



Improving the Function, and Quality of Life with the Analgesic Effect of the Vertebroplasty During the Phase of Induction to the Remission in Patients with Multiple Myeloma of Recent Diagnosis.

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Introduction

Multiple myeloma (MM) is a disorder of plasma cells, which is characterized by bone marrow infiltration with clonal plasma cells, with the consequent production of monoclonal immunoglobulin (paraprotein) and organic damage translated as evidence lytic lesions in the bones, Renal failure, hypercalcemia and anemia. The diagnosis is based on the combination of clinical, cellular, imaging and laboratory features. Although clinical manifestations to establish the diagnosis of MM are not as necessary today.

Normal plasma cells produce immunoglobulins that have the function of antibodies that help the body fight infection and disease. As the number of multiple myeloma cells increases clonally, more immunoglobulins or monoclonal protein or M component are produced reciprocally and abnormally. Multiple myeloma cells damage and weaken bone tissue. Its annual incidence is 6/100000 in the western countries, making it the second most frequent malignant neoplasm of hematology after non-Hodgkin's lymphomas. In 2010, 20,180 new cases per year were estimated in the United States and 10,650 deaths per year. It is more frequent in men with a high incidence in black race. The average age of presentation is 62 years. Bone disease occurs in approximately 80% of patients with a recent diagnosis of MM, and in 70% of cases, bone pain is the first symptom to be reported at the onset of the disease.

Pathologic fractures, lytic lesions and osteoporosis in general, are skeletal related events, which also include the need for radiation therapy or surgery in bone tissue, are highly disabling and can seriously impair the quality of life of patients and reduce their Survival.

The mechanism that causes bone disease in multiple myeloma is based on the fact that neoplastic plasma cells, either directly or indirectly through their interaction with bone marrow stromal cells, induce an alteration in the mechanisms of Bone remodeling, as demonstrated by in vitro culture experiments, promotes bone resorption (increased osteoclast activity) and bone formation is inhibited (reduced osteoblast activity).

Vertebral injuries of all types (put types with their ref) are seen very frequently in patients with multiple myeloma. It is estimated that more than 60% of bone lesions occur in patients with MM involving the spine, and is equated with metastatic bone disease, which is observed in 90% for metastatic prostate cancer, 75% in Breast cancer, and 45% in lung cancer.

Patients with MM present with bone pain in the back or costal region. 80% of patients with a recent diagnosis of MM have osteolytic bone lesions documented by any type of cabinet imaging (type and reference). As a consequence of osteolysis, hypercalcemia and can be observed with or without fracture in the affected bone. Bone loss in MM may not always be clinically observable, as approximately 50% of bone must be reabsorbed and reflected in radiological changes (false neg reference). As a result of bone loss, vertebral fractures are common (55% -70%) in MM. Vertebral fractures can occur in patients with treated and untreated active diseases, as well as in patients with confirmed biopsy remission⁹.

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On the other hand, the vertebral column is the site where the presence of bone plasmocitoma is most frequently observed, which also produces bone affection with deformity or fractures by crushing vertebral bodies. The average incidence is 50% compared to 12% for the pelvis and 9% of the ribs. The dorsal and lumbar regions are affected more frequently, while the cervical spine is rarely involved.

There are three neoplastic lesions of the vertebral body that are amenable to treatment by percutaneous vertebroplasty: aggressive vertebral hemangioma, metastases, lytic lesions and / or plasmacytomas in multiple myeloma^{5,8}. Metastases and myeloma are the tumoral lesions that most often affect the spine.

Vertebral compression fractures are very common in the elderly population. Percutaneous vertebroplasty has been used more frequently to treat painful vertebral fractures, caused by both degenerative changes and metastatic lesions, despite their controversy over usefulness over the years. Although there are currently no precise and specific statistics on patients with multiple myeloma undergoing this procedure, we observed that these patients

Vertebroce mentoplasty

Percutaneous vertebroplasty (PVP) is a minimally invasive radiological method for the treatment of spinal pain, related to osteoporotic vertebral compression, fractures, vertebral metastases, myeloma and aggressive hemangioma. The technique was developed in France after the treatment of a patient with an aggressive hemangioma with epidural extension in C2 in 1984. The outcome of the treatment was C2 and complete pain relief reinforcement. Indications for PVP were later extended to patients with vertebral compression fractures due to osteoporosis and metastases. PVP has been informed that an effective and safe procedure in the last 15 years.

