SH 74: Is there any evidence that adding antibiotics to cements negatively impacts on the integrity of the cement?

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Recommendation: Current evidence suggest that integrity and biomechanical properties bone cement are negatively influenced by the addition of antibiotics into bone cement; and this impact is associated with the type and dose of the added antibiotics, type of the cement, and bone cement mixing techniques.

Strength of recommendation: Strong

Rationale: On January 2025, the existing literature was comprehensively reviewed to determine the available data about the biomechanical properties of bone cement and antibiotics impregnation. PubMed, Scopus and Cochrane were the used search engines; and the search terms included "bone cement", "cement", "antibiotics-impregnated", "antibiotics-loaded". Only the articles on English were reviewed; and case reports, editorial comments and opinion piecies were excluded. Following title and abstract evaluation, none of the retracted results were specifically confined to shoulder arthroplasty and the high majority of the available data were in vitro experimental studies.

The available data is mainly consisted of in vitro experimental studies and no previous clinical reports confined to shoulder arthroplasty was found. The use of antibiotic-impregnated cement in total joint arthroplasty was initially described by Buchholz and Engelbrecht. Subsequently, they reported a 90% success rate for exchange arthroplasty in the context of infection using antibiotics-loaded bone cement (1). Three primary concerns must be addressed before including an antibiotic into bone cement: physical attributes favorable for cement loading, antibacterial efficacy spectrum, and established effectiveness and safety profile (2).

Numerous antibiotic agents have been evaluated as additions to bone cement, although aminoglycosides, especially gentamicin, remain the first and most frequently utilized due to its optimal bacteriological and physicochemical properties (3). Tobramycin is readily accessible as a pharmaceutical-grade powder suitable for human use for extemporaneous cement mixing, while gentamicin is provided as a liquid solution. Liquid gentamicin has been linked to inadequate cement mixing and hardening, with one study indicating an almost 50% decrease in cement biomechanical strength compared to powdered tobramycin, likely due to less homogeneous integration with the cement powder (4). Liquid antimicrobials should typically be avoided in long-term weight-bearing antibiotics-loaded cement applications like fixation or arthroplasty, but may serve as a cost-effective alternative in situations where structural integrity is less critical (e.g., temporary spacers or beads) (4).

Vancomycin is the most extensively researched glycopeptide and lipoglycopeptide antibiotic, considered the basis of antibiotics-loaded cement preparation in orthopedic surgery because of its broad spectrum of gram-positive antibacterial action and its availability as a thermostable powder formulation. The inclusion of an aminoglycoside has been demonstrated to markedly augment vancomycin elution, hence reinforcing the prevalence of this combination's usage (5). Increased dosages of vancomycin have been employed to compensate for restricted

cement elution, however this may compromise mechanical integrity (6). In a previous study, the degree of strength decline following aging was contingent upon the dosage and type of antibiotic administered. Vancomycin-loaded bone cements exhibited reduced bending strengths compared to the control group, regardless of vancomycin concentration, following aging. Conversely, compressive strength was contingent upon the additional concentration and diminished as the concentration grew (7). The optimal concentration that preserves cement characteristics remains undefined; nonetheless, the consensus among most authors indicates that low antibiotic concentrations (ranging from 5 to 10% by weight) are unlikely to negatively impact these properties (8). Attention must be paid to the mixing and manufacturing circumstances when including antibiotics into bone cement in clinical practice, particularly at concentrations over 2.5% per polymer powder (9). Lilikakis et al. indicated that Palamed G and Copal bone cements, along with their formulations including 2.5% and 5% vancomycin, are deemed safe; nevertheless, the incorporation of 10% vancomycin adversely affects their compressive mechanical properties, rendering them unsuitable for clinical application. Furthermore, particular attention must be paid to the mixing process when incorporating antibiotics into bone cement, as samples with identical antibiotic to polymer powder ratios, yet differing manufacturing methods, had markedly distinct mechanical properties (10).

A prior in vitro investigation (11) revealed that both teicoplanin and ciprofloxacin markedly reduced the mean strength values in compression and four-point bending assessments on Days 1 and 15. Teicoplanin markedly reduced the mean strength values at higher doses in both assessments on Day 1 and Day 15, although ciprofloxacin did not produce a significant alteration in these values. A substantial difference was observed in the compression test on Day 1 when comparing the effects of the two antibiotics at the 3200 mg dose. Conversely, notable differences were observed at the 1600 and 3200 mg dosages on Day 15 in the compression test, and at the 3200 mg dose on Day 15 in the four-point bending test.

Amphotericin B, offered in a deoxycholate form and other lipid-associated formulations, is a broad-spectrum antifungal agent classified as a polyene. Amphotericin B is offered in a thermostable powder formulation and is a fairly large (924 Da) lipophilic molecule. An in vitro research indicated that amphotericin B is barely eluted from cement, and its inclusion may enhance cement strength, maybe due to robust covalent chemical interactions between the antifungal and the cement matrix (12). Liposomal amphotericin B may elute more easily than the deoxycholate formulation because of enhanced cement porosity; however, this also compromises the cement's structural integrity, warranting its avoidance in structural applications (13).

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