Effects of an Antiplatelet Agent on the Prevention of Steroid-Induced Osteonecrosis in Rabbits

INTRODUCTION

Nontraumatic osteonecrosis (ON) has been proven to be associated with corticosteroid administration (1). However, the pathogenesis of corticosteroid-induced ON remains unclear. ON is still considered to have an ischemic origin with an interruption of the vascular supply. Numerous reports have suggested that ischemic events, including strokes and cardiovascular diseases, are induced by platelet aggregations based on the dysfunction of the endothelium. Also, some reports have described corticosteroid action on the endothelial cell and the regional endothelial bed dysfunction (2). We hypothesized that platelet aggregation at the damaged vascular endothelium caused by corticosteroid administration may play a role in the pathogenesis of ON. Antiplatelet agents were used widely to prevent ischemic events for the inhibitory effect against platelet aggregation at the damaged vascular endothelium.

The purpose of this experimental study was to evaluate the capacity of an antiplatelet agent to reduce the incidence of corticosteroid-induced ON in rabbits.

METHODS

Rabbits were given a single injection of methylprednisolone acetate (20mg/kg of body weight) intramuscularly into the right gluteus medius muscle. Eighty five adult male rabbits were divided randomly into 2 groups and were treated as follows; one group received an antiplatelet agent (clopidogrel; 5mg/kg/day) mixed with normal saline (5ml/kg/day) which was administered by intragastrically passing the liquid through a rubber gastric tube into the stomach (AP; n = 55), the other group received normal saline alone (5ml/kg/day) intragastrically (NS; n = 30). All rabbits were given drugs or normal saline for 3 weeks, beginning 1 week before the methylprednisolone injection.

Two weeks after the methylprednisolone injection, the rabbits were killed. The diagnosis of ON was determined as previously reported (3). Whole areas of the proximal one-third and distal condyles of both femora and humeri (eight regions) were examined histopathologically for ON.

RESULTS

Four out of 55 rabbits died in the AP group, while no rabbits died in the NS group. The incidence of early histological changes of ON in the AP group was lower (p = 0.04) in comparison to the NS group: 24 of 51 (47%) in the AP group and 31 of 30 (70%) in the NS group.

DISCUSSION

Several reports have suggested associations between the dysfunction of endothelial cells and steroid-induced ON (2). However, no reports revealed any obvious mechanisms of the dysfunction of endothelial cell to ischemia on steroid-induced ON. The present study was the first to verify the preventive effects of an antiplatelet agent to steroid-induced ON in animal model. It indicates that platelet aggregation on the damaged vascular endothelium may be a part of the pathogenesis of steroid-induced ON.

However, in our study, the antiplatelet agent did not completely inhibit the steroid-induced ON. Also, some drugs, including anticoagulant, statin, and anti-oxidative drugs have proven to be preventive to steroid-induced ON (5). It is considerable that pathomechanisms of steroid-induced ON are multifactorial. Some combinations of antiplatelet agents and these drugs are better for preventing the steroid-induced ON in human.

REFERENCES


Poster No. 851 • ORS 2011 Annual Meeting