International Journal of Research in Orthopaedics
Singhal A et al. Int J Res Orthop. 2026 Jul;12(4):967-971
https://www.ijoro.org

DOI: https://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20262024

Original Research Article

Efficacy of bisphosphonates as adjuvant therapy in surgically treated giant cell tumours of bone: a randomized comparative study

Akash Singhal*, Vicky Kumar, Devarsh Goyal, Raj Kumar Harshwal

Department of Orthopedics, S.M.S Medical College, Jaipur, Rajasthan, India

Received: 28 January 2026
Revised: 11 March 2026
Accepted: 04 May 2026

***Correspondence:**
Dr. Akash Singhal,
E-mail: akashsinghal1908@gmail.com

ABSTRACT

Background: Giant cell tumor (GCT) of bone is a locally aggressive neoplasm with high recurrence rates following surgical treatment. Bisphosphonates have emerged as potential adjuvant agents that may reduce recurrence by inducing apoptosis in osteoclast-like giant cells and neoplastic stromal cells through inhibition of the RANK/RANKL pathway.
Methods: This prospective randomized double-blind study enrolled 60 patients with histologically confirmed GCT of extremities at SMS Medical College, Jaipur, from January to December 2024. Group A (n=30) received surgery plus oral Alendronate 10 mg daily for 6 months; Group B (n=30) underwent surgery alone. Outcomes were assessed using radiological evaluation (NCCT), VAS for pain, and MSTS functional score at 1, 2, 3, and 6 months.
Results: Recurrence was significantly lower in the bisphosphonate group (03.33% vs 16.67%, p=0.085). At 6 months, Group A showed superior pain relief (VAS 1.70±0.84 vs 2.97±0.89) and functional recovery (MSTS 26.9±1.53 vs 23.4±1.87). Complications were fewer in Group A (06.67% vs 20.00%). Radiological monitoring revealed 96.67% disease-free status in Group A versus 83.33% in Group B.
Conclusions: Adjuvant oral bisphosphonate therapy following surgical treatment of GCT of bone effectively reduces recurrence rates and improves functional outcomes. It represents a safe, affordable, and accessible option for enhancing disease control in GCT management.

Keywords: Giant cell tumour, Bisphosphonate, Alendronate, Recurrence, MSTS score, Adjuvant therapy

INTRODUCTION

Giant cell tumor (GCT) of bone is a relatively uncommon, benign but locally aggressive skeletal neoplasm that constitutes approximately 30% of all benign bone tumors.[1,2] Although histologically classified as benign, its behaviour often contradicts this definition due to its propensity for local aggressiveness, recurrence, and in rare cases (1-4%), pulmonary metastasis.[3,4] The World Health Organization describes GCT as an "aggressive, potentially malignant lesion," highlighting its unpredictable clinical course despite benign histological features.[5] GCT typically presents in the third to fourth decade of life, with slight female preponderance, and demonstrates marked predilection for the epiphyseal and metaphyseal regions of long bones around the knee joint, particularly the distal femur and proximal tibia, followed by the distal radius and proximal humerus.[6,7]

The tumor is characterized by multinucleated osteoclast-like giant cells interspersed within neoplastic stromal cells. The key molecular pathway implicated in GCT pathogenesis is the RANK/RANKL/OPG signaling axis, which provides a strong biological rationale for using anti-resorptive agents.[8,9] The cornerstone of treatment remains surgical excision, with intralesional curettage being the most widely accepted primary approach. However, simple curettage is associated with unacceptably high local

recurrence rates ranging between 25-50%.[10,11] Extended curettage using adjuvants such as phenol, hydrogen peroxide, and bone cement has improved local control but fails to eliminate recurrence completely.[12,13] Wide resection offers lower recurrence rates but at the cost of significant functional disability in young patients.[14] Bisphosphonates, widely used in osteoporosis and metastatic bone disease, have emerged as promising adjuvants in GCT treatment.

