Bisphosphonates' Use and Risk of Aseptic Loosening Following Total Hip Arthroplasty: A Systematic Review.

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Background

Aseptic loosening (AL) is one of the most common causes of Total Hip Arthroplasty (THA) failure *(1)*. Implant micromotion, microparticle wear debris and macrophage upregulation are the leading theories of AL *(2,3)*. Meanwhile, bisphosphonates (BPs) are drugs with high anti-resorptive activity *(4)*. Their main indication is osteoporosis treatment. However, there is growing interest in the peri- and postoperative use of BPs to mitigate THA AL risk.

Objectives

This systematic review aimed to evaluate:

1. Implant survival and the AL rate in patients with elective THA receiving BPs vs no BPs therapy.
2. Comparison of revision rate, postoperative complications and patients' functional scores in patients with elective THA receiving BPs vs no BPs therapy.

Study Design & Methods

This systematic review was conducted under the PRISMA 2020 guidelines with a pre-registered PROSPERO protocol. Three engines and grey literature were searched up until May 2022. Randomized and non-randomized control trials and comparative cohort studies assessing BP and control therapy after THA survival were included.

Table 1. Functional scores, revision rate and complications between groups.

Author	BP group / Control Group							
	No of patients at final FU	Functional Scores	All-cause revision cases	AL cases	PJI cases	PPF cases	HO cases	Osteolysis cases
Aro et al. (2018)	19/12	HHS: N/S WOMAC: N/S Rand-35: N/S	0/0	0/0	0/0	0/1	N/A	N/A
Khatod et al. (2015)	2292/10586	N/A	29/230 (p<0.001)	23/168 (p=0.004)	N/A	24/33 (p = 0.016)	N/A	N/A
Muren et al. (2015)	30/31	HHS: N/S EQ-5D: N/S	0/0	0/0	0/0	0/0	N/S	N/A
Prieto-Alhambra et al. (2011)	1052/22217	N/A	8/296 (p=0.033)	N/A	N/A	N/A	N/A	N/A
Prieto-Alhambra et al. (2014)	1210/5756	N/A	19/399 (p<0.0001)§	N/A	N/A	N/A	N/A	N/A
Ro et al. (2019)	5276/50287	N/A	162/2689 (p<0.001)	162/2689 (p<0.001)	N/A	N/A	N/A	N/A
Scott et al. (2013)	21/22	N/S	0/1	0/0	0/0	0/0	N/A	N/A
Shetty et al. (2006)	18 /19	N/S	1/0	0/0	0/0	0/0	N/A	2/2
Tapaninen et al. (2010)	7/9	N/S	0/0	0/0	0/0	0/0	N/A	N/A
Yukizawa et al. (2017)	18/12AC (16C)	N/A	0/2 (0)	0/0 (0)	0/2 (0)	0/0 (0)	N/A	N/A
Friedl et al. (2009)	25/25±	HHS, p<0.001	0/0	0/0*	N/A	N/A	N/A	N/A
Formica et al. (2017)	57 hips/137 hips	HHS: 89.1 (5.7)† VAS: 1.1(1)† OHS: 41.3 (5.1)†	14 (p=1)‡	6‡	2‡	1‡	3‡	32‡

Note N/A: not answered, N/S: not significant, BP: bisphosphonate, FU: follow-up, AC: alfacalcidol, C: control, HHS: Harris Hip Score, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index, EQ-5D: EuroQol 5 dimensions, VAS: visual analogue scale, OHS: Oxford Hip Score, THA: total hip arthroplasty, TKA: total knee arthroplasty, PJI: periprosthetic joint infection, AL: aseptic loosening, PPF: periprosthetic fracture, HO: heterotopic ossification, p: p-value.
† mean (SD)
* significant subsidence of stem and medialization and cranialization of cup in control group without signs of loosening
± one patient of the control group was excluded before the analysis
‡ in all groups
§ both THA and TKA

Results

Twelve studies embraced the inclusion criteria. Seven of them were randomized control trials and five were retrospective cohort studies. A total of 99,678 patients and 99,696 THAs were included; 10,025 patients received BPs (BP group), and 89,129 made up the control group. The overall revision and AL rates were lower in the BP group (2.17% and 1.85%) than in the control group (4.06% and 3.2%). Periprosthetic fracture (PPF) cases were higher in the BP group (0.24%) than in the control group (0.04%). Further complication risk was similar between groups. Most studies reported comparable functional scores between groups *(Table 1).* The methodological quality of the included studies varied significantly.

Conclusions

- AL is the most common late THA complication, with multiple factors contributing to its pathophysiology.
- BP treatment after elective THA seems to reduce the overall revision and AL risk.
- On the other hand, the risk for PFF was higher in the BP group.
- Other complications' risk and functional scores were similar between groups.
- Further high-quality studies are needed to validate the results due to the multifactorial AL pathogenesis.

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