

Comparative Study of Single Fraction and Multiple Fraction Palliative Radio Therapy for the Treatment of Bone Metastasis in Multiple Center of Bangladesh

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Abstract: *Background:* The main goal of palliative radiation treatment is to relief pain or dysfunction caused by bone metastasis. Bone metastasis is a very much painful condition in almost all advanced cancer. This observational study aims to compare the efficacy of different radiation fractionation schedule used for the treatment of bone metastasis. *Objective:* To compare the single fraction and multiple fraction radiotherapy in the treatment of metastatic bone pain. *Method:* All patients were explained about the aims, objectives, procedure, risk and benefits of the study. Written informed consent was taken from each patient. Sampling technique was simple random sampling. Every odd number of patients was taken in Group A & every even number patient was taken in Group B. Group A: patients were treated with single (8 Gy) fraction radiotherapy and Group B: patients were treated with multiple fraction (30 Gy) radiotherapy i. e. 300 cGy per fraction in 10 fractions, 5 days a week for two weeks by tele cobalt or LINAC machine. The responses were, Complete response: Absence of pain. Partial response: decrease of pain. The response and toxicities were evaluated at the end of treatment, after 7 days, 14 days, 21 days, 28 days and during the follow - up visits. *Result:* The total number of 60 patients of metastatic bone disease were studied in two groups. Group A included 30 patients received a single fraction of 8 Gy tumor dose and Group B included 30 patients who received 30 Gy tumor dose in 10 fractions over two weeks. Onset of pain relief was 73.33% in Group A and 76.67% in Group B after completion of 4th weeks radiation. After 8th weeks of radiation 80.00% in Group A and 83.33% in Group B are relieved from pain. Complete response in Group A 46.67% and in Group B 53.33%, partial response in Group A 40% and in Group B 43.33% and overall distribution of no response in Group A 13.33% and in Group B 3.34%. *Conclusion:* Single fraction palliative radiotherapy is an acceptable alternative for multiple fractions palliative radiotherapy for the control of metastatic bone pain.

Keywords: Gy - Radiation Unit, Rt – Radiotherapy

1. Introduction

Palliative treatment has significant role to improve the quality of life of cancer patients. Radiation is very effective for pain relief in bone metastasis cases. Almost two thirds of patient will experience improvement in their pain with complete and long lasting pain relief in about half of the patients¹.

Breast cancer e. g. that has only metastasized to the bone has a better prognosis than when breast cancer has spread to visceral organs. The most primary tumors commonly associated with these distal bony metastases are lung, breast, prostate, kidney and thyroid².

Metastatic bone disease is a painful condition that can develop in conjunction with cancers of the breast, prostate, lung or other organs. It occurs when cancer cells at an original site metastasize (travel) to the bone. Metastatic cancer is the most common neoplasm that involves the skeletal system³.

Pain due to cancer is feared by every patient who is diagnosed with cancer because pain is associated with advanced disease specially end stage disease. About three quarters of patient with end stage disease will eventually need pain management⁴.

The time interval from the initial diagnosis of primary tumor to the first evidence of bone involvement can vary greatly. Metastatic lesion of bone may be the first evidence of tumor or latent period may be greater than 10 years⁵ at presentation, secondary deposits may be multiple which aids their recognition or may be single⁶ Individual deposits may come to attention because of pain and swelling or a pathological fracture. If the patient is known to have a primary tumor, secondary deposits in bone don't usually present a diagnostic problem. Difficulties can occur when a secondary deposit is the first indication that a particular patient has a malignancy.

The prognosis of bone metastasis is generally poor; though the course of the disease may be relatively slow over a period of years⁷. The usual presentation of bony metastasis is pain. Possible local mechanisms of inducing bone pain are 1) Release of chemical mediators 2) Increased pressure within the bone 3) Micro fracture 4) Stretching of the Periosteum 5) Reactive muscle spasm 6) Nerve root infiltration 7) Compression of the nerves due to collapse of bone⁸.

Management of painful localized bone metastasis typically utilizes radiation therapy and graduated use of opiate analgesics⁹.

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The aim of treatment is relieving pain as simply and quickly as possible. Analgesic can only increase the pain threshold level for time being but cannot destroy the malignant cells which is responsible for proliferation and elevation of periosteum from which pain occurs. Radiotherapy kills the cells as well as decrease the tumor mass and relieves pain without loss of tissue.

Objectives

General

To compare the role of single fraction and multiple fraction palliative radiotherapy in the management of metastatic bone pain. Symptomatic relief of pain assessed 07, 14 and 28 days after completion of radiation treatment.

2. Materials and Methods

The study was designed as Quasi experimental study.

