

Intralesional Triamcinolone versus Oral Bisphosphonate for Benign Cystic Bone Lesions: A Prospective Comparative Study of Radiological and Pain Outcomes

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Learning Point of the Article:

Intralesional triamcinolone injection is more effective than oral bisphosphonates for treating benign cystic bone lesions, providing significantly superior pain relief, faster radiological healing, and better promotion of internal calcification over a 6-month period.

Abstract

Introduction: Benign cystic bone lesions, particularly solitary bone cysts and aneurysmal bone cysts, predominantly affect children and adolescents, posing significant orthopedic challenges.

Aim: This study was therefore designed to compare intralesional triamcinolone injection and oral bisphosphonate therapy in patients with benign cystic bone lesions, with respect to radiological healing and pain outcomes over a 6-month follow-up period.

Materials and Methods: This prospective study enrolled 60 patients with benign cystic bone lesions at the Department of Orthopedics and Trauma Centre, J.A. Group of Hospitals, Gwalior, India. Patients were randomly allocated to Group A (intralesional triamcinolone injection, n = 30) or Group B (oral bisphosphonate, n = 30). Radiological outcomes were assessed using Cole's modification of the Neer grading system, and pain was measured using the Visual Analog Scale (VAS) at baseline, 1, 3, and 6 months. Statistical analyses included the Mann-Whitney U test and McNemar's test.

Results: Both groups were comparable at baseline for age, gender, pain duration, and side of involvement. At 6 months, Group A demonstrated significantly superior pain reduction (VAS: 1.48 ± 1.33) compared to Group B (VAS: 5.48 ± 1.50 ; $P < 0.001$). Radiological improvement (decrease in Neer grade) occurred in 60% of Group A vs 40% in Group B ($P = 0.03$). Internal calcification and mineralization were significantly more frequent in Group A (40%) than Group B (16.7%; $P = 0.044$). Neer-Cole Grade 1 (complete healing) was achieved in 56.67% of Group A versus 23.33% of Group B.

Conclusion: Intralesional triamcinolone injection demonstrated superior efficacy compared to oral bisphosphonate in managing benign cystic bone lesions with respect to pain reduction, radiological improvement, and promotion of calcification. Bisphosphonates remain valuable as adjunctive or alternative therapy in specific clinical scenarios. Larger randomized controlled trials with long-term follow-up are warranted.

Keywords: Solitary bone cyst, aneurysmal bone cyst, intralesional triamcinolone, bisphosphonate, neer-cole grading, pathological fracture, benign bone lesion.

Introduction

Benign cystic bone lesions, including solitary (unicameral) bone cysts (SBCs) and aneurysmal bone cysts (ABCs), represent a

clinically important group of pediatric bone disorders. SBCs predominantly affect the proximal humerus (approximately 70% of cases) and proximal femur (approximately 25% of cases) in

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skeletally immature patients [1, 2]. These fluid-filled lesions are generally benign but carry a significant risk of pathological fracture, growth disturbance, and, in rare instances, growth arrest [3].

The etiology of SBCs remains incompletely understood. Proposed mechanisms include venous obstruction with resultant increased intra-cystic pressure, active bone resorption mediated by the cyst lining, chronic inflammation, and traumatic events [4,5]. The cyst fluid is typically clear to amber and contains a complex mixture of histiocytes, inflammatory cells, giant cells, and prostaglandins [6].

Management of SBCs encompasses a broad spectrum of modalities: Injection therapies (corticosteroids, bone marrow aspirate, demineralized bone matrix, calcium sulfate pellets), mechanical curettage, flexible intramedullary nailing, and multimodal combinations [7,8]. Despite this range, outcomes remain variable. Traditional curettage and bone grafting carry high recurrence rates, prompting a shift toward minimally invasive approaches. Among these, intralesional injection of triamcinolone acetonide – a synthetic glucocorticoid – has gained wide acceptance, although reported healing rates have varied considerably across studies [9,10,11,12].

Despite the theoretical basis for bisphosphonates (BP) use in bone cysts, comparative data against established treatments such as triamcinolone injection remain scarce. This prospective study was therefore designed to compare intralesional triamcinolone injection and oral bisphosphonate therapy in patients with benign cystic bone lesions, with respect to radiological healing and pain outcomes over a 6-month follow-up period.

