain [1]. Its prevalence is estimated to 73% in breast and about 68% in prostate cancer [2]. Over the past few decades, several radiopharmaceuticals have been developed with bone seeking properties that provide palliation of pain to multiple areas of skeleton without any significant hematological or soft tissue toxicity [3].

Sm-153 is the most widely used radioisotope for metastatic bone pain palliation for all lesions showing up in bone scintigraphy not only in patients with cancer prostate (osteoblastic metastases), but even in those presenting with a mixed pattern of osteolytic and osteoblastic metastases, like those seen in breast cancer [4].

Nature of the Study

This is a retrospective clinical study on 110 patients who underwent single dose of Sm-153 EDTMP for therapy of painful metastatic bone lesions.

Aim of the study was to evaluate the overall therapeutic response and report if there is a significant correlation of metastatic bone pain response with gender, pathology of primary cancer, patient's age as well as extent of the metastatic bone dissemination.

Treatment Design

Sm-153 EDTMP therapy was performed according to the Vienna protocol [5]. The protocol is defined as follows: A single dose of 30 mCi (1.1 GBq) Sm-153 EDTMP was administered through a slow intravenous injection on an outpatient basis. Whole body bone Scintigraphy was performed usually on the next day, anyway, about 20 hours after radionuclide application to achieve complete blood clearance, using large field of view double headed γ-camera, LEHR-collimation, energy window 20%, 103 KeV, acquisition mode contionusely 15 cm/min, early images(<4 hours) showed significantly lower quality.

The study included patients had been treated at Department of Nuclear Medicine, Medical University of Vienna, Austria. All patients were followed up for 12 weeks, conventional bone scintigraphy (Tc-99m MDP), analgesic consumption (according to WHO Analgesia Scale which based on analgesia requirements for each patient), pain symptoms, blood cell count were recorded by the patients and/or family members during each visit. The patient was allowed to adjust the dose of his/her medications if symptoms changed. The patients were asked to get the haemogram 3 and 6 weeks after therapy up to 12 weeks

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Received November 17, 2017; **Accepted** November 20, 2017; **Published** November 27, 2017

Citation: Elzahry M, Diab W, Sinzinger H (2017) Assessment of Bone Pain Response in Cancer Patients Receiving Single Dose of Sm-153 EDTMP Therapy. J Nucl Med Radiat Ther 8: 349. doi: 10.4172/2155-9619.1000349

and provide the report to the physician telephonically. At the end of 12 weeks, the patient was asked to come to the clinic for subsequent detailed assessment and recording of data.

This study was approved by the Ethics Commission at the Medical University of Vienna and the Vienna General Hospital (AKH), each patient was explained the details of the procedure, benefits and side effects of therapy and the follow-up protocol and all patients provided written informed consent.

Statistical Analysis

Date entry and data analysis were done using SPSS version 16 (Statistical Package for Social Science). The data of the patients were retrospectively collected. Continuous variables were summarized as means and standard deviations, while categorical variables were summarized as numbers and percentage. "Independent-samples T test" was used to test for significance between two variables. For all P-values<0.05 were selected as significant.

Design and Methodology

This retrospective analysis included 110 patients, 63 (57.2%) males [age range; 52-89 years] and 47 (42.7%) females [age range: 35-84 years], their primary cancer were prostate and breast cancer, respectively. The majority of the patients have more than 10 metastatic bone lesions on conventional bone scintigraphy representing 71% of all patients (78/110) (Table 1).

Before initiating treatment, all patients performed conventional bone scintigraphy to prove the evidence of metastatic bone dissemination. Bone pain was significant in all patients Pain severity was assessed clinically and according to WHO Analgesia Scale. Pain severity was evaluated based on analgesia requirements according to WHO Analgesia Scale.

Results

A total of 110 cancer patients received a single dose of Sm-153 EDTMP therapy for palliation of painful bone metastases, 93.6% (103/110) showed overall therapeutic response and 6.4% (7/110) showed only no response at all. 61% (67/110) of patients were completely pain-free, 32.6% (36/110) were partially responded to therapy (Table 2).

Pain response is assessed in all 110 patients after administration of the single dose of Sm-153 EDTMP depending on their gender (pathology of primary cancer), patient's age and the extent of metastatic bone lesions.

