DECREASE OF STEROID RELATED AVASCULAR NECROSIS OF THE FEMORAL HEAD UNDER NITRATE PATCH CO-TREATMENT

INTRODUCTION:
Avascular necrosis of the femoral head (FHN) is a common complication with disabling effect for young patients after high dose corticosteroid treatment [1]. Recently, we could show that steroids have a vasoconstrictive effect on lateral epiphyseal arteries of the femoral head (FH) which could lead to FH ischemia and subsequent necrosis [2]. In the current study we investigated the preventive effect of a nitrate patch on steroid related avascular necrosis of the femoral head in a New Zealand white rabbit model.

MATERIALS AND METHODS:
New Zealand White rabbits (male; 3 – 4.5Kg bodyweight) were injected with 20mg/Kg bodyweight methyprednisolone (GC group; n=6). Control animals (n=6) were treated with phosphate buffered saline (PBS). A third group (GC+N; n=6) received additionally to the methylprednisolone a nitrate patch (0.675mg per day). 4 weeks after methylprednisolone injection (i.m.) the animals were sacrificed. For histology and immunohistochemistry, tissue samples were fixed in 3% paraformaldehyde, embedded in paraffin, sectioned, dewaxed, irradiated at 750 W in a microwave oven in 0.01 M sodium citrate buffer, pH 6.0 (twice for 5 min), sections blocked with 3% hydrogen peroxide (endogenous peroxidases) and subsequently with normal serum (1:5 in Tris-buffered saline) of the species in which the primary antibody was raised, immunostained with anti-VEGF or anti-VEGFR-2 followed by biotinylated secondary antibodies and a peroxidase-labelled streptavidin-biotin staining technique; nuclei were counterstained with hemalum. Hematoxylin Eosine (HE), AZAN, Goldner, Ladewig and van Giesson staining were performed according to standard protocols. For quantification of empty lacunae, a histologic sign of FHN [3], histomorphometry was performed.

RESULTS:
Histomorphometry revealed a significant increase of empty lacunae in glucocorticoid (GC) treated animals compared to controls and GC+N treated animals (p<0.001). No significant different in empty lacunae count was detected between the GC+N group and controls (Figure 1). HE staining revealed the different osteocyte amount in the GC versus GC and nitrate patch treated groups (Figure 2).

DISCUSSION:
The current study demonstrates an increased number of empty osteocyte lacunae, which represent a pathologic feature of osteonecrosis, in the GC group. A decrease of empty lacunae was counted in the GC animals after additional treatment with a nitrate patch. This hints to an FHN preventive effect of the nitrate treatment. Also lovastatin, a lipid clearing agent, has been shown to have a preventive effect on FHN in a chicken model [4]. Future investigation has to state the beneficial use of nitrate patches in patients receiving high dose GC treatment in order to prevent FHN. Besides advances in understanding implant loosing [5], this may be a step towards FHN prevention.

REFERENCES:

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