Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/18819
DOI URL: http://dx.doi.org/10.21474/IJAR01/18819

RESEARCH ARTICLE

TO ANALYZE THE ROLE OF ORAL ALENDRONATE ON CLINICO RADIOLOGICAL SHORT-TERM OUTCOME OF LEGG CALVE'S PERTHES DISEASE

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Manuscript Info

Manuscript History
Received: 30 March 2024
Final Accepted: 30 April 2024
Published: May 2024

Key words:-
Legg-Calvé-Perthes Disease, Alendronate, Bisphosphonate

Abstract

Background: Legg-Calvé-Perthes disease (LCPD) also known as Juvenile idiopathic avascular necrosis of the femoral head in a skeletally immature patient. The aim of this study is to analyze the role of oral Alendronate on clinico radiological short-term outcomes of Legg Calve's Perthes disease.

Methodology: The Prospective open-ended cohort study was carried out on 36 patients of 18 years of age of either sex with unilateral idiopathic painless limp diagnosed to be Perthes disease enrolled as per inclusion-exclusion criteria. Patients were divided into two groups, with group I containing patients less than 8 years of age and group II of patients above 8 year of age fulfilling the inclusion criteria-exclusion criteria. Both the groups were further divided randomly into subgroups A and B, subgroup A was received standard treatment as per the protocol, while subgroup B to be given oral alendronate along with standard treatment protocol. All patients were evaluated as per history, clinical and radiological examinationsat the time of initial presentation, and at 3months, 6 months, 9 months and12 months.

Results: Clinical and radiological outcomes were significantly better when LCPD cases were handled with conventional treatment along with oral Alendronate.

Conclusion: Outcomes were significantly better when LCPD cases were handled with conventional treatment along with oral Alendronate. Although, to increase the reliability of the study a large multicentric study with a large sample size is required.

Introduction:-

Legg-Calvé-Perthes disease (LCPD) also known as Juvenile idiopathic avascular necrosis of the femoral head in a skeletally immature patientshas a history of as old as 100 years. Majority of children diseased are in the age between 2-14 years. Permanent deformity and premature arthritis are two major late complication associated with this [1**].**It's a childhood disorder in which the blood flow to the ball portion of the hip joint (femoral head) is momentarily cut off, causing the bone to die.

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Juvenile idiopathic avascular necrosis of the femoral capital epiphysis, was recognized as a seprate disorder for more than 100 years ago (**2). Several retrospective (4-5) and few prospective studies (3) had defined the final deformities of the femoral head after** and operative and nonoperative treatments.

Avascular necrosis of the capital epiphysis is an idiopathic condition in which there is interruption of blood flow to femoral capital epiphysis.The reasons behind disruption of blood flow are not certain, resulting in epiphyseal osteonecrosis, which is accompanied by necrotic tissue resorption, reconstruction and remodelling, and the replacement of necrotic bone with healthy new bone(**6).** Bisphosphonates are bone anti-resorptive drugs that have become the standard of care for postmenopausal osteoporosis and other disorders characterized by pathological bone loss and increased bone turnover. Bisphosphonates ability to suppress osteoclast activity has sparked interest as a potential treatment for diseases that are typically treated with orthopaedic surgery. Their use has also been investigated for the treatment of conditions that occur as a result of orthopaedic surgical operations, as well as for the treatment of LCPD(**7).**

The use of antiresorptive agents like bisphosphonates (BPs), in avascular necrosis of femoral capital epiphysis in experimental model documents that they preserve the trabecular structure of the bone and inhibit the resorption mediated by osteoclast and helps in new bone formation as well. The bisphosphanates already has a established role in postmenopausal osteoporosis to decrease fracture risk and improve BMD (**8),** and bone pain in fibrous dysplasia, osteogenesis imperfecta, tumoral osteolysis related bone complication and reduce hypercalcemia in childhood malignancies (**9) and in paget's disease they alter the abnormal bone formation**, however their use in LCPD is relatively not proved but the use of bisphosphate in adult AVN has been proved in intermediate term studies suggesting that it will prevent further head collapse, reduces pain, improve function and reduce the need for total hip arthroplasty **(10)**. There is limited clinical evidence to support the use of bisphosphonates in juvenile conditions characterized by osteonecrosis. A critical appraisal of the existing research is merited given the paucity of data demonstrating efficacy and safety for these vulnerable patient populations. Further well-designed studies are needed to establish appropriate guidelines for paediatric applications of these drugs. Adult hip arthritis is more likely in children who have had Legg-Calve-Perthes disease, particularly if the hip joint heals in an irregular shape. The joint will wear out prematurely if the hip bones do not fit together well after healing. Children with Legg-Calve-Perthes syndrome who are diagnosed after the age of six are more likely to have hip problems later in life. The younger the child is when the hip joint is diagnosed with Legg Calve's Perthes disease, the more likely it is to heal in a regular, round form(**11).**