Vertebroplasty could be performed as a complement to radiotherapy to provide immediate pain relief and stabilization. It has been suggested that PV can be performed in patients in whom surgery is contraindicated in order to prevent further collapse of the vertebral body and improve pain relief.

The effectiveness of this treatment in pain control, biomechanical stability of the spine and therefore the increase in life expectancy worldwide reaches between 80 and 90% ¹²

Bone Cement

The polymethyl methacrylate requires high temperatures for its polymerization. The carbonaceous bone cement of hydroxyapatite has very compatible properties and fabrics. Calcium phosphate cement is a good substitute that has bone conduction and biocompatibility.

The high-viscosity and radio-opaque cement resulting from the combination of a powder composed of a copolymer of methyl methacrylate, barium sulfate and benzoyl peroxide with a liquid composed mainly

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of a methyl methacrylate monomer. When polymerized, the cement hardens causing an exothermic reaction. Deramond et al. Appreciated, in vitro, that this thermal elevation does not cause Neurological damage. It should be noted that the liquid component is a potent lipid solvent and may cause contact dermatitis. The polymerization time of the cement can be delayed by cooling its components before use and keeping the cement in an ice bath 19.

Functional Scales

The use of measures of functional capacity was introduced in oncology in the late 1940s to evaluate both the possibility of chemotherapy treatment and the consequences of this on patients. The predictive power of survival of the Karnofsky Functional Scale was recognized, thanks to different studies to verify its validity and viability.

Karnofsky Performance Status Scale

Introduced in the scientific literature in 1948 and since then it has become one of the most used (Adams, Britt, Godding et al., 1995). It represents a standardized tool used in the field of oncology, initially developed to measure the functional status or abilities (mainly physical) of people with cancer to perform their daily activities (National Cancer Institute, 2007). This scale is a method to estimate the functional status of the patient and a measure of progression and outcome of the disease.

Barthel Index

The Barthel Index was first used in the chronically ill hospitals of Maryland in 1955. One of the objectives was to obtain a measure of the functional capacity of chronic patients, especially those with neuromuscular and musculoskeletal disorders. The greatest need was to find a useful tool to periodically assess the evolution of these patients in rehabilitation programs.

It is a generic measure that assesses the level of independence of the patient with respect to the accomplishment of some basic activities of the daily life, by means of which different scores and weights are assigned according to the capacity of the subject examined to carry out these activities.

Analog Visual Scale (EVA)

It subjectively evaluates the intensity or severity of the perceived pain, both chronic and acute, allowing the patient to express the severity of their pain and making it possible to obtain a numerical value of

the pain, where in a line of 0 to 10 cm the pain is indicated, considering To 0 as absence and to 10 cm as the worst possible pain.

Likert Satisfaction Scale

It is a type of summative scale, implemented by Likert (1932), who introduces them for the first time to measure attitudes, from techniques of measurement of the personality (Morales Vallejos, 2000). This method measures all items with the same intensity the attitude that you want to measure and it is the respondent who gives a score, usually one to five, depending on their position against the affirmation suggested by the item. The final attitude that is assigned to the respondent will be the average of the score that it gives to each of the items of the questionnaire.

Justification

The increase in life expectancy worldwide leads to an increase in the probability of developing oncological diseases, as well as other chronic degenerative diseases such as osteoporosis, which can consequently cause fractures of the vertebral bodies, generating chronic pain syndromes By compromising the biomechanics of the spine.

Vertebral fractures in cancer patients are associated with high morbidity, reduction in quality of life and an increase in mortality. The increase in the requirement of opioids by these patients can be very high, due to the metastatic bone lesions, this indicates to us that the conservative treatment with opioid drugs is not effective. The decrease in efficacy may suggest a fundamental difference in the mechanisms of bone pain against inflammatory pain.