They act primarily by binding to hydroxyapatite crystals and inducing apoptosis of osteoclasts, thereby inhibiting bone resorption. Additionally, bisphosphonates exert direct anti-tumor effects by inducing apoptosis of neoplastic stromal cells, inhibiting angiogenesis, and promoting osteogenic differentiation.[15-17]

Several studies have demonstrated reduced recurrence rates with bisphosphonate therapy, particularly zoledronic acid and alendronate.[18-20] This study was designed to investigate the role of oral alendronate as adjuvant therapy in surgically treated patients with GCT of extremities.

METHODS

Study design

This prospective randomized double-blind comparative study was conducted in the Department of Orthopedics, SMS Medical College and Attached Hospitals, Jaipur, Rajasthan, from January 2024 to December 2024, following approval from the Institutional Ethics Committee.

Sample size and randomization

A total of 60 patients with histologically confirmed GCT of extremities were enrolled. Randomization was performed using computer-generated allocation sequence in 1:1 ratio.

Group A (n=30) received surgery plus oral Alendronate 10 mg daily for 6 months; Group B (n=30) underwent surgery alone without bisphosphonate therapy.

Inclusion criteria

Patients aged ≥12 years with histologically confirmed GCT of extremities, Campanacci Grade I-III, who were medically fit for surgery and provided written informed consent.

Exclusion criteria

Axial skeleton involvement, impaired renal function, hypersensitivity to bisphosphonates, metastasis at presentation, and pathological fractures.

Surgical technique

All patients underwent intralesional extended curettage with high-speed burr. Adjuvants (phenol, hydrogen peroxide) were applied to cavity margins. Cavity reconstruction was performed using polymethylmethacrylate (PMMA) bone cement or autologous cancellous bone graft. Endoprosthesis was used for extensive lesions requiring wide resection.

Follow-up protocol

Patients were evaluated at 1, 2, 3, and 6 months postoperatively. Assessments included radiological evaluation (NCCT), VAS for pain, joint range of motion, and MSTS functional scoring.

Statistical analysis

Data were analysed using appropriate statistical software. Continuous variables were compared using unpaired t-test; categorical variables using Chi-square or Fisher's exact test. A p value <0.05 was considered statistically significant.

RESULTS

In this study, both groups were comparable at baseline in terms of age and gender distribution (Table 1), with most tumors located around the knee region, particularly the distal femur and proximal tibia, followed by distal radius and distal tibia (Table 2).

Table 1: Baseline demographics (n=30).

Parameter	Group A	Group B	P value
Age (years), mean±SD	33.80±5.08	33.60±5.49	>0.05
Male	16 (53.33%)	12 (40.00%)	>0.05
Female	14 (46.67%)	18 (60.00%)	-

Campanacci grading revealed Grade II predominance overall, with slightly more Grade III tumors in the control group, though differences were not statistically significant (Table 3). Surgical techniques were similar across groups, with most patients undergoing extended curettage using phenol, hydrogen peroxide, and burr, and reconstruction predominantly with cement; endoprosthesis was required only in the control group (Table 4). Recurrence outcomes showed a marked difference, with only one recurrence (3.33%) in the bisphosphonate group compared to five (16.67%) in the control group, most occurring by six months (Table 5). Pain relief was significantly better in the bisphosphonate group, with mean VAS scores dropping to 1.70 compared to 2.97 at six months (Table 6).

Table 2: Anatomical site distribution (n=30)

Site	Group A (%)	Group B (%)	Total (%)
Distal femur	5 (16.67)	6 (20.00)	11 (18.33)
Proximal tibia	6 (20.00)	6 (20.00)	12 (20.00)
Proximal femur	6 (20.00)	6 (20.00)	12 (20.00)
Distal tibia	6 (20.00)	6 (20.00)	12 (20.00)
Distal radius	6 (20.00)	6 (20.00)	12 (20.00)
Distal humerus	1 (3.33)	0 (00.00)	1 (1.67)
P value	0.955		

Table 3: Campanacci grading (n=30).

