



Outcome of study on zoledronic acid induced pain and fever at day care oncology of a tertiary care hospital in Karachi, Pakistan

Arifa Aziz^{1*}, Adnan Jabbar², Shafaq Zubair³, Muhammad Nawaz Khan Niazi⁴, Afsheen Feroz⁵, Sadaf Firdous⁶, Samrina Imran⁷

¹ Staff Medical Officer, Supervisor at Day care Oncology Department of Oncology The Aga Khan University Hospital, Karachi, Pakistan

² Medical Oncologist, Department of Oncology, the Aga Khan University Hospital, Karachi, Pakistan,

^{3, 4} Medical Officer, Day care Oncology, Department of Oncology, The Aga Khan University Hospital, Karachi, Pakistan

⁵ Head Nurse, Day care, Radiation Oncology, The Aga Khan University Hospital, Karachi, Pakistan

⁶ Registered Nurse, Day care Oncology, Department of Oncology, The Aga Khan University Hospital, Karachi, Pakistan

⁷ Nursing Manager, Department of Oncology, The Aga Khan University Hospital, Karachi, Pakistan

DOI: <https://doi.org/10.33545/26649322.2020.v2.i1a.4>

Abstract

Objective: It was observed with patients who received zoledronic acid that there were complaints of increase in pain and fever therefore to know the intensity of both, this project was initiated to measure grade of pain and fever with zoledronic acid and to identify the preventive measures taken to counter the effects caused by zoledronic acid.

Method: We collected data of a total of 72 patients who were electively admitted at daycare oncology, The Aga Khan University Hospital, Karachi from 4th of April, 2019 till 12th of July, 2019. A questionnaire form was prepared by a multidisciplinary team of medical oncologist, daycare nursing staff and Staff medical officer. A consensus was made to identify the following mentioned side effects.

1. Pain ^[1]
2. Fever ^[2].

Result: Out of 72 patients it was seen that after getting injection of Zoledronic acid only 21 patients reported with low grade fever whereas the rest of them were symptomless and 15 patients out of 72 went through mild pain either in the body or some specific part such as legs or arms, 02 of them experienced moderate pain and 02 had severe pain, while 53 patients went through no symptom at all.

Conclusion: Most of the patients had mild pain and low grade fever. These symptoms were adequately managed with paracetamol tablet.

Keywords: zoledronic acid, pain, paracetamol

Introduction

Zoledronic acid is a bisphosphonate administered to patients by intravenous infusion. Reactions during infusion are very occasional and may present with flu like symptoms, musculoskeletal pain, gastrointestinal effects, eye inflammation and fever with shivering ^[3]. This may appear approximately in two weeks but most of the reactions are very mild and disappear within 48 hours following an infusion^[11]. Patients that, during or after receiving zoledronic acid, complain of pain and fever use of paracetamol is sufficient in controlling mild pain and fever ^[4].

Method

This prospective observational study is designed to analyze and measure the side effects of Zoledronic acid induced body pain and fever in cancer patients. We collected data of a total of 72 patients who were electively admitted at daycare oncology, Aga Khan University Hospital Karachi from 4th of April, 2019 till 12th of July, 2019.

Their initial assessment was performed which includes the height, weight, sex, diagnosis and zoledronic acid cycles per protocol identified. A questionnaire form was prepared by a

multidisciplinary team of medical oncologist, daycare nursing staff, Staff medical officer/Supervisor at day care oncology. A consensus was made to identify the following mentioned side effects and data was collected:

1. Pain,
2. Fever.

Furthermore it also includes the onset of symptoms with its occurrence and management. Data was collected using questionnaire form and a pain scale as a reference and results documented accordingly. The Medical Record numbers were noted alongside of the patient's name, their side effects and the relevant management data collected.

Inclusion Criteria

Patients aged more than 18 years of both genders who received this drug at day care oncology were included.

Exclusion Criteria

Patients who were less than 18 years age, received injection Zoledronic Acid in ward or have history of arthritis were excluded from the data collection.

Results

Out of 72 patients it was observed that after getting the injection of Zoledronic acid only 21 patients reported with low grade fever whereas the rest of them experienced nothing and 15 patients out of 72 went through mild pain either in body or some specific part such as legs or arms, 02 of them experienced moderate pain and 02 had severe pain, while 53 patients were symptomless as shown in below figures and tables.

