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Differential Impact of Corticosteroids on Human Mesenchymal Stem Cells

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Introduction: Previous studies have shown the deleterious effects of corticosteroids on chondrocytes, suggesting a potentiation of degenerative joint disease. Mesenchymal stem cells (MSCs) are direct progenitors of chondrocytes and other musculoskeletal tissue and serve an important anti-inflammatory role. Further evaluation is needed on how corticosteroids interact with this regenerative and reparative cell population. This study assessed the cytotoxicity of corticosteroids on MSCs.

Methods: Human MSCs were isolated and cultured from adipose tissue obtained from 20 patients undergoing primary total hip arthroplasty (THA). MSCs were exposed for 60 minutes to one of the following corticosteroid preparations: betamethasone sodium phosphate-betamethasone acetate (6 mg/mL), dexamethasone sodium phosphate (4 mg/mL), methylprednisolone (40 mg/mL), or triamcinolone acetonide (40 mg/mL). In each treatment group, cells were exposed to 8 different titrations: 0%, 3.125%, 6.25%, 12.5%, 25%, 50%, 75%, and 100%. Cells were allowed to recover in standard culture media for 24 hours and then cell viability was measured using cellular proliferation assays and live-dead cell fluorescent immunostaining.

Results: Exposure to corticosteroids decreased MSC viability in a clear dose-response fashion. However, cell viability was statistically different at every tested concentration between the four corticosteroids ($p < 0.001$). Subsequent pairwise comparisons demonstrated that dexamethasone supported significantly greater cell viability than the other corticosteroids at every concentration ($p < 0.001$). At concentrations between 6.25% and 25%, betamethasone mediated a significant decrease in cell viability when compared to the remaining treatment modalities ($p < 0.001$). These outcomes were maintained after adjusting for age, gender or indication for THA. The cellular proliferation assays and live-dead cell fluorescent staining counts demonstrated positive correlation (r-squared = 0.90).

Conclusion: Intra-articular corticosteroids have a profound, yet differential impact on MSCs. Corticosteroids are frequently used to reduce inflammation in both the perioperative and outpatient setting, hindering innate regenerative capacity in exchange for temporary analgesia. Our study suggests that this risk is potentially mitigated with dexamethasone.