So we feel committed to helping in an early and as successful way as possible to patients with pathological disorders and established spinal injuries, properly derived from Multiple Myeloma. We propose the possibility of performing a joint and established therapy for this type of patients, with the purpose of incorporating it in a brief way to perform normal activities in their daily life, seeking greater independence of the same, therefore, we consider vertebroce mentoplasty an alternative Feasible and well-founded, to treat both bone pain and pathological fractures of the vertebral bodies, which, if not treated early, can lead to fatal and irreversible damage.

Objectives

General:

1. To determine the analgesic effect of patients with multiple myeloma undergoing vertebroplasty and its functional repercussion in activities of daily living in patients of the Pain Clinic Service of the National Cancer Institute from January 2004 to October 2015.
2. To determine the pain in patients submitted to vertebroplasty versus those treated with bisphosphonates and radiotherapy, according to the analogue visual scale.
3. To identify a better response regarding the functionality of patients undergoing vertebroplasty, thus incorporating them into activities of their daily life after procedure, through the Karnofsky and Barthel scales.
4. Identify better response in terms of satisfaction of patients submitted to vertebroplasty according to Likert scale.

Specific:

- To know the sociodemographic characteristics of gender and age of patients with Multiple Myeloma treated in the Pain Clinic.
- To identify the frequency of pathological fracture in patients with multiple myeloma undergoing vertebroplasty.

Variables:

Variable Type Description Units

Quantitative clinical file Number assigned to each patient in a personalized way

Clinical stage Discrete qualitative Correlates the progression of the disease to other organs or system I
II, III

Diagnosis Algologic Qualitative discrete Syndromic pain diagnosis according to its etiopathogenesis and location Type of pain:

- Somatic

- Neuropathic

- Bone pain

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Date of diagnosis of the disease Quantitative continuous Reported in record as date of the oncological diagnosis Expressed in: day, month and year

Gender

Qualitative nominal

To define gender of the patient

- Female
- Male
- Discrete Quantitative Age Given by patient's age Years
- Date of first visit to pain clinic Continuous quantitative Date patient visits at clinic of pain clinic for the first time Expressed in: day, month and year
- Clinical treatment of MM Nominal Qualitative Related to drugs and other therapies to preserve bone architecture QT: Chemotherapy
- RT: Radiotherapy
- Bisphosphonates

Types of injuries Qualitative nominal Referring to the types of lesions in bone tissue in patients with Multiple Myeloma Líticas

Blast

Magnetic Resonance Dichotomous Qualitative Column Image study performed on patients with MM to confirm the presence of bone lesions If performed

Unrealized

Pathological fracture Qualitative dichotomous To confirm the commitment of spinal injury as a factor causing functional limitation in patients With fracture

No fracture

Impossibility of ambulation Qualitative dichotomous Determines whether patients with MM retain the ability to wander If wandering

Does not roam

Bone pain Dichotomous Qualitative Patient-related symptom of involvement of bone tissue in the spine With Bone Pain

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No bone pain

Clinical treatment of pain Qualitative nominal Related to drugs selected for pain management and interventional therapy Pharmacological:

- Bisphosphonates

Interventionist:

-Vertebroce mentoplasty

EVA Quantitative continuous Visual Analog Scale: used at the first consultation and consultation after the performance of vertebroce mentoplasty in the clinic of pain, to obtain a numerical value on the intensity of pain expressed by the patient Scale from 0 (absence of pain) to 10 (Severe, unbearable pain)

Karnofsky scale Continuous quantitative Scale of functionality in cancer patients Values from 0 to 100, increase in tenths.

0 = Death

100 = Normal

Barthel Index Quantitative Continuous Generic measure that assesses the level of independence of the patient for activities of daily living Values from 0 to 100 points.

Self-employed: 100

Partial dependence: 71-99

Moderate dependency: 51-70

Severe dependence: 31-50

Great dependence: 0-30

Likert Scale Continuous quantitative Scale of satisfaction, employed after treatment of vertebroplasty 5 = Completely satisfied

4 = Fairly satisfied

3 = Neither satisfied nor dissatisfied

2 = Not satisfied

1 = Totally dissatisfied

Methodological Design

1. Type of study

Retrospective, cross-sectional study.

2. Universe and Sample

The universe is constituted by 119 cases reported with the diagnosis of Multiple Myeloma, consulted in the Pain Clinic during the period from January 2004 to October 2015, of which 64 patients underwent vertebroplasty.

The total available will be taken as a sample.