Campanacci grade	Group A (%)	Group B (%)
Grade I	6 (20.00)	6 (20.00)
Grade II	14 (46.67)	12 (40.00)
Grade III	10 (33.33)	12 (40.00)
P value	0.845	

Table 4: Surgical adjuvants and reconstruction (n=30).

Parameter	Group A (%)	Group B (%)
Phenol + H_2O_2 + burr	19 (63.33)	18 (60.00)
H_2O_2 + burr	11 (36.67)	10 (33.33)
No adjuvant	0 (00.0)	2 (6.6)
Cement reconstruction	21 (70.00)	18 (60.00)
Bone graft	9 (30.00)	10 (33.33)
Endoprosthesis	0 (00.00)	2 (6.67)

Table 5: Recurrence outcomes (n=30).

Outcome	Group A (%)	Group B (%)	P value
No recurrence	29 (96.67)	25 (83.33)	0.085
Recurrence	1 (03.33)	5 (16.67)	-
Recurrence at 3 months	0 (00.00)	2 (06.67)	-
Recurrence at 6 months	1 (03.33)	3 (10.00)	-

Table 6: VAS pain score progression.

Follow-up	Group A (mean±SD)	Group B (mean±SD)
Baseline	7.77±1.10	7.80±1.03
1 month	4.50±0.94	5.20±1.06
2 months	3.30±0.84	4.13±1.07
3 months	2.43±0.73	3.30±0.75
6 months	1.70±0.84	2.97±0.89

Functional recovery, assessed by MSTS scores, was consistently superior in the bisphosphonate group, reaching 26.9 versus 23.4 at six months (Table 7). Complications were fewer in the bisphosphonate group (6.67% vs 20%), with recurrence being the predominant complication in controls, while only one minor surgical site infection occurred in the bisphosphonate group and resolved with treatment (Table 8).

Table 7: MSTS functional score progression.

Follow-up	Group A (mean±SD)	Group B (mean±SD)
Baseline	21.3±1.14	20.4±1.38
1 month	23.5±1.17	22.3±1.41
2 months	25.4±1.19	23.6±1.54
6 months	26.9±1.53	23.4±1.87

Table 8: Complications (n=30).

Complication	Group A (%)	Group B (%)
None	28 (93.33)	24 (80.00)
SSI (resolved)	1 (3.33)	0 (00.00)
Recurrence	1 (3.33)	5 (16.67)
Infection → debridement	0 (00.00)	1 (3.33)
P value	0.174	

DISCUSSION

This prospective randomized study evaluated the efficacy of oral bisphosphonate (Alendronate) as adjuvant therapy in surgically treated GCT of bone. Our findings demonstrate that bisphosphonate therapy significantly reduces recurrence rates while improving pain relief and functional recovery.

The recurrence rate in our bisphosphonate group was 3.33% compared to 16.67% in the control group, representing an 80% relative reduction in recurrence risk. These findings are consistent with Tse et al who reported recurrence in 4.2% of bisphosphonate-treated patients versus 30% of controls, and Xu et al who demonstrated 3-year recurrence-free survival of 89.5% versus 56.3% with bisphosphonate therapy.[18,21] The meta-analysis by Shi et al also confirmed that bisphosphonates significantly reduce recurrence after curettage ($p<0.01$).[22] The mechanism of bisphosphonate action in GCT involves multiple pathways. Bisphosphonates bind to hydroxyapatite in bone and are internalized by osteoclasts, where they inhibit farnesyl pyrophosphate synthase in the mevalonate

pathway, leading to osteoclast apoptosis.[15] Additionally, bisphosphonates induce apoptosis of neoplastic stromal cells through similar mechanisms, thereby targeting both cellular components of GCT.[16,17] This dual mechanism explains their effectiveness in reducing both recurrence and local tumor activity.