All patients included in the study were informed about the nature of the study. They were explained about the aims, objectives, procedure, risk and benefits of the procedures in easily understandable language. Written informed consent was taken from each patient. It was assured that all information from the patients would be kept secret.

Cytologically or histologically proven malignant disease with the painful bone metastases in single or multiple sites without pathological fracture. No history of previous radiotherapy on the treatment site. Patient able to determine subjectively the amount of pain. Age up to 70 years. Any sex Radiologically proved 30 patients each in Group A and Group B.

Sampling technique was done by simple random sampling. Every odd number of patients was taken in Group A every even number patient was taken in Group B.

Two groups of patients were studied.

Group A: One group was treated with single (8 Gy) fraction radiotherapy and

Group B: Another group was treated with multiple fraction (30 Gy) radiotherapy i. e. 300 cGy per fraction in 10 fractions, 5 days a week for two weeks by telecobalt or ortho- voltage machine.

Following procedures were followed to evaluate the patient's condition before treatment:

Complete history and physical examination. Location and size of lesions were recorded prior to treatment. Histopathological examination reports which had already been done by taking biopsy either from primary or from metastatic bony lesion. Laboratory studies - CBC with differential and platelet count. Kidney function test. Liver function test. Radiologic studies - X - ray of affected part. Radio isotope bone scan. Registration of analgesic consumption. Pain assessment was done by visual analog scale.

Patients were managed symptomatically with antibiotics, oral mouth wash, steroids, antiemetics, vitamins, blood transfusion, and nasogastric tube feeding etc. according to

their needs throughout the treatment period. All patients were advised to take proper skin care during treatment.

The radiation was given by a telecobalt or LINAC machine. Group A (Single fraction group) received a single fraction of 8 Gy whereas Group B (Multi fraction group) received 30 Gy in 10 daily fractions over two weeks. The prescribed dose was the maximum absorbed dose in single field and the central dose for opposed fields. The treated fields, if possible, a 2 cm margin on each side of the metastasis and for spine metastasis one unaffected vertebral body on each side. At treatment planning critical organs were generally not considered to be a problem. Treatment area was marked on the skin with gentian violet placing the patient on the table. Patient's position was correlated with the position of the patient at the machine during treatment. Anatomical landmarks and the field size were noted on the radiation therapy card, which helped to remark on the skin of treatment volume when necessary.

Evaluation after treatment included patients' complete history and physical examination, toxicity of the treatment, pain response evaluation by visual analog scale, laboratory studies - CBC with differential and platelet count, kidney function test, Liver function test, radiological studies - X - ray of affected part. Follow up was performed weekly i. e. 1st, 2nd, 3rd, 4th and 8th weeks after completion of radiation.

The responses were classified by 3 (three) parameters.

Complete response: Absence of pain in treatment site.

Partial response: A decrease in the pain score by at least two points on visual analog scale. No response: No relief of pain.

Progression: Pain does not relief but increase in pain score.

The following outcome variables were studied

Age, Sex, Smoking habit, Clinical features, Primary sites, Affected sites, Histological variety, Radiological variety, Response to therapy on: - Affected part, Histological variety.

Data obtained from the study was compiled and analyzed with computer by SPSS (Statistical Package for Social Sciences). Results were presented in tables and figures.

3. Results

The total number of 60 patients of metastatic bone disease was studied in two Groups. Among the 60 patients, 3 patients were excluded because of willingness to withdraw from the study for personal reason & 7 patients were lost follow up. Group A received a single fraction of 8 Gy tumor dose containing 30 patients and Group B included 30 patients who received 30 Gy tumor dose in 10 fractions over two weeks.

Table I: Distribution of Patients according to age

Age in Year	Group A		Group B	
	No. of Patient	Percentage	No. of Patient	Percentage
30 - 39	1	3.33	01	3.33
40 - 49	09	30	08	26.67
50 - 59	15	50	15	50
60 - 69	05	16.67	06	20
Total	30	100	30	100

Table II: Distribution of Patients according to primary sites

Primary site	Group A		Group B	
	No. of Patient	Percentage	No. of Patient	Percentage
Lung	10	33.33	11	36.67
Prostate	08	26.67	08	26.67
Breast	07	23.33	06	20
Thyroid	02	6.67	02	6.67
Unknown	01	3.33	01	3.33
Kidney	02	6.67	02	6.67
Total	30	100	30	100

Table III: Distribution of patients according to sites of bony metastasis

Primary site	Group A		Group B	
	No. of Patient	Percentage	No. of Patient	Percentage
Vertebrae	20	66.67	21	70
Pelvis	05	16.67	04	13.33
Limbs	03	10	04	13.33
Ribs	02	6.66	01	3.34
Total	30	100	30	100