The basic aim of this study is to analyze the role of oral Alendronate on clinico radiological short-term outcomes of Legg Calve's Perthes disease. Also, this study was helpful in analyzing the role of bisphosphonate on hip function, short-term outcome, and quality of life at the end of one year. Further, the study also helped in observing the role of bisphosphonate in short-term radiological outcomes in children with unilateral Perthes disease.

Inclusion Criteria

Patients less than 18 years of age of either sex with unilateral idiopathic painless limp diagnosed to be Perthes disease based on clinical and radiological picture and willing to participate in the study.

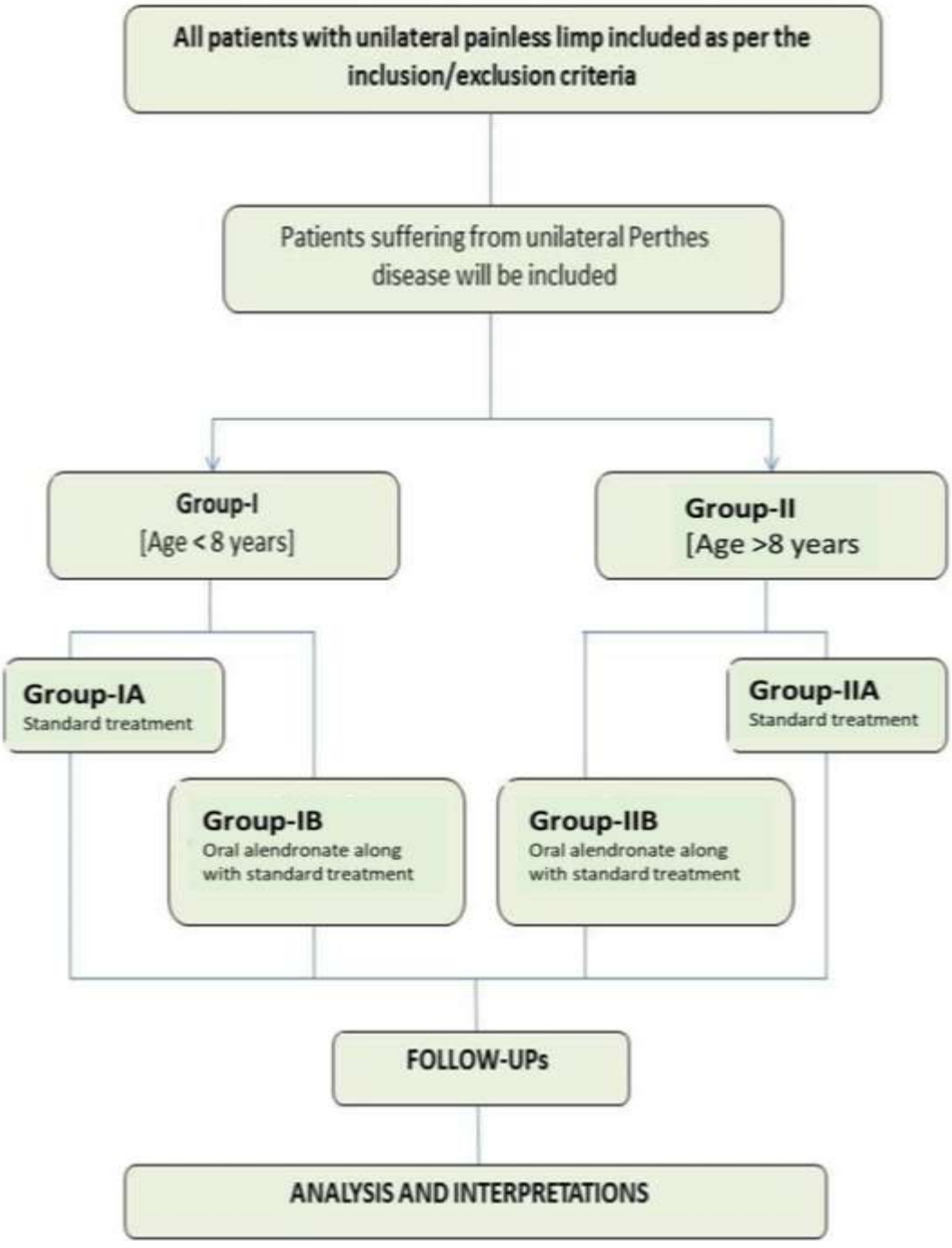
Exclusion Criteria

1. Patient previously operated or under treatment.
2. Patients with previously collapsed hip due to some other pathology.
3. Patients diagnosed to be a case of transient synovitis of hip, sequelae of septic arthritis of hip, SCFE, or child suffering from muscular dystrophy.
4. Patient not willing to be the part of the study.
5. Patient with bilateral pathology

Material and Methods:-

The Prospective open-ended cohort study was carried out in the Department of Orthopaedics, King George's Medical University, Lucknow, Uttar Pradesh, India. A total of 36 patients of 18 years of age of either sex with unilateral idiopathic painless limp diagnosed to be Perthes disease based on the clinical and radiological picture were enrolled as per inclusion-exclusion criteria. All patients with unilateral painless limp included as per the inclusion-exclusion criteria were evaluated as per history, clinical examination, and radiological pictures at the time of initial presentation. Patients suffering from unilateral Perthes disease were included in the study. The lateral pillar

