Paper - Basic Science

Paper Session: PTOA

Phosphodiesterase-5 Inhibition Improves Bone Regeneration at Early Stages of Traumatic Avascular Necrosis of the Femoral Head in Rats

Andre Luiz Campos Pessoa*; Victor Hugo Vieira De Oliveira Araujo MSc; ANA LUCIA ROSA NASCIMENTO MSc; Nelson Elias PhD; Jorge José De Carvalho PhD*
Rio de Janeiro State University, Rio de Janeiro, Brazil

Purpose: Posttraumatic avascular necrosis of the femoral head (ANFH) affects young patients and may lead to functional limitation and joint replacement, with total hip arthroplasty, which is a costly procedure. Proposed methods to optimize ischemic tissue regeneration have been reported. Phosphodiesterase-5 inhibitors act by inhibiting the degradation of guanosine 3′,5′-cyclic monophosphate in the nitric oxide pathway, increasing its bioavailability and promoting vascular endothelial growth factor (VEGF)-mediated neovascular recruitment and the induction of tissue regeneration in traumatized bone.

Methods: 30 male Sprague Dawley rats (6 months old) were subjected to an experimental model of traumatic ANFH, divided into 2 groups, according to the administration of 5 mg/kg sildenafil or water (control group). Rats were then sacrificed at 7, 14, and 21 days. Histological (Goldner's trichrome), histochemical (periodic acid-Schiff [PAS]) and immunohistochemical (VEGF and osteopontin) techniques were used to quantify bone and vascular responses.

Results: Higher levels of VEGF ($P < 0.01$) and osteopontin ($P < 0.01$) im munostaining in the epiphysis, greater formation of osteoid tissue ($P < 0.01$ on day 7; $P < 0.05$ on day 14), and higher levels of PAS staining ($P < 0.01$ on day 7) were observed in the sildenafil-treated group.

Conclusion: The present study demonstrated that sildenafil optimized bone tissue regeneration by increasing VEGF signaling and osteopontin expression, with increased bone formation (osteoid and carbohydrate macromolecule deposition) in the early stages following traumatic ischemic insult. Thus, sildenafil treatment may improve the prognosis of patients with osteonecrosis.