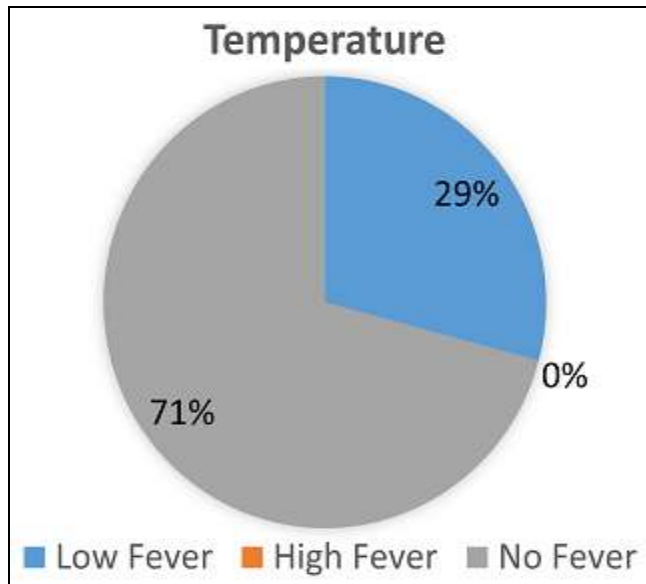


Figure 1: Temperature Percentage

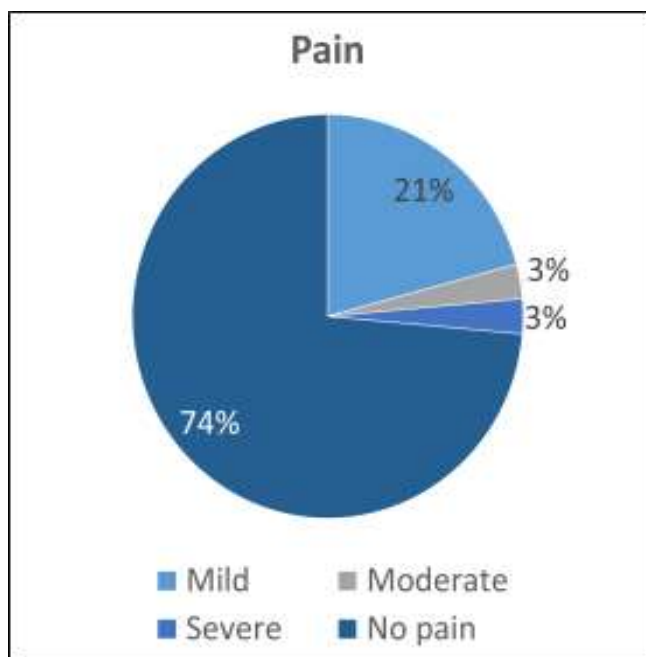


Fig 2: Pain Percentage

Table 1

temperature	# of patients
Low fever	21
High fever	0
no fever	51
total	72

Table 2

pain	# of patients
mild	15
moderate	2
severe	2
No pain	53
total	72

Table 3

pain	scale
Mild pain	1-3
moderate	4-6
Severe pain	7-10

Discussion

The aim of this study is to identify the percentage of patients receiving Zoledronic acid who developed fever and musculoskeletal pain. Fever is the most common adverse effect associated with zoledronic acid infusion. Flu-like syndromes including fever, chills, and bone pain; these symptoms generally did not require treatment and symptoms resolved within 24 to 48 hours after administration of drug. Intravenous zoledronic acid, often causes influenza-like symptoms and severe musculoskeletal pain but when we compare our study in which most patients practiced mild symptoms and were not very severe only 02 patients experienced severe pain out of 72 patients, 21 patients reported with low grade fever and 15 patients went through mild pain whereas the rest of them experienced nothing.

One study showing symptoms appears in 30% of patients post first dose followed by a decreasing pattern lowering up to 6.6% post second dose and to reach 2.8% post third dose. but in our study pain and low grade fever was observed irrespective of number of cycles and can occur in first dose with same intensity in 3rd or 4th dose.

Therefore counseling of patients before starting treatment is essential. Acetaminophen before intravenous zoledronic acid may be considered to control acute reactions [5]. During our study it was observed that side effects occurred maximally within 24 to 36 hours after intravenous administration of zoledronic acid and were self-limiting symptoms within 2 to 3 days [6]. A study reported that acute phase reactions were presented as pyrexia in 16.1% of patients, myalgia 9.5%, flu-like symptoms 7.8% and arthralgia 6.3% [7].

Patients who developed post infusion fever and muscular pain should be given paracetamol or ibuprofen soon after

administration of zoledronic acid

In another study, the importance of vitamin D supplementation before the dose, to reduce the incidence of these symptoms has also been mentioned ^[8].

Conclusion

1. The patients are advised to take tablet paracetamol 1000 mg 2 hours before administration of zoledronic acid.
2. If the patient develops any of the acute-phase reactions, suitable supportive care with acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) is advised.
3. If patients report severe musculoskeletal pain, the physician may consider to stop the treatment with zoledronic acid.

Conflict of interest

There is no conflict of interest.

Way Forward

Side Effects reported after zoledronic acid infusion administration are occasional and can be easily managed with paracetamol or non-steroidal anti-inflammatory medicines.

Also, those who have a repeated history of developing fever and pain post infusion can be managed by prior administration of paracetamol to minimize the post zoledronic infusion side effects.

References

1. Mc Caffrey. M Pain Assessment and Intervention in Clinical Practice, 1991.
2. Springhouse Fever in handbook of signs & symptoms. (3rd edition), Lippincott Williams & Wilkins, 2006.
3. Reid IR, Gamble GD, Mesenbrink P. Characterization of and risk factors for the acute-phase response after zoledronic acid. The Journal of Clinical Endocrinology and Metabolism. 2010; 95:4380-4387.
4. Tanvetyanon T, Stiff PJ. Management of the adverse effects associated with intravenous bisphosphonates. Annals of oncology. 2006; 17:897-907.
5. Adami S. The acute phase response after bisphosphonate admin. Calcified tissue inter. 1987; 41:326-31.
6. Luca DC. Safety and tolerability of Zoledronic acid other bisphosphonates in osteoporosis management. Drug Health Patient Saf. 2010; 2:121-37.
7. Laura LL, Dawn AD, Stephen JQ, Philippa B, Emma R, Tania MW, *et al.* Zoledronic acid reduces knee pain and bone marrow lesions over 1 year: a randomized controlled trial. Ann Rheum Dis. 2012; 71:1322-8.
8. Bertoldo F, Pancheri S, Zenari S. Serum 25-hydroxyvitamin D levels modulate the acute-phase response associated with the first nitrogen-containing bisphosphonate infusion. J Bone Miner Res. 2010; 25:447-54.