classification system was used to classify the disease type on the X-ray pelvis with both hip AP views. Patients were divided into two groups, with Group I containing patients less than 8 years of age and Group II of patients above 8 years fulfilling the inclusion-exclusion criteria. Both the groups were further divided randomly into subgroups A and B, and subgroup A received standard treatment as per protocol, while subgroup B was given oral alendronate along with standard treatment protocol. In order to improve the containment of femoral head abduction brace/Broom stick brace was applied in patients below 8 years of age (i.e. Group I patients), and varus derotation osteotomy (VDO) was done in patients above 8 years of age (i.e. Group II patients). To improve the contour we give oral alendronate 5mg/day for children <40kg and 10mg/day for above 40kg for a total duration of one yearand clinic radiological examination was done at an interval of every three months. All patients were advised to meet the age-related dietary reference intake for calcium and vitamin D; supplemental calcium and vitamin D were added in quantities to meet the dietary reference intake if the dietary intake was inadequate.



Standard Treatment Protocol

Patient of age <8 years

1. Broom stick/abduction brace
2. Calcium
3. Vitamin D3
4. Quadriceps drill exercise
5. Symptomatic treatments
6. Physiotherapy

Patient of age >8 year

1. Varus derotation osteotomy
2. Calcium
3. Vitamin D3
4. Quadriceps drill exercise
5. Symptomatic treatments
6. Physiotherapy

Outcome Variable

Clinical outcome

1. Mean age
2. Gender
3. Laterality
4. Shortening
5. Limping
6. Range of motion
7. Trendelenburg gait
8. Harris hip score

Radiological outcome

Herring lateral pillar classification

Group A- No involvement of lateral pillar, with full height maintained

Group B- Greater than 50% of lateral pillar height maintained

Group C- Less than 50% of lateral pillar height maintained

Results:-

The demographic parameters.

The mean age of patients in Group-IA & Group-IB is 6.12±1.23 & 6.27±1.35, with an insignificant difference among them (p=0.7881). Similarly, the mean age of patients in Group-IIA & Group-IIB is 13.27±2.68 & 13.96±2.73 with an insignificant difference among them (p=0.6306).