Table IV: Distribution of patients according to radiological appearance of bone

Types of Lesion	Group A		Group B	
	No. of Patient	Percentage	No. of Patient	Percentage
Osteolytic	16	53.34	17	56.67
Osteo sclerotic	07	23.33	08	26.67
Mixed (both lytic and sclerotic)	07	23.33	05	16.66
Total	30	100	30	100

Table V: Distribution of patients according to histological variety

Types of Tissue	Group A		Group B	
	No. of Patient	Percentage	No. of Patient	Percentage
Adeno carcinoma	14	46.67	13	43.33
Squamous cell carcinoma	08	26.66	08	26.67
Follicular	01	3.33	02	6.66
Papillary	01	3.33	01	3.33
Sarcoma	02	6.67	02	6.66
Small cell Ca	02	6.67	01	3.33
Undifferentiated	02	6.67	03	10
Total	30	100	30	100

Table VI: Complete response of pain according to histological typing

Histological type	Group A		Group B	
	Complete Response	Percentage	Complete Response	Percentage
Adeno carcinoma	6	42.85	7	53.85
Squamous cell Carcinoma	5	62.5	5	62.5
Follicular	1	100	1	50
Papillary	1	100	1	100
Sarcoma	0	00	1	50
Small cell Ca	1	50	0	50
Undifferentiated	0	00	0	00
Total	14		15	

Overall distribution of complete response of patients

14 patients of Group A and 15 patients of Group B were completely responded. Overall distribution of complete response of pain is shown in Table VII.

Table VII: Overall distribution of complete response of patients

Group	No of patient	Complete Response	Percentage
Group A	30	14	46.67
Group B	30	15	53.33

Table VIII: Overall distribution of Partial Response of patients

Group	No of patient	Partial Response	Percentage
Group A	30	12	40
Group B	30	13	43.33

Distribution of Patients according to onset of pain relief

Onset of pain relief for the two treatment Groups which was 73.33% in Group A and 76.67% in Group B after completion of 4thweek radiation. It is observed that, after 8th week of radiation 80.00% in Group A and 83.33% in Group B are relieved from pain. Onset of pain relief is shown in Table IX.

Table IX: Distribution of Patients according to onset of pain relief

Week	Pain relief (Complete & Partial)			
	Group A		Group B	
	No. of Patient	Percentage	No. of Patient	Percentage
1stWeek	13	43.33	12	40
2ndWeek	19	60	20	66.67
3rdWeek	20	66.67	21	70
4thWeek	22	73.33	23	76.67
8thWeek	24	80	25	83.33

4. Discussion

The study was carried out with an aim to compare the effect of single fraction radiotherapy & multiple fraction radiotherapy in metastatic bone pain. The present study findings were discussed and compared with the previously published relevant studies.

Metastatic bone disease is common particularly in older age people¹⁰. The present study showed that the patient with metastatic bone cancer were mostly at advanced age. Peak age was between 50 - 59 year. This study coincides with the study¹¹.

The most commonly involved primary site was lung, which is 31.8% in Group A, 32.6% in Group B. Next common sites are prostate 22.7%, Breast 25%, Unknown Primary 13.6% in Group A and 26%, 17.3%, 8.7% in Group B respectively. This study corresponds with the study of the effect of single fraction compared to multiple fractions on painful bone metastasis: a global analysis of the Dutch bone metastasis study¹².

In this study, vertebrae were most common sites of involvement, which were 72.7% in Group A & 71.7% in Group B respectively. This study correlates with the study of multiple and single fraction palliative radiotherapy in bone

secondaries - A prospective study¹³. Next common sites are Pelvis, Limb & Ribs which are 11.4%, 11.4%, 4.5% in Group A and 10.9%, 15.2%, 2.2% in Group B respectively. This also correlates¹³.

Radiological study revealed lytic nature of the involved site in 54.5% of cases, 22.7% being sclerotic, and 22.7% mixed in Group A and 56%, 26%, 18% respectively in Group B. It corresponds with Multiple & Single fraction palliative study - A prospective study¹³.

According to histological typing in Group A adenocarcinoma representing of about 45.5%, squamous cell ca 27.3%, Undifferentiated 9%. In Group B they were 39%, 26%, 13% respectively.

In response to radiotherapy in Group A complete response was achieved in 35% adenocarcinoma, 75% of sq cell carcinoma, 100% papillary ca, 50% small cell ca, 25% undifferentiated ca. In Group B they were 38%, 83%, 100%, 50% and 33% respectively.

In comparative study complete response was observed 46.66% in Group A & 50% in Group B. Partial response in Group A was 40% & Group B it was 43.33% observed 8thweek after completion of treatment. Onset of pain relief for the two treatment Groups which was 68% in Group A and 67.4% in Group B after completion of 4thweek radiation. It is observed that, after 8thweek of radiation 81.8% in Group A and 86% in Group B are relieved from pain.