Gender/pathology of primary cancer

Breast cancer patients expressed high partial response to pain (40.4%) as compared to prostate cancer (27%), while prostate cancer patients expressed a high complete cure (63.5%) as compared to breast cancer (57.4%). Generally, the overall response to pain among breast cancer patients is higher (97.8%) than that of prostate (90.5%). Statistically there is no such difference among prostate and breast cancer patients in their response to pain (all P-values>0.05) as shown in Table 2.

Age (years)	Ca prostate	Ca breast
Mean ± SD	71.1 ± 8.3	58.3 ± 13.2
Range	52 – 89 y	35 – 84 y
Gender		
Males	63/57.3	0
Females	0	47/42.7
Extent of bone lesions (n/%)		
Less than 10 lesions	20/31.7	12/25.5
More than 10 lesions	43/68.3	35/74.5
All values expressed in number/percentage		

Table 1: Demographic characterstics.

Age

Data in Table 3 describes the difference in pain response among the different age groups of prostate and breast cancer patients. The patients are divided according to age into 2 groups, the first group representing the patients who aged 70 years old or younger and the second group representing the patients who are older than 70 years old. In both age groups, the prostate cancer patients who were older than 70 years expressed high complete cure (71.8%) than that of breast cancer patients (33.4%), while the older breast cancer patients expressed a high partial response (66.6%) to therapy as compared to prostate cancer patients at the same age group, 9.7% of prostate cancer patients expressed no response to therapy while the all breast cancer patients achieved overall response to therapy. Statistically, there is no significant difference in pain response among the both age groups of prostate and breast cancer patients (P-values>0.05).

Extent of bone metastases

Cancer patients who have more than 10 bone lesions on bone scan expressed a high complete response (60.3%) after the first dose of therapy as compared to those who have less than 10 bone lesions (50%). Generally, the rate of the response among the cancer patients having more than 10 bone lesions shows an equal percentage (78.2%) as compared to the other group of the patients who have less than 10 bone lesions (78.1%) with no statistical difference in pain response between the both groups of patients (P-values >0.05).

Discussion

Radionuclide therapy has been gaining popularity m the management of painful osseous metastases. This form of palliative therapy has the advantages of targeting all the involved sites but limiting the dose to normal tissue [6]. Radionudide therapy was used in patients with widespread metastatic disease, who would not benefit much from other therapies [7].

There are several studies discussed the efficacy of Sm-153 EDTMP as a palliative radionuclide therapy for metastatic bone pain and

Variables	Ca prostate	Ca breast
Total n/%	63/57.3	47/42.7
Duration (12 weeks) (n/%)		
Complete response	40/63.5	27/57.4
Partial response	17/27	19/40.4
No response	6/9.5	1/2.2
All values expressed in number/percentage		

Table 2: Therapeutic response to Sm-153 EDTMP therapy.

Variables	≤ 70 y (n=69)		>70 y (n=41)	
	Ca prostate	Ca breast	Ca prostate	Ca breast
Total n /%	(31/45)	(38/55)	(32/78.1)	(9/21.9)
Complete response	17/54.8	25/65.8	23/71.8	3/33.4
Partial response	11/35.5	12/31.6	6/18.7	6/66.6
No response	3/9.7	1/2.6	3/9.5	0
All values expressed in number/percentage				

Table 3: Sm-153 EDTMP therapy induced pain response *vs.* patient's age.

Variables	≤ 10 bone lesions (n=32)		>10 bone lesions (n=78)	
	Ca prostate	Ca breast	Ca prostate	Ca breast
(n/%)	(20/62.5)	(12/37.5)	(43/55)	(35/45)
Complete response	12/60	4/33.4	30/69.7	17/48.6
Partial response	5/25	4/33.3	4/9.3	10/28.6
No response	3/15	4/33.3	9/21	8/22.8
All values expressed in number/percentage				

Table 4: Sm-153 EDTMP therapy induced pain response *vs*. extent of bone metastases.