We observed that the males are more in both categories of Group I and in Group IIB. The male & female patients in Group-IA are 7(70.00%) & 3(30.00%), Group-IB are 6(60.00%) & 4(40.00%) respectively, with the insignificant difference among them (p=0.6392). Similarly, the male & female patients in GroupIIA are 4(50.00%) & 4(50.00%), Group-IIB are 5(62.50%) & 3(37.50%) respectively, with the insignificant difference among them (p=0.6143)

As per laterality, the right one is more impacted than the left one in both categories of Group I and Group IIA. The right & left impacted patients in Group-IA are 6(60.00%) & 4(40.00%), Group-IB are 7(70.00%) & 3(30.00%) respectively, with the insignificant difference among them (p=0.6392). Similarly, the right & left impacted patients in Group-IIA are 5(62.50%) & 3(37.50%), Group-IIB are 4(50.00%) & 4(50.00%) respectively, with the insignificant difference among them (p=0.6143).

The mean shortening at the time of initial presentation was 00±00 & 00±00 in Group-IA & Group-IB respectively, and 1.23±0.21 & 1.16±0.20 in Group-IIA & Group-IIB respectively with the insignificant difference among them (p=0.751). After 12 months follow up the mean shortening was found 00±00 & 00±00 in Group-IA & Group-IB respectively, and the mean shortening of patients in Group-IIA & Group-IIB was 1.17±0.18 & 1.19±0.19 with the insignificant difference among them (p=0.8320), so in group with oral alendronate along with standard treatment i.e.

Group-IIA the mean shortening was improved as compared to group without oral alendronate i.e. group-IIB but insignificant difference among them (p=0.8320).

Limping is more often a painless phenomenon than painful in all categories. The baseline of limping presence and absence in Group-IA is 10(100.00%) & 0(00.00%) and for Group-IB is 10(100.00%) & 0(00.00%). Similarly, the baseline of limping presence and absence in Group-IIA is 8(100.00%) & 0(00.00%) and for Group-IIB is 8(100.00%) & 0(00.00%) with the significant difference among them, and after 12 months follow up, Limping is more often Absent in all categories except Group IA. The limping presence and absence in Group-IA is 5(50.00%) & 5(50.00%), and for Group-IB is 0(00.00%) & 10(100.00%) with a significant difference among them (P=0.0098*). Similarly, the limping presence and absence in Group-IIA is 3(37.50%) & 5(62.50%) and for Group-IIB is 0(0.00%) & 8(100.00%) with the insignificant difference among them (P=1.922), so the limping was significantly improved in groups who was taking oral alendronate along with standard treatment i.e. Group-IB and Group-IIB.

The mean baseline for a range of motion in patients including Group-IA is 116.7±5.9 for flexion, 16.9.2±5.1 for Abduction, 18.10±3.5 for Adduction, 16.12±5.2 for I Rotation and 26.14±6.1 for E Rotation. In Group-IB is 116.2±5.9 for flexion, 16.5±5.6 for Abduction, 18.8±3.3 for Adduction, 16.9±5.8 for I Rotation and 26.11±6.7 for E Rotation. The insignificant difference among them is recorded. Similarly, the mean baseline for a range of motion in patients including Group-IIA is 116.4±5.3 for flexion, 16.6±5.3 for Abduction, 18.8±3.7 for Adduction, 16.10±5.3 for I Rotation and 26.12±6.4 for E Rotation. In Group-IIB is 116.9±5.7 for flexion, 16.11±5.8 for Abduction, 18.13±3.2 for Adduction, 16.15±5.7 for I Rotation and 26.12±6.5 for E Rotation. The insignificant difference among them is recorded, and after 12 months follow up, Flexion is observed to show the maximum range of motion, followed by Abduction mostly in all categories of both the groups. The mean range of motion in patients including Group-IA is 122.9±3.7 for flexion, 38.10±2.4 for Abduction, 28.73±1.4 for Adduction, 28.14±1.6 for I Rotation and 35.7±1.8 for E Rotation. In Group-IB is 122.11±3.3 for flexion, 38.14±2.9 for Abduction, 28.14±1.8 for Adduction, 28.14±1.3 for I Rotation and 35.12±1.2 for E Rotation, the significant difference among them is recorded for Abduction (p<0.000), Adduction (p=0.0255), and I Rotation p<0.0001. Similarly, the mean range of motion in patients including Group-IIA is 122.14±3.5 for flexion, 38.12±2.7 for Abduction, 28.13±2.2 for Adduction, 28.5±1.4 for I Rotation and 35.14±1.10 for E Rotation. In Group-IIB is 122.11±3.2 for flexion, 38.13±2.3 for Abduction, 28.5±1.3 for Adduction, 28.14±1.6 for I Rotation and 35.12±1.8 for E Rotation. The significant difference among them is recorded.

