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Review

Effect of zoledronic acid on reducing femoral bone mineral density loss following total hip arthroplasty: A meta-analysis from randomized controlled trails

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HIGHLIGHTS

- To assess the efficiency of zoledronic acid on reducing femoral periprosthetic BMD loss in THA.
- Four randomized controlled trials (RCTs) were included in the meta-analysis.
- Intravenous administration of zoledronic acid could significantly reduce periprosthetic bone mineral density loss.

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ABSTRACT

Objective: This meta-analysis aimed to assess the efficiency of intravenous administration of zoledronic acid on reducing femoral periprosthetic bone mineral density loss in patients undergoing primary total hip arthroplasty (THA).

Methods: A systematic search was performed in Medline (1966–2017.07.31), PubMed (1966–2017.07.31), Embase (1980–2017.07.31), ScienceDirect (1985–2017.07.31) and the Cochrane Library (1966–2017.07.31). Fixed/random effect model was used according to the heterogeneity tested by I^2 statistic. Sensitivity analysis was conducted and publication bias was assessed. Meta-analysis was performed using Stata 11.0 software.

Results: Four studies including 185 patients met the inclusion criteria. The present meta-analysis indicated that there were significant differences between groups in terms of periprosthetic bone mineral density in Gruen zone 1 (SMD = 0.752, 95% CI: 0.454 to 1.051, P = 0.000), 2 (SMD = 0.524, 95% CI: 0.230 to 0.819, P = 0.000), 4 (SMD = 0.400, 95% CI: 0.107 to 0.693, P = 0.008), 6 (SMD = 0.893, 95% CI: 0.588 to 1.198, P = 0.000) and 7 (SMD = 0.988, 95% CI: 0.677 to 1.300, P = 0.000).

Conclusion: Intravenous administration of zoledronic acid could significantly reduce periprosthetic bone mineral density loss (Gruen zone 1, 2, 4, 6 and 7) after THA. In addition, no severe adverse events were identified. High-quality RCTs with large sample size were still required.

1. Introduction

Total hip arthroplasty (THA) is successful surgical procedure for treatment of end-stage joint osteoarthritis. With the aging population, the incidence of THA is has risen sharply. It was reported that more than 330 thousand of THAs were performed in the United States in 2011. By 2030, the demand of THA is expected to increase to 500 thousand producers annually [1–3]. However, the implantation of femoral component may lead to osteopenia of the proximal femur due to stress shielding [4]. Periprosthetic bone loss after THA is associated with reduced bone mineral density which increase the risk of migration, implant loosening, and periprosthetic fractures [5–7].

Substantial studies have focused on the periprosthetic bone mineral density after THA and the development of osteolysis. Bisphosphonates are anti-resorptive agent which promotes bone

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mineralization and inhibits the biological effect of osteoclasts [8–10]. Several randomized controlled trials (RCTs) has confirmed its beneficial effect on preserving periprosthetic bone in cementless THA. Zoledronic acid is a third-generation of bisphosphonate drug given intravenously to treat bone diseases [11]. It could rapidly reduce bone turnover rates in adult patients at high risk of fractures. In addition, zoledronic acid has the potential efficacy in protecting against osteoporotic fractures and improving periprosthetic bone quality [12]. Currently, no approved therapy for bone mineral density loss associated with THA has been applied because of the small sample size, short-term follow up and low evidence level of the published studies. Based on the beneficial effects, zoledronic acid has been recommended to be applied in THA as routine.

Currently, the intravenous administration of zoledronic acid for reducing periprosthetic bone loss in THA was seldom reported. Thus, there is a lack of scientific evidence. Therefore, we perform a meta-analysis from RCTs to assess the efficiency of intravenous administration of zoledronic acid on reducing femoral periprosthetic bone mineral density loss in patients undergoing primary THA.

2. Methods

This meta-analysis was reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. All analyses were based on previous published studies, thus no ethical approval and patient consent are required.

