The use of calcium phosphate bone cement in fracture treatment: a meta-analysis of randomized trials

CRD summary
This review concluded that the use of calcium phosphate bone cement for the treatment of fractures in adults was associated with lower prevalence of pain compared to patients receiving no graft material. A decreased loss of fracture reduction compared to autogenous bone graft was reported. The conclusions were reasonable, but should be viewed as tentative until further research is available.

Authors' objectives
To compare the effects of calcium phosphate bone cement with alternatives on functional and radiographic outcomes in adults with metaphyseal fractures of the upper and lower extremities.

Searching
Two reviewers independently searched MEDLINE, EMBASE, CINAHL, AMED and Cochrane Central Register of Controlled Trials up to September 2006. Several other sources were searched including trial registers and conference proceedings. The reference lists of included studies were searched and manufacturers and experts in the field contacted. The search terms were provided. Studies were sought in all languages and regardless of publication status.

Study selection
Randomised controlled trials (RCTs) comparing the use of calcium bone cement to alternatives or to no treatment for bone fractures of the appendicular skeleton of adults were included. The outcomes of interest were functional (pain or impairment), radiographic (fracture-healing or subsidence) and rate of infection. Three different types of calcium phosphate were used in the included studies (most commonly the Norian Skeletal Repair System). The comparator was fracture treatment with no substitute or (in three studies) included autogenous iliac crest bone graft. The fractures were in a range of different sites and primarily through trabecular, cancellous bone. The mean age of participants receiving the intervention ranged from 36 years to 84 years. Two reviewers independently screened studies for inclusion. Disagreements were resolved through consensus.

Assessment of study quality
Studies were assessed for method of randomisation, allocation concealment, baseline comparability, similarity of care programmes, blinding of patients and outcome assessors, statement of primary outcome, sample size calculation, statistical analysis and loss to follow-up. Quality of reporting was also assessed using the Detsky score (score expressed as a percentage). Two reviewers independently carried out quality assessment. Disagreements were resolved by consensus.

Data extraction
The relative risk (RR) and relative risk reductions (RD), with 95% confidence intervals (CI) were extracted for dichotomous outcomes and mean differences (95% CI) for continuous outcomes. In one study ordinal data were transformed to categorical to allow statistical pooling. Two reviewers independently extracted data. Authors of the primary studies were asked to verify the accuracy and provide any additional data required (five responded). Disagreements were resolved by consensus.

Methods of synthesis
Where appropriate data were available, studies were pooled in a random-effects meta-analysis. Statistical heterogeneity was assessed using Cochrane’s $X^2$ (p<0.1) statistic and $I^2$. The sub-group analyses of interest were specified in advance: type of control group (autogenous bone graft or no graft); type of fracture (radial, tibial, femoral or multiple); and study quality score (<70% or ≤70%). Publication bias was assessed using a funnel plot.

Results of the review
Fourteen RCTs were included (1,093 participants; 1,179 fractures). Nine studies reported concealment of allocation
using sealed envelopes. Full blinding was not possible as calcium phosphate cement is radiodense. There were
imbalance between groups at baseline in four studies. Three studies did not report a intention-to-treat analysis. On the
Detsky scale assessing quality of reporting, scores ranged from 50 per cent to 90 per cent.

Three (n=455 patients) of the eight studies reporting a pain outcome were pooled. The prevalence of pain was lower at
the fracture site in the intervention group (calcium bone cement) compared to control (RR 0.57, 95% CI: 0.33, 0.99,
p=0.04). In the subgroup analysis there was no statistically significant difference in pain when the intervention was
compared to autogenous bone graft (one RCT, n=22), but there was a significant pain benefit when the intervention was
compared to a no-substitute comparator (two RCTs, n=432).

Appropriate data were not available for pooling of the five studies reporting functional outcome. The findings from
these five studies were mixed.

There was no significant difference between intervention and control prevalence of infection (seven RCTs, n=718), RR
0.74 (95% CI: 0.19, 2.87), in fracture healing (four RCTs, n=216) and in prevalence of loss of fracture reduction (five
RCTs, n=599), RR 0.54, 95% CI: 0.26, 1.13). There was significant heterogeneity. When the intervention was
compared to autogenous bone graft alone in a subgroup analysis there was a statistically significant benefit in favour of
the intervention (three RCTs, n=166) for loss of fracture reduction, but not when compared to no substitute. There was
a benefit with the intervention for tibia fractures (two RCTs, n=146), but not with other fractures. The authors stated
that funnel plots did not suggest publication bias.

**Authors’ conclusions**
The use of calcium phosphate bone cement for the treatment of fractures in adults is associated with lower prevalence
of fracture site pain compared to controls managed with no graft material. Use of calcium phosphate bone cement also
decreased loss of fracture reduction when compared to autogenous bone graft. However, the benefits needed to be
confirmed a large, definitive RCT.

**CRD commentary**
This review had clearly stated inclusion criteria. Studies were sought from a wide range of sources. Appropriate
methods were used to minimise the risk of error and bias in the review process. The synthesis seemed appropriate. The
subgroup analyses were specified in advance.

The results of the subgroup analyses need to be viewed cautiously due to the small number of studies available for some
of the subgroups: whether or not there was a statistically significant result in the subgroup analyses may have been
influenced by the number of participants in the analysis.

Using a quality score to investigate the impact of quality on a meta-analysis has limitations. However, overall study
quality was comprehensively assessed and taken into consideration in the interpretation of the findings. This was a well-
conducted review, but due to limitations in the evidence available the conclusions cannot be considered definitive.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated that a methodologically sound RCT with patient-relevant outcomes was required.

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