Trendelenburg GAIT is most often observed to be present in all categories of both groups. The baseline of GAIT presence and absence in Group-IA is 6(60.00%) & 4(40.00%) and for Group-IB is 7(70.00%) & 3(30.00%), with the insignificant difference among them (P=0.6392). Similarly, the baseline of GAIT presence and absence in Group-IIA is 7(87.50%) & 1(12.50%) and for Group-IIB is 8(100.00%) & 0(00.00%) with the insignificant difference among them (P=0.3017), and after 12 months follow up, Trendelenburg GAIT is most often observed to be absent in all categories of both groups, except for Group-IA. The GAIT presence and absence in Group-IA is 5(50.00%) & 5(50.00%) and for Group-IB is 2(20.00%) & 8(80.00%), with an insignificant difference among them (P=0.1596). Similarly, the GAIT presence and absence in Group-IIA is 6(75.00%) & 2(25.00%) and for Group-IIB is 1(12.50%) & 7(87.50%) with the significant difference among them (P=0.0117).

On comparing the Harris Hip Score in the patients, it was found that the baseline mean Harris Hip score in Group-IA was 46.92±16.51 and Group -IB was 47.81±15.63. However, in Group-II, mean HHS score were 46.13±14.51 (Group-IIA) and 47.02±13.96 (Group-IIB). No significant differences was observed. At 12 months follow-up, the mean Harris Hip Score in Group-IA was 54.34±3.76 and Group -IB was 58.43±3.36. However, in Group-II, mean HHS score at were 55.01±3.72 (Group-IIA) and 59.04±3.95 (Group-IIB). Significant differences was observed among them.

While observing the Herring lateral Pillar, it is recorded that Herring lateral Pillar is reported to be maximum in subgroup A, followed by B and then C, in both the categories of Group IA. However, it is reported to be maximum in Subgroup A & C in Group IIA and in Subgroup B in Group IIB. The baseline of Herring lateral Pillar Classification in subgroups A, B & C in Group-IA is 5(50.00%), 3(30.00%) & 2(20.00%) and for Group-IB is 6(60.00%), 3(30.00%) & 1(10.00%), with the insignificant difference among them (P=0.8089). Similarly the baseline of Herring lateral Pillar Classification in subgroups A, B & C in Group-IIA is 3(37.50%), 2(25.00%) & 3(37.50%) and for Group-IIB is 2(25.00%), 4(50.00%) & 2(25.00%) with the insignificant difference among them

(P=0.5866), and after 12 months follow up the Herring lateral Pillar Classification in subgroups A, B & C in Group-IA is 6(60.00%), 4(40.00%) & 0(0.00%) and for Group-IB is 10(100.00%), 0(00.00%) & 0(00.00%), with the significant difference among them (P=0.0253). Similarly, Herring lateral Pillar Classification in subgroups A, B & C in Group-IIA is 3(37.50%), 2(25.00%) & 3(37.50%) and for Group-IIB is 5(62.50%), 3(37.50%) & 0(0.00%) with the insignificant difference among them (P=0.1572).

Table 1:- Herring Lateral Pillar classification at baseline and follow up.