Name of Author	Cases (n) and diagnosis	Response(R)	Percentage(%)	Duration(T)
Wang RF	9 with confirmed malignancies	overall R	77.8	>3 weeks
Dolezal J	43 females with breast cancer	overall R	72	3 months
Gonzalez CL	277 prostate, breast and others	overall R	54	> 3 weeks
Coronado M	28 breast, 27 prostate	complete R	21	3 m
Lakovou I	36 female with breast cancer	complete R	52	16 weeks
Tripathi M	86 from various primaries	overall R	73	>16 weeks
Serafini AN	118 from various malignancies	overall R	43	During 16 weeks
Vina JC	94 prostate, breast and others	overall R	85	(7 days – 3 months)
Beiki D	16 breast, prostate, thyroid and paraganglioma	complete R	75	At 8th week
R: Response; D: Days; W: Weeks; M: Months; (N): Number				

Table 5: Overview of relevant studies with Sm-153 EDTMP.

calculation of the overall or/and complete response rate of bone pain in relation to the time of therapy as shown in Table 4. Previous relevant studies (Table 5), reported a great variation of pain response rate in relation to the time of therapy among cancer patients with different confirmed primaries. For example, Vina et al. reported a high overall therapeutic response 85% of 94 patients over 3 months [8], this response rate is slightly higher as compared with Wang RF study (77.8% after 3 weeks) [9]. The other two studies of González et al. and Tripathi et al. reported 75% *vs*. 73% within 4 months) [10,11], while Serafini et al. and Lakovou et al. registered a low response rate to pain in (43 *vs*. 52%, respectively) through 16 weeks [12,13].

In the present study, overall response rate was 93.6% within the time of follow up (3 months after the first dose of Sm-153 EDTMP). As compared with the other relevant studies discussed in Table 5, this rate of response considered fairly high as compared to Serafini et al. study who achieved only 43% of pain response during the same duration of time, taking into consideration that the number of our patients was nearly similar to his population (118 and 110) respectively [12].

Complete responders in this study were 67/110 (61%) while 36/110 (32.6%) of patients showed partial pain response and only 7/110 (6.4%) of patients expressed no response to therapy. This compared with Dolezal et al. study which showed 42% of patients expressed complete response, 30% partial response and 28% non-responders [14], while at Lakovou et al. study, pain palliation was complete in 52% of the patients, partial in 31% and absent in 16% [13].

Coronado M. study recorded a very low rate of complete response to therapy (21%), partial response (40%) with (24%) of patients showed absent response to therapy [15]. After injection of 153Sm-EDTMP, response was recognized in 90.3% prostate cancer and 97.9% of breast cancer patients, a total of 7/110 prostate and breast cancer patients did not respond to therapy. As compared with other studies showed 40 to 85.5% response rates in cancer breast and 70 to 80% response rate in cancer prostate [16-18], we reported insignificant difference in therapeutic response rate between prostate and breast cancer (90.5% and 97.8% respectively), this finding also recorded by Tripathi et al. as well as Baczyk et al. who did not show any significant difference in response rate among prostate and breast cancer patients (80.6% and 80.4%) respectively [11,19].

Statistically, there is no difference in therapeutic response among different age groups of the patients, 94.2% of responders was younger than 70 years and 92.6% of responders older than 70 years while 5.8% of non-responders was younger than 70 years and 7.4% of non-responders older than 70 years which is also compatible with the findings of Beiki et al. and Sinzinger et al. [5,20]. A comparative analysis also was designed to identify the factors related to therapeutic response between responders and non-responders by Tian. The mean and range of age in the groups were 54 ± 10.9 years (27-72 years) and 57 ± 11.1 years (30-82 years), respectively. However, statistically, there was no difference between the two groups [21].

Study limitations

1. Disadvantage of this study is that it is a retrospective one, that data collection was limited because a number of patients died.
2. Advantage is that it was conducted on a fairly high number of patients followed of a single site with a quite extensive work-up program.

Conclusion

The results of this study showed that a single dose of 153Sm-EDTMP offers an effective treatment option in patients with painful metastatic bone disseminations irrespective to their gender, age, primary tumor pathology as well as to the bone lesions extent. Overall, 61% of cancer patients were completely pain free after a single dose of Sm-153 EDTMP, 33% partially responded and less than 10% showed no response.

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