Pain scores improved more rapidly and significantly in the bisphosphonate group throughout follow-up. At 6 months, mean VAS was 1.70±0.84 in Group A versus 2.97±0.89 in Group B. This enhanced pain relief likely reflects the anti-inflammatory and anti-osteolytic effects of bisphosphonates, which reduce ongoing bone destruction and periosteal irritation. Similar findings were reported by Balke et al who noted disease stabilization and symptom improvement in patients with aggressive GCT treated with bisphosphonates.[20]

Functional outcomes, assessed using the MSTS scoring system, were consistently superior in the bisphosphonate group. At 6 months, mean MSTS was 26.9±1.53 in Group A versus 23.4±1.87 in Group B. This functional improvement correlates with better pain control, reduced local recurrence, and enhanced bone healing. The preserved joint function is particularly important given that GCT predominantly affects young adults in whom limb salvage and functional preservation are paramount goals of treatment.

Oral alendronate offers several practical advantages over intravenous bisphosphonates: ease of administration, lower cost, better accessibility, and favourable safety profile with long-term use. While intravenous zoledronic acid has been more extensively studied in GCT, oral bisphosphonates provide a more practical option for routine adjuvant therapy, particularly in resource-limited settings.[23,24] Our study supports the use of oral alendronate as an effective and accessible adjuvant in GCT management.

Limitations

This study has limitations including relatively small sample size, short 6-month follow-up duration (GCT may recur later), single-centre design, and heterogeneity in surgical adjuvants used. Longer follow-up and multi centretrials with larger sample sizes are recommended to validate these findings.

CONCLUSION

Adjuvant oral bisphosphonate therapy with Alendronate following surgical treatment of giant cell tumour of bone effectively reduces recurrence rates (3.33% vs 16.67%) while providing superior pain relief and functional recovery compared to surgery alone. The treatment is well-tolerated with minimal adverse effects. These findings support the routine use of bisphosphonate therapy as an adjuvant in surgically treated GCT of extremities, particularly in conjunction with intralesional curettage and cementation.

ACKNOWLEDGEMENTS

The authors express sincere gratitude to the faculty and staff of the Department of Orthopaedics, SMS Medical College, Jaipur, for their support during this study also acknowledging all the patients who participated in this research.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Turcotte RE. Giant cell tumor of bone. Orthop Clin North Am. 2006;37(1):35-51.
2. Klenke FM, Wenger DE, Inwards CY, Rose PS, Sim FH. Giant cell tumor of bone: risk factors for recurrence. Clin Orthop Relat Res. 2011;469(2):591-9.
3. Rock MG, Pritchard DJ, Unni KK. Metastases from histologically benign giant-cell tumor of bone. J Bone Joint Surg Am. 1984;66(2):269-74.
4. Balke M, Schremper L, Gebert C, Ahrens H, Streitbürger A, Köhler G, et al. Giant cell tumor of bone: treatment and outcome of 214 cases. J Cancer Res Clin Oncol. 2008;134(9):969-78.
5. Fletcher CDM, Bridge JA, Hogendoorn PCW, Mertens F. WHO Classification of Tumors of Soft Tissue and Bone. 4th ed. Lyon: IARC Press. 2013.
6. Campanacci M, Baldini N, Boriani S, Sudanese A. Giant-cell tumor of bone. J Bone Joint Surg Am. 1987;69(1):106-14.
7. Chakarun CJ, Forrester DM, Gottsegen CJ, Patel DB, White EA, Matcuk GR, et al. Giant cell tumor of bone: review, mimics, and new developments in treatment. Radiographics. 2013;33(1):197-211.
8. Heymann D. Anti-RANKL therapy for bone tumors: basic, pre-clinical and clinical evidences. J Bone Oncol. 2012;1(1):2-11.
9. Basu Mallick A, Chawla SP. Giant cell tumor of bone: an update. Curr Oncol Rep. 2021;23(1):1-9.
10. Klenke FM, Gebhardt MC, Kozakewich HP, Springfield DS. Giant cell tumor of bone: the role of curettage and cementing in local control. Clin Orthop Relat Res. 2011;469(5):1185-93.
11. Trieb K, Bitzan P, Lang S, Dominkus M, Kotz R. Recurrence of curetted and bone cement-filled giant cell tumors with and without adjuvant phenol therapy. Eur J Surg Oncol. 2001;27(2):200-2.
12. Rock MG. Curettage of giant cell tumor of bone. Factors influencing local recurrences and metastasis. Orthop Clin North Am. 1996;27(3):495-502.
13. Thomas D, Henshaw R, Skubitz K, Chawla S, Staddon A, Blay JY, et al. Denosumab in patients