Selection Criteria

A) Exclusion criteria

Patients undergoing spinal surgery within one year.

Patients who do not have a diagnosis of Multiple Myeloma.

Patients received prior to January 2004.

B) Criteria for inclusion

Any patient with a diagnosis of Multiple Myeloma.

Patients receiving bisphosphonate therapy, radiation therapy.

Patients with and without bone pain who belong to the Pain Clinic service.

Patients with studies that certify lytic type bone lesions and are potential candidates for vertebroplasty.

Instrument Data Collection

A data sheet from the Multiple Myeloma Clinic database was used to collect data from patients with this diagnosis and receive care at the INCAN Pain Clinic in the period of January 2004 to October 2015. In addition to gathering and verifying information with data sent by our official network of the National Institute of Cancerology (INCANET), reviewing each file to cross-check information and obtain solid and reliable data.

Procedure Data Collection

We proceed to capture data in Excel and later in IBM SPSS 21.0 statistical tabulation system for data analysis.

Plan Of Tabulation and Analysis

The results were summarized as odds ratio (OR) and their respective 95% confidence intervals (CI). The data of all the patients were inserted in an electronic sheet using the program SPSS 21.0 for the statistical analysis. In all cases, a p value <0.05 was considered statistically significant.

Results

We reviewed 126 records of patients diagnosed with Multiple Myeloma, of which 119 patients were referred to the pain clinic, who also met the inclusion and exclusion criteria, for evaluation and management. These patients had a mean age of 59 (\pm 12. 63) years, with a minimum age of 28 years and a maximum of 87 years. Regarding gender, 54.6% (65) were male and 45.4% (54) were female. (Table 1)

Gender	Frequency	Percentage
Female	54	45.4
Male	65	54.6
TOTAL	119	100

Table 1. Relationship by gender in patients with multiple myeloma treated in pain clinic

Patients with multiple myeloma belonged to different states of the country, including Mexico City (43.1%), Mexico (21.9%), Mexico (21.9%), Puebla (11.8%) and Michoacán 7), among others. (Table 2)

Status	Frequency	Percentage
Chiapas	2	1,7
Cohuila	1	0,8
Federal District	43	36,1
Mexico state	21	16,9
Guanajuato	3	2,4

Guerrero	4	3,4
Hidalgo	1	0,8
Jalisco	1	0,8
Michoacan	7	5,9
Morelos	3	2,5
Oaxaca	8	6,7
Puebla	14	11,8
San Luis Potosi	1	0,8
Tlaxcala	2	1,7
Veracruz	5	4,2
Zacatecas	2	1,7
TOTAL	119	100

Table 2. Relationship of patients with Multiple Myeloma seen at the Pain Clinic

88% (104) of the patients reported as main symptom bone pain, of the 279/5000

While 79% (94) had significant data on pathological fracture and vertebral collapse. Of the group of patients, 26.9% (32) presented difficulty or impossibility for ambulation. (Table 2)

Table 2. Impossibility to walk

All patients with a diagnosis of Multiple Myeloma had spine imaging studies, regardless of whether or not they had bone pain. The data obtained indicated that the study of choice was spinal magnetic resonance, in 93.3% (111) of the patients, and 6.7% (8) had simple x-ray, or in the absence of computed tomography of the spine. (Table 3).

	Frequency	Percentage
Valid NO	8	6.7
SI	111	93.3
TOTAL	119	100.0

Table 3. Patients with imaging study: Magnetic Resonance of Spine

Of all patients, 21% (25) had no pathological fracture in the spine, while the remaining 79% (94) presented fracture data. (Table 4)

	Frequency	Percentage
Valid NO	25	21.0
SI	94	79.0
TOTAL	119	100.0

Table 4. Presence of pathological fracture in the vertebral column

Of the total number of patients with myeloma treated by our service in the period of eleven years (January 2004 to October 2015), 114 (96%) received radiotherapy indicated by hematology service complying with their established treatment protocol; In addition to the use of bisphosphonates, used in 99% (118) of the patients. A total of 54% (64) of the patients were candidates and submitted to vertebroplasty, while the remaining 46% (55) were not submitted to it. (Figures 1 and 2).

