INPLASY PROTOCOL

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The author declared no potential conflict of interest.

The effect of teriparatide on the reduction of fragility fracture-related pain: a systematic review and meta-analysis

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Review question / Objective: **The purpose of the meta-analysis is to determine the analgesic effect of teriparatide on the fragility fracture of osteoporosis patients. RCTs and observational studies were included.**
Condition being studied: **Osteoporosis characterized by bone mass loss and bone microarchitecture disruption, leading to an increased risk of fracture. The most common location of fragility fractures are the spine, hip, wrist, humerus, and pelvis. About 40% of patients with osteoporosis in China developed fragility fractures. The risk of secondary fractures was increased among patients with previous osteoporotic fractures. Teriparatide (recombinant human parathyroid hormone [PTH]1-34), as an anabolic medication, increases bone formation by stimulating osteoblasts. Teriparatide had been proven to be effective to decrease the risk of fractures and improve bone mineral density. There were studies explored the analgesic effect on pain caused by osteoporotic fragility fractures, but the conclusions were various.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 May 2020 and was last updated on 29 May 2020 (registration number INPLASY202050108).

INTRODUCTION

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METHODS

Participant or population: Patients with fragility fractures.

Intervention: Teriparatide.

Comparator: Placebo or traditional drug used for osteoporosis.

Study designs to be included: RCTs and observational studies.

Eligibility criteria: Inclusion criteria: 1) RCTs and observational studies. 2) Patients with fragility fractures. 3) Studies reporting pain and relevant assessments on fragility fractures. Studies focused on fractures unrelated to osteoporosis or the pain of patients was not evaluated were excluded.

Information sources: PubMed, Embase and Cochrane Library databases were searched to identify randomized controlled trials (RCTs) and observational studies comparing the effect of teriparatide with control on the reduction of fragility fracture-related pain. In addition, we checked the reference lists of the articles manually to identify other potentially eligible publications.

Main outcome(s): Assessments of pain after treatment of patients with fragility fractures.

Quality assessment / Risk of bias analysis: Methodological quality and risk of bias of RCTs were assessed using the tools from the Cochrane Handbook. A total of 8 domains were assessed according to the standard from the instructions provided in the Cochrane Handbook: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants; 4) blinding of personnel; 5) blinding of outcome assessment; 6) incomplete outcome data; 7) selective reporting; 8) other biases (baseline imbalance, the similarity in using cointerventions between groups, and inadequate statistical analysis). The Jadad Scale, with total score of 7 points, contains 2 questions were used to evaluate observational studies. The scale focused on randomization, masking and the reporting of dropouts and withdrawals. 0 to 3 points means poor quality, and 4 to 7 points means high quality.

Strategy of data synthesis: The main outcomes were pain assessed by its relative measurements such as visual analog scale (VAS), The Japanese Orthopedic Association (JOA) low back pain scores, Charnley pain score, numeric rating scale and Qualeffo-41. As for continuous data reported in the studies as mean values with standard deviations (SD), the mean difference (MD) or the standardized mean difference (SMD) with 95% confidence intervals (CI) were generated as the effective measures. The main outcome was pain evaluation, but the trials included had various measurement for pain assessment. For data using the same measurement, an MD and the 95% CIs were generated. As for data using different scales, we generated the SMD with 95% CIs. If SD was not provided, SE or CI were collected to calculate SD. Data of dichotomous outcomes were calculated as a risk ratio (RR) with 95% CIs. Forest plots were generated using all relevant data showing a summary with 95% CIs. Heterogeneity between studies was assessed using I2 analysis. We first used fixed effect (FE) model to create forest plots. If the results showed I2 was over 50%, indicating substantial heterogeneity among studies included, random effect model was superseded by random effect (RE) model to re-create the forest plots. We using funnel plots to evaluate the possibility of publication bias visually.

Review Manager 5.3 (Cochrane IMS, Copenhagen, Denmark) were used for statistical analysis. We perform subgroup analyses on the different drugs used on participants of control groups (risedronate or alendronate).

Subgroup analysis: We perform subgroup analyses on the different drugs used on participants of control groups (risedronate or alendronate).

Sensibility analysis: The sensitivity analysis was performed using the following method: For analysis with I2 > 50%, we change into the RE model to see if the results changed. We excluded each paper in order and record the change of MD and 95% CIs, if the value of I2, MD and 95% CI changed significantly, the excluded paper was the origin of heterogeneity.

Country(ies) involved: China.

Keywords: Teriparatide; Fragility fracture; Pain; systematic review.

Contributions of each author:
Author 1 - Peixu Wang - Author 1 drafted the manuscript.
Author 2 - Wei Sun - The author provided statistical expertise.
Author 3 - Fuqiang Gao - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 4 - Zirong Li - The author read, provided feedback and approved the final manuscript.