Herring Lateral pillar classification	**Group-I (n=20)**		**p-value**	**Group-II (n=20)**		**p-value**
	Group IA	**Group IB**		**Group IIA**	**Group IIB**	
Baseline	**A** 5 (50.00%)	6 (60.00%)	X = 0.4242	3 (37.50%)	2 (25.00%)	X=1.067
	B 3 (30.00%)	3 (30.00%)	P = 0.8089	2 (25.00%)	4 (50.00%)	P=0.5866
	C 2 (20.00%)	1 (10.00%)		3 (37.50%)	2(25.00%)	
At 3rd month	**A** 5(50.00%)	7(70.00%)	X=0.8667	3(37.50%)	3(37.50%)	X=0.4
	B 3(30.00%)	2(20.00%)	P=0.6483	2(25.00%)	3(37.50%)	P=0.8187
	C 2(20.00%)	1(10.00%)		3(37.50%)	2(25.00%)	
At 9th month	**A** 6(60.00%)	9(90.00%)	X=5.6	3(37.50%)	3(37.50%)	X=1.667
	B 4(40.00%)	0(00.00%)	P=0.0608	2(25.00%)	4(50.00%)	P=0.4346
	C 0(0.00%)	1(10.00%)		3(37.50%)	1(12.50%)	
At 12th months	**A** 6(60.00%)	10(100.00%)	X=5	3(37.50%)	5(62.50%)	X=3.7
	B 4(40.00%)	0(00.00%)	P=0.0253*	2(25.00%)	3(37.50%)	P=0.1572
	C 0(00.00%)	0(00.00%)		3(37.50%)	0(0.00%)	

Discussion:-

Avascular necrosis of the capital epiphysis also known as Legg-Calve'-Perthes disease (LCPD), was identify as a different entity from a century ago**(2,12-13).** Two recent prospective multicenter studies **(3,5)** and several extensive retrospective studies **(4,14- 15)** have supplied critical information about femoral head deformity following current nonoperative and surgical treatments. In a multicenter prospective cohort study among childrenover 6 years of age at the time of diagnosis with >50% femoral head necrosis, were treated by three different methods i.e. physiotherapy, abduction brace and VDRO. After 5 years of follow up they observe that VDRO gave significant better outcome than brace and physiotherapy, and 43% of patients had a spherical femoral head (Stulberg Class I or II outcomes) five years following femoral varus osteotomy**(3).**

Similarly, A prospective multicenter study of patients between 6 year to 12 year of age at the time of diagnosis, were managed by bracing, physiotherapy, salter innominate osteotomy and VDRO, and on follow up they found that there were no difference in outcome between patients treated with bracing and physiotherapy, there were also no difference in outcome between patients treated with salter innominate osteotomy and VDRO. In patients <8 years of age, treatment did not have a significant effects either operative and non operative, but the outcome was significantly better after surgical treatment in patients >8 years of age. Patients who underwent a Salter innominate osteotomy or femoral varus osteotomy for the treatment of developmental dysplasia of the hip found that 41% of those receiving the Salter innominate osteotomy and 62% of those receiving the femoral varus osteotomy exhibited spherical femoral heads classified as Stulberg Class I or II by the time skeletal maturity was reached **(5).**In light of the foregoing, the purpose of this study was to determine the effect of oral Alendronate on the clinic radiological short-term outcome of Legg Calve's Perthes disease. We observed no changes in clinico-demographic characteristics between subgroups in the present study. However, the outcomes were significantly better when LCPD cases were handled with conventional treatment and oral Alendronate.Multiple peer-reviewed studies**(16-20)**suggest that current surgical interventions, including femoral varus osteotomy and Salter innominate osteotomy, do not reliably produce a spherical femoral head, especially in patients diagnosed after eight years of age. A deeper understanding of the mechanism underlying femoral head deformity resulting from ischemic necrosis led to the development of biologic therapies for treating osteonecrosis of the femoral head in juveniles **(16-18).** This approach aims to address the underlying pathologic processes that contribute to the collapse of the femoral head. These processes include the imbalance between osteoclast-mediated bone resorption and the delayed new bone formation observed in histological samples from animal models of avascular necrosis as well as femoral head specimens from patients diagnosed with Legg-Calvé-Perthes disease**(19-20).**Given these findings, researchers employed the use of

bisphosphonates (BPs), which are antiresorptive medications, inhibit osteoclast-mediated resorption in experimental models of ischemic necrosis of the femoral head. The hypothesis was that this would preserve the trabecular architecture of the necrotic bone, minimize deformity, and maintain the trabecular framework to support new bone formation. The present study builds upon previous experimental investigations that demonstrated significant positive outcomes when using Alendronate in avascular necrosis of the femoral head cases.