Materials and Methods

Study design and setting

This prospective comparative study was conducted at the Department of Orthopedics and Trauma Centre, J.A. Group of Hospitals, Gwalior, Madhya Pradesh, India. The study received approval from the Institutional Ethics Committee (No. 1067/IEC-GRMC/2022, dated September 01, 2022), and written informed consent was obtained from all participants or their legal guardians before enrollment.

Participants

Sixty patients of all age groups diagnosed with benign cystic bone lesions were enrolled and randomly allocated into two equal groups of 30 each. Inclusion criteria comprised patients of any age with a radiologically confirmed benign bone cyst who provided consent for examination and follow-up. Exclusion criteria included: refusal to consent, malignant bone tumors,

bone marrow diseases, chronic corticosteroid use, ongoing chemotherapy, contraindications to steroid use, pregnancy, and significant medical comorbidities. Sample size was computed using the formula: $n = 2s^2 (Z\alpha/2 + Z1-\beta)^2 / (\mu1-\mu2)^2$.

Interventions

Group A patients underwent intralesional injection of triamcinolone acetonide. Pre-operatively, routine blood investigations, serology, chest radiograph, electrocardiogram, and plain radiograph of the affected region were obtained. The injection was administered in the operating theater under strict aseptic conditions with C-arm fluoroscopic guidance. The cyst was punctured with two needles; its contents were aspirated with one needle while radiological contrast was injected simultaneously with the other needle to confirm the cystic nature and exclude ABCs, followed by instillation of triamcinolone acetonide [7].

Group B patients were prescribed oral bisphosphonate. Patients were instructed to take the medication on an empty stomach with one to two glasses of plain water and to remain upright for at least 30 min post-ingestion to minimize the risk of esophageal irritation.

Outcome measures

Radiological assessment used Cole’s modification of the Neer

Table 1: Demographic and clinical characteristics of study participants

Variable	Group A (n=30) (%)	Group B (n=30) (%)	Total (n=60) (%)
Age (years)			
<20	10 (33.3)	18 (60.0)	28 (46.7)
20–30	16 (53.3)	4 (13.3)	20 (33.3)
30–40	3 (10.0)	4 (13.3)	7 (11.7)
>40	1 (3.3)	4 (13.3)	5 (8.3)
Gender			
Male	21 (70.0)	17 (56.7)	38 (63.3)
Female	9 (30.0)	13 (43.3)	22 (36.7)
Side involved			
Right	16 (53.3)	16 (53.3)	32 (53.3)
Left	14 (46.7)	14 (46.7)	28 (46.7)
Pain duration (months)			
6–12	16 (53.3)	13 (43.3)	29 (48.3)



Table 2: Comparison of mean age, pain duration, and continuous variables between groups

Variable	Group A (mean±SD)	Group B (mean±SD)	P-value	Test used
Age (years)	23.44±7.78	22.52±11.63	0.732	Independent t-test
Pain duration (months)	13.76±9.71	10.48±6.87	0.134	Independent t-test

SD: Standard deviation

grading system [13]: Grade 1: Cyst distinctly visible; Grade 2: Cyst visible but multilocular and opaque; Grade 3: Sclerosis around or within a partially visible cyst; Grade 4: Complete healing with total obliteration. Pain intensity was assessed using the 10-point Visual Analog Scale (VAS) at baseline and at 1, 3, and 6 months post-treatment. Internal calcification and mineralization were documented as present or absent on follow-up radiographs.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences v21.0. Continuous variables were compared with the independent samples t-test for normally distributed data and the Mann–Whitney U test for non-parametric data. Categorical variables were analyzed using chi-square or Fisher’s exact test. McNemar’s test was used for paired ordinal data (Neer-Cole grading before and after treatment). Statistical significance was set at P < 0.05.

Results

Demographic and clinical characteristics

The majority of participants (46.7%) were under 20 years of age, consistent with the known predilection of benign bone cysts for the skeletally immature [1, 2]. Group A had a higher proportion of patients aged 20–30 years (53.3%), whereas Group B had a greater proportion under 20 years (60%). Overall, males constituted 63.3% of participants, with a higher male proportion in Group A (70%) than Group B (56.7%); this difference was not statistically significant (P = 0.290). Mean age was 23.44 ± 7.78 years in Group A and 22.52 ± 11.63 years in Group B (P = 0.732). Mean pain duration was 13.76 ± 9.71 months

in Group A and 10.48 ± 6.87 months in Group B (P = 0.134), indicating comparable baseline chronicity. Both groups had identical right/left-side distribution (53.3%/46.7%, respectively; P = 1.000) (Tables 1 and 2).

