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The effect of contrast media on the synovial membrane

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Abstract

Objective: To examine the effect of intra-articular injection of contrast media, sorbitol and normal saline on the synovial membrane.
Materials and methods: Sixty three rabbits (126 knees) were used in this study. We injected the knees with amidotrizoate, ioxaglate, iopamidol, iotrol and diluted gadolinium-DTPA (2 mmol/l). Normal saline and sorbitol 27.25% were used for comparison. A histological and histochemical examination of the knees was carried out 1, 2, 10, 20, 30, 40 and 60 days after the injection.
Results: On histological examination, the knees injected with normal saline, ioxaglate and gadolinium-DTPA had a normal appearance. Intra-articular injection of amidotrizoate, iopamidol, iotrol and sorbitol caused early, mild and transient histological changes of the synovium (synovial hyperplasia, infiltration by leucocytes). Furthermore, the knees injected with amidotrizoate presented with late, extensive histological changes (severe synovial hyperplasia, moderate vascular dilatation, severe infiltration by leukocytes).
Conclusion: The results suggest that the chemical structure and not the osmolality of the contrast media is the main cause for the histological changes of the synovium.

Keywords: Arthrography; Contrast media effects; Histology; Rabbit knees; Synovium

1. Introduction

Arthrography is a valuable examination in the evaluation of the glenohumeral joint [1–3] and other articulations. Transient post-procedural pain and swelling are not uncommon following arthrography, especially in the glenohumeral joint [4,5]. These symptoms and signs have been attributed to a direct irritant effect of contrast media on the synovium or joint distension caused by additional influx of fluid into an already distended joint [4]. Studies have demonstrated transient histological changes of the synovial membrane up to 10 days after injection of contrast material into the joint [6–12]. The authors describe the histological alterations of the rabbit synovial membrane up to 60 days, following intra-articular injection of both ionic, non-ionic (low, high osmolality), paramagnetic contrast agent, sorbitol and normal saline. This study aims at describing, in addition to the early alterations of the synovium, the late changes as well.

2. Materials and methods

Sixty three young adult New Zealand male and female white rabbits (126 knees), weighing 3–4.5 kg each were used in this investigation according to the guidelines of the National Institutes of Health for use of laboratory animals. The rabbits were premedicated with Ketamine I.M., 20 mg/kg of body weight, Xylazine I.M., 10 mg/kg of body weight and Atropine I.M., 0.3 mg. Anesthesia was maintained with Ketamine 5 mg/kg/h and Dormicum 0.25 mg/kg/h intra-

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Table 1
Characteristics of substances injected in the knee joints ($n = 126$)

Solutions	n	Iodine (mg/ml)	Osmolality (mosm/kg)
Amidotrizoate[a] (Urografin 76%, Schering)	27	370	2100
Ioxaglate[a] (Hexabrix, Querbet)	16	320	600
Iopamidol[b] (Solutrast-300, Bracco)	21	300	616
Iotrol[b] (Isovist, Schering)	15	300	320
2 mmol/l gadolinium-DTPA (Magnevist, Schering)	12	–	290
Sorbitol 27.25%	21	–	1800
Normal saline	14	–	300

[a] Ionic.
[b] Non-ionic.

venously. Under fluoroscopy, careful knee joint puncture with a hypodermic needle (25 G), under antiseptic conditions, was employed and 1.5 ml of contrast agents, sorbitol and normal saline were injected into the knees (Table 1). Different substances were injected into the knees of the same rabbit. One substance was injected into one knee and another substance into the other of the same rabbit. The animals were sacrificed, with an intravenous overdose of Nembutal, after 1, 2, 10, 20, 30, 40, 60 days (Table 2). The knees were examined histologically for possible pathological changes. Paraffin sections of each specimen were stained with hematoxylin–eosin (H–E), PAS and Giemsa stain. The following pathological alterations were evaluated: synovial hyperplasia, vascular dilatation and leucocytic infiltration: These pathological changes were semiquantitatively evaluated as follows: 0 = no changes, + = mild, ++ = moderate, +++ = severe. Synovial hyperplasia was graded as mild when there were two to four layers of synovial cells, moderate when there were four to five layers of synovial cells and scattered synovial villi formation and severe when more than five layers of synovial cells and extensive synovial villi formation were seen. Vascular dilatation was graded as mild when less than two dilated vessels at low power ($\times 40$) view were seen, moderate when two dilated vessels were seen and severe when more than two dilated vessels were seen. Inflammation was graded as mild when scattered chronic inflammatory cells were seen, moderate when focal aggregates of inflammatory cells were seen and severe when there was a diffuse chronic inflammatory cell infiltrate. In addition, the knees of two rabbits, which had not been injected by any intra-articular solution (control rabbits) were examined to determine the normal appearance. To evaluate the association between the grade of histological changes (nominal 4-level) and the osmolality (interval variable) the ETA asymmetric test [11] was used. Statistical analysis was performed by using the SPSS software (SPSS ver 6, Inc., Chicago).

Table 2
Time of pathologic examination of the knee joints ($n = 126$)

Injected substances	Days							
	1	2	10	20	30	40	60	Total (n)
Amidotrizoate	4	4	4	4	5	2	4	27
Ioxaglate	3	3	2	2	2	2	2	16
Iopamidol	3	3	3	3	3	3	3	21
Iotrol	3	3	3		3		3	15
Gadolinium-DTPA	3	3	2		2		2	12
Sorbitol 27.25%	3	3	3	3	3	3	3	21
Normal saline	2	2	2	2	2	2	2	14

3. Results

The histological examination (Table 3) of the knees injected with normal saline, ioxaglate and gadolinium-DTPA revealed a normal appearance. The knees injected with the non-ionic agents iopamidol and iotrol presented with a transient mild hyperplasia of the synovium and a mild infiltration by leukocytes in one knee of the two animals: at 2 and 10 days with iopamidol and 1 and 2 days with iotrol. The knees injected with sorbitol presented with a transient mild synovial hyperplasia in one knee of the two animals, on 1 and 2 days (Fig. 1).

Intra-articular injection of amidotrizoate caused early, mild and transient histological changes, such as mild synovial hyperplasia and infiltration by leukocytes in one knee of the two animals on day 1 and day 2.

The knees which were also injected with amidrozitoate presented late and extensive histological changes such as severe synovial hyperplasia, moderate vascular dilatation and severe infiltration by leukocytes in one knee of the three animals, on days 20, 30 and 40 (Figs. 2 and 3).

Examination of the control rabbits revealed normal lining cells and fibrous and fatty tissue with no inflammation (Fig. 4).

The osmolality had no significant association with the histological changes (ETA = 0.23).

4. Discussion

There are few reports of histological abnormalities of the synovial membrane following intra-articular injections of contrast media.

Fichtner and Weiss [6] studied the effects of 1 ml of urografin 76% and 1 ml of glucose 50% on the synovial membrane of the knee in rats and detected histological changes 3 h to 1 day after injection that were less severe with the contrast media than with the glucose solution. No abnormalities were seen 2 days after the procedure. Bodnya et al. [7] analyzed the effect of tri-iodinated contrast media (diatrizoates and acetrizoates) on the synovium of the knee in rats. After 2 h they observed transient and reversible inflammatory changes consisting of round-cell infiltration, edema, mucoid degeneration, desquamation of the integument and areas of hemorrhage; these changes decreased after 2 days and had almost disappeared by the fourth day and for this reason they