While BPs have been shown to increase the BMD and reduce fracture risk inpostmenopausal osteoporosis **(8,21)**and reduces bone pain in fibrous dysplasia **(9)**, and prevent fracture risk in osteogenesis imperfecta **(22)**, tumoral osteolysis related bone complication prevention**(23)**, to malignancies associated hypercalcemia prevention**(24)** and reduces the pagets disease related abnormal bone turnover **(25). Agarwala et al., 2005(26)**; **Agarwala et al., 2009 (27)**; **Lai et al., 2005(28)**; and **Nishii et al., 2006(10)**Studies have shown that in adults with osteonecrosis of the femoral head, Bisphosphonates (BPs) may provide benefits over intermediate time periods. Specifically, BPs may help reduce pain, improve hip function, prevent additional femoral head collapse, and postpone the need for joint replacement surgery. These potential effects of BPs were observed in research examining intermediate-term outcomes. However, the clinical data supporting BPs in juvenile osteonecrosis is minimal and needs further evaluation. The current study demonstrated that Alendronate is effective regardless of the patient's age. Additionally, instances younger than 8 years had better results than ones older than 8 years.

A recent multicenter prospective study found that children of all ages with severe Lateral Pillar C, LCPD had poor radiographic outcomes regardless of whether they received nonsurgical or surgical therapy, necessitating the discovery of innovative interventions to avoid femoral head deformity **(5)**. A pathologic healing mechanism characterized by an imbalance between bone resorption and creation has been implicated in the development of collapse in juvenile femoral head osteonecrosis. By reducing osteoclastic bone resorption, BP treatment has the potential to avoid significant femoral head deformity during the fragmentation phase of LCPD. Numerous limitations exist in the literature, most notably the scarcity of published Level IV studies now available for review.

The patient demographics comprised a diverse group with a variety of osteonecrosis etiologies and phases. Only one study followed a systematic approach for initiating and administering BP medication, which is crucial for evaluating the drug's effects on femoral head collapse prevention and function improvement. Additionally, most studies did not include a clear radiographic classification of osteonecrosis pre- and post-treatment, The lack of baseline and follow-up radiographic data makes it challenging to evaluate the degree of deformity at the start and end of bisphosphonate use. Radiographic evidence from animal studies characterizing the geometry of the femoral head along with correlating histologic data examining bone microarchitecture imply that bisphosphonates disrupt the physiological process of femoral head deterioration. However, these results have yet to be corroborated in human research.

Controversies surrounding the use of BP therapy to treat LCPD include the drug's restricted dispersion in necrotic bone, its lack of anabolic effect on bone, its inability to improve mechanical qualities directly, however in growing skeletal long-term effect of bisphosphonate in not known but the uptake of bisphosphate in avascular bone is not certain. Radioactive blood pressure tracing research in piglets has shown that 14C-ibandronate binds preferentially to the vascularized areas of the infracted femoral head **(16)**. Although this is a clinical study, it is not comparable to an experimental study. However, we observed a positive effect of Alendronate in LCPD cases, which may represent Alendronate's involvement in bone growth, particularly in the femoral head region. This experimental study result explains why several dosing regimens for oral and intravenous delivery are recommended.

By injecting 14C-ibandronate into necrotic femoral heads in the piglet model, it was established that the drug had a wide distribution and reasonable retention over time**(29)**. While a single local injection can significantly reduce the dose required to achieve the desired impact of reducing femoral head deformity, this strategy also involves a separate surgical procedure that adds to the damage to the ischemic bone. The retention of necrotic bone in the absence of new bone development on the necrotic framework, as demonstrated in various animal studies, thus raises the possibility that BP therapy may have an effect on bone formation in LCPD. A perfect biological treatment for LCPD would balance bone resorption and creation during the fragmentation/resorptive phases. This spurred research into the use of a combination of BP (antiresorptive) and BMP-2 (anabolic) therapy in the treatment of osteonecrosis of femoral head **(30).** The study found that compared to the control group, individuals who received the combined therapy experienced a decrease in the asphericity of the femoral head and a decrease in the number of osteoclasts, as well as an increase in trabecular bone volume and osteoblast surface area. These findings suggest that BMP-2 has an additive effect on bone formation when combined with the other therapies.