Tumor site distribution

Cystic lesions were distributed across multiple long-bone sites. The most common locations were proximal humerus left side (13% overall), distal femur left side (12%), and proximal tibia left side (12%). Group A had a higher proportion of distal femur left side and proximal tibia left side lesions (20% each), while Group B showed a greater concentration in the proximal humerus left side (27%). These site differences are relevant given variations in blood supply and mechanical loading that may influence treatment response (Table 3) [14].

Radiological outcomes

A statistically significant difference in radiological outcomes was observed between groups (P = 0.03). In Group A, 60% of patients demonstrated a decrease in radiological grade, compared with 40% in Group B. An increase in radiological grading (worsening) was noted in 10% of Group A and 30% of Group B, while 30% of patients in each group showed stable grades. Internal calcification and mineralization were present in 40% of Group A patients versus 16.7% in Group B, a statistically significant difference (P = 0.044) (Table 4).

Neer-cole grading improvement

McNemar’s test confirmed statistically significant within-group improvements in both Group A ($\chi^2 = 10.57, P = 0.001$) and Group B ($\chi^2 = 7.11, P = 0.008$). Group A achieved an overall improvement rate of 56.67%, with 66.67% of patients initially at Grade 3 and 50% initially at Grade 4 advancing to Grade 1. Group B demonstrated an overall improvement rate of 23.33%;

Table 3: VAS pain score comparison at baseline and follow-up time points

Time point	Group A (mean±SD)	Group B (mean±SD)	P-value*
Baseline (VAS)	9.23±0.77	9.43±0.73	0.307
1 Month	7.48±1.16	9.04±0.67	<0.001
3 Months	5.36±1.47	7.76±0.92	<0.001
6 Months	1.48±1.33	5.48±1.50	<0.001

***Mann-Whitney U test. SD: Standard deviation, VAS: Visual analog scale**



Table 4: Radiological outcomes and internal calcification at 6 months

Outcome measure	Group A (n=30) (%)	Group B (n=30) (%)	P-value
Radiological grading – decrease	18 (60)	12 (40)	0.03
Radiological grading – stable	9 (30)	9 (30)	—
Radiological grading – increase	3 (10)	9 (30)	0.03
Internal calcification present	12 (40)	5 (16.7)	0.044
Neer-cole grade 1 achieved	17 (56.67)	7 (23.33)	0.001
Chi-square test/Fisher's exact test as appropriate			

among those initially at Grade 4, only 11.11% improved to Grade 1, while 55.56% reached Grade 3, suggesting moderate rather than complete healing.

Pain outcomes (VAS scores)

Both groups exhibited comparable baseline pain levels (VAS: Group A 9.23 ± 0.77 , Group B 9.43 ± 0.73 ; $P = 0.307$). At 1 month, Group A already showed significantly lower VAS scores (7.48 ± 1.16) compared to Group B (9.04 ± 0.67 ; $P < 0.001$). This divergence progressively widened: At 3 months, scores were 5.36 ± 1.47 versus 7.76 ± 0.92 ($P < 0.001$), and at 6 months, 1.48 ± 1.33 versus 5.48 ± 1.50 ($P < 0.001$) in Group A and Group B, respectively. By 6 months, the triamcinolone group had achieved near-complete pain resolution, while the bisphosphonate group retained clinically significant pain.

Discussion

This study compared intralesional triamcinolone injection and oral bisphosphonate therapy for benign cystic bone lesions and found that triamcinolone was significantly superior with respect to pain reduction, radiological improvement, and promotion of internal calcification. These findings contribute to the ongoing discourse on optimal management of these lesions, for which no universally accepted standard of care exists [3,14].

The predominance of young patients (46.7% under 20 years) in our cohort is consistent with established epidemiology showing that SBCs account for approximately 3% of all primary bone tumors, with 85% of cases arising in children and adolescents [14]. The male predominance observed (63.3%) mirrors previously reported gender distribution patterns in SBCs [1,2]. The equal distribution of side involvement and comparable baseline pain duration across groups strengthened the internal validity of our comparisons.

