

Influence of doxycycline on the epiphyseal plate cartilage of the rats in experimental osteoarthritis, induced by iodoacetate

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Abstract

In 36 Wistar rats with the iodoacetate-induced experimental osteoarthritis (OA), effects of doxycycline, given orally, were determined on histochemical reactions of glycosaminoglycans (GAG) in the epiphyseal plate cartilage.

The epiphyseal plate of rats with OA was reduced in height (especially the proliferative zone), cell columns were disorganized, many chondrocytes were irregular and polygonal, their nuclei were pycnotic, the intensity of GAG staining was irregular and predominantly reduced, which can be interpreted as signs of degeneration. A concomitant administration of doxycycline in the second group of rats prevented, to some extent, the negative effects of iodoacetate on chondrocytes and led to a more pronounced intensity of GAG reactions in the matrix of the epiphyseal plate.

Key words: osteoarthritis, mono- iodoacetate, doxycycline.

Introduction

In the previous work, we studied histochemical reactions of GAG in the articular cartilage of rats, treated with iodoacetate, suggesting that a concomitant administration of doxycycline had some protective potential on the content of GAGs in chondrocytes and the articular matrix [1].

The aim of the present study was to determine, whether or not doxycycline might play any role of the GAGs histochemical

reactions in the epiphyseal plate cartilage of the rats in experimental osteoarthritis, induced by iodoacetate.

Material and methods

The procedure of the experiment was previously described [1]. Shortly, on the first day, iodoacetate was given to the left posterior knee joint (I group).

The second group of the rats additionally received doxycycline through the gastric tube in doses, comparable with those, used in men. The rats were sacrificed after 7, 14, 21 days (6 rats in each group). Tissue sections were stained with H+E and Safranin O.

Results

In the epiphyseal cartilages from the control right posterior knee joints, four well defined zones: the resting, proliferative, hypertrophic and mineralized, can be determined. The epiphyseal plates in the first group of rats were predominantly strongly reduced in height and, in most areas, the organization of cell columns was severely disturbed. Many of the chondrocytes were of irregular shape and with pycnotic nuclei.

The intensity of GAG staining was predominantly reduced. Focal loss of chondrocytes, negative staining of GAG with fibrillations perpendicular splits, clefts and irregular lacunae were often observed. A great intensity of changes, which can be interpreted as signs of degeneration or necrosis, was observed in almost all the rats Table 1.

Similar histological and histochemical changes were observed in the second group of rats but in 8/18 animals, they were somewhat less pronounced Table 1. The epiphyseal plates were higher, the organization of cell columns was partly preserved, the number of chondrocytes was focally increased with positive GAG histochemical reactions in their vicinity.

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Table 1. Approximate evaluation of histological and histochemical changes in the rats with iodoacetate osteoarthritis, treated with doxycycline.

Group	I			II		
	7	14	21	7	14	21
Days	7	14	21	7	14	21
Intensity of lesions						
• Less pronounced	-	-	-	-	-	-
• More pronounced	2/6	-	-	3/6	2/6	3/6
• Severe	4/6	6/6	6/6	3/6	4/6	3/6

Legend

Counter- the number of rats with lesions

Denominator- the number of rats in subgroup.

Discussion

Intraarticular injections of iodoacetate in experimental animals induce degenerative changes of the articular cartilage, which are similar to osteoarthritis in men [2]. This model is used to study the effects of some non-steroidal and steroidal drugs in the course of osteoarthritis treatment [3, 4].

The results of this study indicate that iodoacetate, injected to the joint, damages not only the superficial articular cartilage but it deeply penetrates the joint structures with similar lesions in the epiphyseal plate cartilage.

Some investigations have shown that matrix metalloproteinase inhibitors, among them doxycycline, are partially protective against cartilage and subchondral bone damage, induced by iodoacetate [3, 4].

As in the previous study [1], in some rats, treated with doxycycline, we observed signs of focal chondrocyte proliferation and of matrix GAG production, what may have indicated a normalizing effect of this drug. Nevertheless, the results of this study need verification by other methods of investigation. They

must also be evaluated with an appropriate caution in the extrapolation of results to human osteoarthritis.

References

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