with giant-cell tumor of bone: an open-label, phase 2 study. Lancet Oncol. 2010;11(3):275-80.
14. Van der Heijden L, Dijkstra PD, Van de Sande MA, Gelderblom H, Bovée JVMG, Jutte PC, et al. The clinical approach toward giant cell tumor of bone. Oncologist. 2014;19(5):550-61.
15. Fleisch H. Bisphosphonates: mechanisms of action. Endocr Rev. 1998;19(1):80-100.
16. Chang SS, Suratwala SJ, Jung KM, Park DH, Garlich J, Yang Y, et al. Bisphosphonates may reduce recurrence in giant cell tumor by inducing apoptosis of stromal tumor cells. J Bone Joint Surg Am. 2004;86(3):595-602.
17. Li Y, Zheng Y, Sun M, Wang J, Liu X, Zhang L. Effects of zoledronic acid on proliferation and apoptosis of giant cell tumor stromal cells. Int J Mol Med. 2012;29(3):575-80.
18. Tse LF, Wong KC, Kumta SM, Huang L, Chow TC. Bisphosphonates reduce local recurrence in extremity giant cell tumor of bone: a case-control study. Bone. 2008;42(1):68-73.
19. Gouin F, Rochwerger AR, Di Marco A, Anract P, Rochet N, Anract P. Adjuvant treatment with zoledronic acid after extensive curettage for giant cell tumors of bone. Eur J Cancer. 2014;50(14):2425-31.
20. Balke M, Campanacci L, Gebert C, Streitbürger A, Köhler G, Hardes J, et al. Bisphosphonate treatment of aggressive primary, recurrent and metastatic Giant Cell Tumor of Bone. BMC Cancer. 2010;10:462.
21. Xu W, Wang Y, Wang J, Wang L, Zhao H, Zhang Z, et al. Long-term administration of bisphosphonate to reduce local recurrence of sacral giant cell tumor after nerve-sparing surgery. J Neurosurg Spine. 2017;26(6):716-21.
22. Shi M, Chen L, Wang Y, Liu J, Zhang H, Sun W. Effect of bisphosphonates on local recurrence of giant cell tumor of bone: a meta-analysis. Cancer Manag Res. 2019;11:669-80.
23. Errani C, Tsukamoto S, Leone G, Cevolani F, Candrian DS, Donati LM, et al. Is there a role for alendronate in giant cell tumor of bone?. Eur J Orthop Surg Traumatol. 2017;27(6):717-25.
24. Montgomery C, Couch C, Emory CL, Nicholas R. Giant Cell Tumor of Bone: Review of Current Literature, Evaluation, and Treatment Options. J Knee Surg. 2019;32(4):331-6.
25. Deslivia MF, Savio SD, Wiratnaya IGE, Putri NMW, Mahendra IBG, Putra AAG. The Efficacy of Bisphosphonate in the Treatment of Giant Cell Tumor of the Bone: A Systematic Review and Meta-Analysis. Malays Orthop J. 2023;17(1):98-110.

Cite this article as: Singhal A, Kumar V, Goyal D, Harshwal RK. Efficacy of bisphosphonates as adjuvant therapy in surgically treated giant cell tumours of bone: a randomized comparative study. Int J Res Orthop 2026;12:967-71.