The significant reduction in VAS pain scores in the

triamcinolone group at all-time points corroborates the well-established anti-inflammatory mechanism of corticosteroids. Triamcinolone inhibits the cyclooxygenase pathway and suppresses pro-inflammatory cytokines and prostaglandins, which are known to be elevated in the cyst fluid of SBCs [6,15]. A randomized controlled trial by Wright et al. similarly demonstrated the superiority of methylprednisolone acetate over bone marrow injection, with a 42% versus 23% healing rate, respectively, using the same Neer radiographic grading criteria employed in our study [13].

The significantly higher rate of internal calcification and mineralization in Group A (40% vs. 16.7%, $P = 0.044$) supports the hypothesis that triamcinolone promotes osteoblast differentiation and stimulates deposition of bone matrix proteins, contributing to cyst stabilization and healing [10,15]. Pavone et al. reported an 82.6% good response rate with corticosteroid injection in unicameral bone cysts over long-term follow-up, further supporting the utility of this approach [9].

BP primarily inhibits osteoclast-mediated bone resorption through the mevalonate pathway, preventing prenylation of essential small GTPases in osteoclasts [11,12]. Third-generation nitrogen-containing BP additionally exhibits anti-proliferative, pro-apoptotic, and angiostatic effects, which are relevant to the pathophysiology of cystic bone lesions [12,16]. Cornelis et al. reported pain relief within 6 weeks and ossification in nearly all patients with unresectable benign bone tumors treated with BP, suggesting a role particularly where corticosteroids are contraindicated [16].

In terms of radiological Neer-Cole grading, Group A achieved Neer Grade 1 (complete healing) in 56.67% of patients versus 23.33% in Group B. Interestingly, Group B patients initially at Grade 4 tended to improve to Grade 3 rather than achieving complete resolution, suggesting BP facilitates partial, rather than complete, healing. Deslivia et al.'s systematic review and meta-analysis on bisphosphonate use in giant cell tumors similarly found lower recurrence rates with BP therapy (odds ratio 0.15; 95% confidence interval 0.05–0.43), indicating their capacity to stabilize but not necessarily fully resolve bone lesions [17].

While triamcinolone demonstrated superior outcomes, the potential adverse effects of corticosteroids – including immunosuppression, glucocorticoid-induced osteoporosis, and adrenal suppression with repeated injections – must be carefully weighed, particularly in pediatric populations [15,18]. BP, by contrast, has a favorable safety profile in young patients



when administered according to evidence-based consensus guidelines [18]. This makes BP a viable alternative for patients with corticosteroid contraindications or for long-term bone stabilization.

The combination of the two modalities represents an interesting avenue for future investigation: triamcinolone for rapid pain relief and calcification promotion, with BP providing longer-term antiresorptive support. Sclerotherapy approaches, such as that evaluated by Purnomo using triamcinolone acetate as a single sclerosing agent for ABC with full lesion resolution over 3 years, also deserve further systematic study [19].

Limitations

This study's limitations include the relatively small sample size (n = 60), a 6-month follow-up period that may not capture late recurrence, the absence of quality-of-life metrics, and non-blinded outcome assessment. Differences in tumor site distribution between groups – though not statistically controlled – may have introduced site-specific confounding. The oral route of bisphosphonate administration, compared to the direct intralesional delivery of triamcinolone, represents an inherent pharmacokinetic disparity. Future randomized controlled trials with larger samples, longer follow-up, intralesional bisphosphonate arms, and patient-reported outcomes are warranted.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

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Conclusion

Intralesional triamcinolone showed superior pain relief and radiological healing compared with oral BP in benign cystic bone lesions. Intralesional steroids are preferable for accessible lesions where image-guided injection can be performed effectively, although technical difficulty may arise in deep or anatomically complex locations. Oral BP remains a useful non-invasive alternative for inaccessible lesions or patients unsuitable for corticosteroid therapy, despite a comparatively slower response. Further long-term multicenter studies are required to define optimal treatment selection.

Clinical Message

Intralesional triamcinolone injection is significantly more effective than oral bisphosphonates for the management of benign cystic bone lesions, offering superior pain relief and more robust radiological healing. Patients treated with triamcinolone achieved a 56.67% complete healing rate compared to only 23.33% in the bisphosphonate group, while also demonstrating significantly higher rates of internal calcification. Although bisphosphonates remain a viable alternative for patients with corticosteroid contraindications, triamcinolone's rapid anti-inflammatory and osteogenic effects make it the preferred primary intervention. Consequently, for pediatric and adolescent patients with symptomatic bone cysts, triamcinolone should be considered the first-line treatment to optimize clinical and structural outcomes.

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