2.1. Search strategy

Potentially relevant studies were identified from electronic databases including Medline (1966–2017.07.31), PubMed (1966–2017.07.31), Embase (1980–2017.07.31), ScienceDirect (1985–2017.07.31) and the Cochrane Library (1966–2017.07.31). The following key words were used on combination with Boolean operators AND or OR: “total hip replacement OR arthroplasty”, “zoledronic acid”, and “bone loss”. No restrictions were imposed on language. The bibliographies of retrieved trials and other relevant publications were cross-referenced to identify additional articles. The search process was performed as presented in Fig. 1.

2.2. Inclusion and exclusion criteria

(1) Participants: Only published articles enrolling adult participants that with a diagnosis of end-stage of hip osteoarthritis and prepared for unilateral total hip arthroplasty.
(2) Interventions: The intervention group received intravenous zoledronic acid for preventing periprosthetic bone loss after THA.
(3) Comparisons: The control group was received normal saline infusion.
(4) Outcomes: Bone mineral density measured in the frontal plane, throughout seven Gruen zones (Fig. 2) by means of dual-energy X-ray.
(5) Study design: only clinical randomized control trials (RCTs) were regarded as eligible in our study.

2.3. Selection criteria

Two reviewers independently scanned the abstracts of the potential articles identified by the above searches. Subsequently, the full text of the studies that met the inclusion criteria was screened, and a final decision was made. A senior author had the final decision in any case of disagreement regarding which studies to include.

2.4. Data extraction

Two of the authors independently extracted data from the included studies. Corresponding authors were consulted for details of data were incomplete. The following data were extracted and recorded in a spreadsheet: first author names, publication year, samples size, baseline characteristics, intervention procedures, and outcome parameters. Other relevant data were also extracted from individual studies. Primary outcomes were bone mineral density measured by means of dual-energy X-ray.

2.5. Quality assessment

Quality assessment of the included RCTs was assessed by two authors independently which used the Cochrane Collaboration's tool. We conducted “risk of bias” table including the following key points: random sequence generation, allocation concealment, blinding, incomplete outcome data, free of selective reporting and other bias, each item was recorded by “Yes”, “No”, or “Unclear”. Each risk of bias item was presented as a percentage across all included studies. The percentage indicated the proportion of different levels of risk of bias for each item.

The quality of the evidence for the main outcomes in present meta-analysis were evaluated using the Recommendations Assessment, Development and Evaluation (GRADE) system including the following items: risk of bias, inconsistency, indirectness, imprecision and publication bias. The recommendation level of evidence is classified into the following categories: (1) high, which means that further research is unlikely to change confidence in the effect estimate; (2) moderate, which means that further research is likely to significantly change confidence in the effect estimate but may change the estimate; (3) low, which means that further research is likely to significantly change confidence in the effect estimate and to change the estimate; and (4) very low, which means that any effect estimate is uncertain.

2.6. Data analysis and statistical methods

Pooling of data was carried out using Stata 11.0 software (The Cochrane Collaboration, Oxford, United Kingdom). Statistical heterogeneity was evaluated based on the value of P and I^2 using standard chi-square test. When I^2 >50%, P < 0.1 was considered to be significant heterogeneity, random-effect model was used for meta-analysis. Otherwise, fixed-effect model was performed. Sensibility analysis is conducted to assess the origins of heterogeneity. The results of dichotomous outcomes were expressed as risk difference (RD) with 95% confidence intervals (CIs). For continuous various outcomes, mean difference (MD) or standard mean difference (SMD) with a 95% confidence intervals (CIs) was applied for assessment.

3. Results

3.1. Search result

A total of 236 studies were identified through the initial search. By scanning the abstracts, 232 reports that did not meet inclusion criteria were excluded from the current meta-analysis. No gray literature was included. Finally, four RCTs [13–16] which published between 2009 and 2017 were included in the present meta-analysis. These studies included 95 patients in the experimental groups and 90 patients in the control groups.