Reports of various studies and results of the present prospective study indicate that there is no significant difference between speed of onset and overall incidence of pain relief following single and multiple fractions of radiation in metastatic bone pain.

It is to be noted that in spite of large treatment fields in some patients no significant early toxicity was observed in both groups and side effects were generally mild in nature and tolerated. Adverse effects are mainly skin reaction, nausea & vomiting. Rate of toxicities occurring in both Group were almost same. This observation correlates with the observations¹³.

5. Conclusion

External beam radiation therapy is one of the major indication for Metastatic bone pain control. The disease is efficiently treated by the use of either single fraction or multifraction radiotherapy without any significant difference in response and early toxicities. so it can be concluded as the *Single fraction palliative radiotherapy is an acceptable alternative for multiple fractions palliative radiotherapy for the control of metastatic bone pain.*

6. Conflicts of interest

The Authors declared that they have no conflicts of interest.

References

- [1] Bates, T. A review of local radiotherapy in the treatment a bone metastasis and cord copression. Int. J. Radiat. Oncol. Biol. Phys.1992; 23: 217 - 221.
- [2] Rosier R N; Keefe R. I; Sahasrabdha D. M; Bone Tumors. Philip Rubin, Clinical Oncology, A multidisciplinary approach for the physicians & students .8 edition Philadelphia, W. B Saunders Company 2001; 632 - 648.
- [3] Devita Jr., Vincent T., Hellman S, Rosenbergh S. A.: Cancer Principle & Practice of Oncology, 7 Phildelphia 2005; 2570 - 2585.
- [4] Cleeland, C. S. Cancer - related symptoms Sem. Radiat. Oncol.2000; 10: 175 - 190. edition. Lippincott - Raven
- [5] Alam, M. Levine, E Bone Metastasis. In Moosa ARC, S Chimpff SC. Robson MC (Eds). Comprehensive Textbook of Oncology. Volume II. USA: Williams and Williams CO.1991; 1638 - 1652.
- [6] Salisbury JS. Byers PD. Non - ectoblastic Non cariliagious. Neoplasm. In: Salisbury JS, Byers PD (eds). Diseases of
- [7] bones and joints cell biologics, mechanism and pathology. London: Champma and Hall Medical Publications.1994; 376 - 437.
- [8] Bomford C. K., Kunkler I, H., Sherrif S. B Walter & Millers Textbook of Radiotherapy, Radiation Physics, Therapy & Oncology.6 edition, Edinburgh Chrchull Livingstone.2003; 580 - 582.
- [9] Mercadante, S. Malignant bone pain: Pathophysiology & treatment pain 1997; 69: 1 - 18.
- [10] Mcquay, H. J., Collins, S. L. Carroll, D. & Moore, R. A. Radiotherapy for the palliation of painful bone metastases (Cochrane Review). In: The Cochrane Library, Chichester, UK, John Willey & Sons Ltd.2003.
- [11] Falkmer, U., Jarhult, J., Wersall, P. & Cavallin - Stahi, E, A sistemic Overview of radiation therapy effects in skeletal metastatic Acta Oncol.2003; 42: 620 - 633.
- [12] Akhter PS; Uddin MM; Afroz S Metastatic Bony Cancer - A 25 Months study. Journal of Bangladesh College of Physicians and Surgeons 1996; 14: 69 - 74.
- [13] Steenland, E., Leer, J. W., Van Houwelingen, H., Post, W. J., Van Denhout, W. B., Kievit, J., DE Haes, H., Martijn, H., Oei, B., Vonk, E., Vander Steen - Banasik, E., Wigenraad, R. G., Hoogenhout, J., Warlamrodenhuis, C., Van Tienhoven,
- [14] G., Wanders, R., Pomp, J., Van Reijn, M., Van Mierlo, I., Rutten, E., Leer, J. and Van Mierlo, T., The effect of single fraction compared to multiple fractions on painful bone metastases: a global analysis of the Dutch Bone Metastasis Study Radiother. Oncol 1999; 52: 101 - 109.
- [15] Sze, W. M., Shelley, M. D., Held, I., Wilt, T. J & Mason, M. D. Palliation of metastatic bone pain: Single fraction versus Multifraction radiotherapy - A systematic review of randomized trials. Clin. Oncol.2003; 15: 345 - 352.
- [16] Sarkar, S. K., Pahari, B. and Majumdar, D. Multiple and single fraction palliative radiotherapy of bone secondaries - A prospective study. Ind. J. Radiol. Imaging 2002; 12: 281 - 284.