Graph 1. Treatment provided to patients of the Pain Clinic with diagnosis of Multiple Myeloma

The relationship obtained according to the Visual Analog Scale (EVA) of patients submitted to vertebroplasty was expressed in two stages, prior to and subsequent to the procedure. Prior to vertebroplasty, 67% of patients had an EVA greater than 4 points (moderate to severe pain). Significant change in outcome after the procedure reported that 92% of patients achieved significant pain relief, with VAS less than 4 points (mild pain). Graph 3.

Graph 3. Relationship of Visual Analog Scale in patients submitted to Vertebro plasty

At the post-vertebroplasty review visit, the Likert Satisfaction Scale, which yielded satisfactory results, was applied to each patient, expressing that 51% (33) of the patients reported being completely satisfied with the procedure, 42% (27) patients Fairly satisfied, and 7% (4) patients report a neutral or indifferent stance, since they do not indicate improvement or increase of pain. Graph 6.

Graph 6. Satisfaction Scale LIKERT applied in the first consultation after Vertebroplasty

Discussion

Multiple myeloma is a hematological neoplasm consisting of the clonal proliferation of plasma cells, usually producing immunoglobulins. It represents approximately 1% of all cancers and 10% of the haematological type. Therefore, it has become more important in its diagnosis and early multidisciplinary management. According to the study carried out in patients of the Pain Clinic with the diagnosis of Multiple Myeloma in the eleven-year period (January 2004 to October 2015), we found that 94% of the patients with this diagnosis were referred by the hematology service, For an assessment and joint management in favor of the patient almost immediately. It is important to note that vertebral injuries in this type of patients constitute a considerable proportion of the total vertebral body compression fractures, which is why it is important not to fall into a subclinical spectrum, allowing them to progress gradually, leading to complications that could Be irreversible.

We can also point out that 88% of the patients consulted in our service presented bone pain in the axial axis or vertebral column, whose symptom had repercussions on the patient's functionality, where 27% of them presented an impossibility for ambulation, limitation in their Daily activities of life, such as bathing, eating, dressing, etc.

According to the demographic data found, 53% of the patients with multiple myeloma treated at the pain clinic belong to the Federal District and State of Mexico, the remaining 47% are transferred from the interior of the country to receive multidisciplinary treatment at our center. Patients with a mean age of 59 years, correlated with the median age of 62 years exposed according to the Mexican Diagnostic Guide of MM 2009, of which 55% are male, and the remaining 45% are female.

Vertebral destructive processes lead to mechanical alterations of the spine, neurological disorders of the spinal compression type, equine tail syndrome or nerve root lesions. Percutaneous procedures of vertebroplasty and kyphoplasty are safe, especially when using imaging techniques such as fluoroscopy or techniques guided by tomography. The incidence of complications is very low, the literature reports a small number of methylmetacrylate leaks that are asymptomatic and are not detected by fluoroscopy²³. In our study we found that 93% of the patients had Magnetic Resonance of Spine, as an image study of choice before confirmation of the diagnosis or suspected fracture or vertebral compromise, which was confirmed in 79% of the cases attended.

The high morbidity and mortality associated with compressive vertebral fractures has led to the development of minimally invasive techniques for its management. This is why the hematology service of our institute seeks early management of these patients, both in their diagnosis and in the beginning of treatment of choice to treat oncological pathology, as well as the initiation of bisphosphonates and radiotherapy to treat Bone pathology, which is confirmed by the data obtained, which reflect that 99% of the patients have bisphosphonate therapy at the time of being captured by the Pain Clinic Service.

Likewise, 96% of the patients received radiotherapy as a treatment of choice in the presence of the most frequent symptom, such as bone pain, present in 88% of known cases. After evaluating each case comprehensively and taking into account its previous treatments and responses, it is proposed a safe percutaneous therapy with great impact in the treatment of bone lesions, such as Vertebroce mentoplasty, which has become the cornerstone in the treatment of bone pain and that reached great acceptance on the part of the patients, because thanks to her many recover their functionality in daily activities and therefore their independence. We found that 54% of the patients were treated with vertebroplasty, and in a consultation after that procedure, 92% of the pain in these patients was achieved in relation to the previous consultation. In addition, we apply simultaneously scales of functionality such as Karnofsky and Barhtel.