The existence of heterotopic ossification in the hip joint capsule was one warning conclusion from this investigation. Prior to implementing this therapy in the clinical context, it is critical to adjust the BMP-2 dose and perfect the injection technique. Additionally, the present study demonstrates favorable outcomes, implying that Alendronate has an anabolic impact on necrotic bone in LCPD patients. Numerous experimental studies indicate that ischemic necrosis of the young femoral head weakens the cartilage and bone mechanically **(31)**. The possibility that BP therapy can immediately restore the necrotic femoral head's mechanical characteristics is slim, as this restoration is dependent on new bone creation occurring over time. Given the protracted nature of the healing process, especially in older patients experiencing Legg-Calvé-Perthes disease, a treatment plan combining protected weight-bearing and a biologic medication to regulate bone resorption and formation may be the optimal approach for minimizing mechanical issues and ensuring long-term success.

In general, significant side effects associated with blood pressure medication are infrequent in children when the drug is used judiciously**(32-35).** Transient pyrexia with flu-like symptoms is the most often reported adverse effect following intravenous treatment; gastrointestinal problems have also been noted. Jaw osteonecrosis has not been recorded in children. One of the unanswered uncertainties concerns the long-term impact of repeated BP administration on the normal growing skeleton.The medication may only be necessary during the initial resorptive stages of the condition. While some data on the systemic skeletal effects of bisphosphonate therapy have been published in paediatric patients with osteogenesis imperfecta, additional research is warranted **(36–38)**, data on children with normal skeletons are scarce. In multiple animal investigations **(39-42)**, The study observed decreased growth in long bones that was presumed to have a dose-dependent effect when high doses of bisphosphonates (BPs) were administered to rapidly growing test subjects. However, such growth suppression was not noted in several clinical cases. Another study found maintenance of height z-scores in a small group of children treated with pamidronate for fibrous dysplasia over periods ranging from 1.2 to 9.1 years**(34)**, as well as in another review of 17 individuals with LCPD treated with zoledronic acid for an 18-month period **(33)**. The preceding observations from numerous research and the current study's findings indicate that BPs may have a role in preventing the femoral head from collapsing during osteonecrosis.

Although numerous problems surrounding the standardization of the ideal blood pressure dose, the optimal timing to initiate treatment and the most effective drug delivery method remain unknown. There are potential drawbacks to bisphosphonate therapy that include decreased dispersion within necrotic bone after systemic administration, the lack of a bone anabolic effect, and the absence of an immediate improvement in the mechanical characteristics of the affected femoral head. Due to limited relevant clinical evidence, the use of bisphosphonate therapy for Legg-Calvé-Perthes disease to prevent femoral head deformity and enhance long-term functional outcomes remains an area of debate.

Other basic sciences and clinical studies are required to determine the efficacy and safety of BP treatment in LCPD, emphasizing the potential deleterious effects on necrotic bone remodeling and the remainder of the growing skeleton. Again, the present study's limitations were due to the small sample size and single-centric design. It is respectfully suggested that further multicenter studies with larger sample sizes be undertaken in order to strengthen the reliability and broad applicability of the findings presented in the current research.

Conclusion:-

Outcomes were significantly better when LCPD cases were handled with conventional treatment along with oral Alendronate.Other basic sciences and clinical studies are required to determine the efficacy and safety of BP treatment in LCPD, emphasizing the potential deleterious effects on necrotic bone remodeling and the remainder of the growing skeleton.

A recent multicenter prospective study found that children of all ages with severe Lateral Pillar C LCPD had poor radiographic outcomes regardless of whether they received nonsurgical or surgical therapy, necessitating the discovery of innovative interventions to avoid femoral head deformity [5]. A pathologic healing mechanism characterized by an imbalance between bone resorption and creation has been implicated in the development of collapse in juvenile femoral head osteonecrosis. By reducing osteoclastic bone resorption, BP treatment has the potential to avoid significant femoral head deformity during the fragmentation phase of LCPD. Numerous limitations exist in the literature, most notably the scarcity of published Level IV studies now available for review.

Additional multicentric studies with large sample sizes are strongly recommended by the author to strengthen the validity and generalizability of the findings of the current study.

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