In vivo physiological changes in the synovial membrane of the knee during reperfusion after arthroscopy

A STUDY USING THE MICRODIALYSIS TECHNIQUE

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We have used in vivo microdialysis to monitor postoperative physiological events in the synovial membrane after arthroscopy. The levels of lactate were significantly higher in the synovial membrane than in the reference tissue (subcutaneous fat) and there was a significant increase in lactate after operation. Blood flow, measured as the ethanol ratio, was stable in both tissues.

Our findings show that there was an increase in the local production of lactate since the levels of lactate in blood and the reference tissue were comparable and did not show a significant increase. There was also a consumption of glucose in the synovial membrane which was not observed in the reference tissue. The levels of pyruvate were higher in the synovial membrane.

A state of reperfusion occurs in the synovial membrane after moderate trauma such as standard arthroscopy of the knee. Microdialysis should be further evaluated in studies of the in vivo physiology of the synovial membrane.

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The synovial joint is an organ which simultaneously ensures stability and movement. The synovial membrane is rich in blood vessels and has an important part in the physiology and metabolism of the joint. Disturbances in synovial metabolism can play a pathophysiological role in the response to trauma as well as in inflammatory and degener-

ative disorders of the joints. The synovial membrane is arranged in folds which occasionally penetrate deep into the interior of the articular cavity. Synovial fluid is produced by the synovial layer of the membrane and apart from facilitating sliding of the articular surfaces it also supplies nutrients and oxygen to the avascular articular cartilage.¹ Arthroscopy is a commonly used procedure especially when intra-articular pathology is to be diagnosed or treated. It causes a reduction of blood flow as a result of compression of the synovial blood vessels caused by joint irrigation under pressure. The events following tissue injury during surgical trauma may also cause vasoconstriction because of the release of substances such as catecholamines and serotonin and also because of hypothermia.^{2,3} These are reversed at the end of the surgical procedure when the joint is emptied of fluid and there is a state of hyperaemia with increased tissue blood flow. During mechanical, traumatic and also primary inflammatory joint disorders, the synovial membrane is affected and increased amounts of synovial fluid may be present. Distension of the joint by synovial fluid may lead to compression of the synovial blood vessels resulting in an altered physiological state. Apart from this, the increased production of synovial fluid may also produce a change in its composition.

There have been no studies of the in vivo metabolism of the synovial membrane as determined by the microdialysis technique. Quantification of the degree and course of anaerobic metabolism in the synovial membrane after surgery is of interest since analysis of basic physiological changes is important to understand better the physiology of the metabolism of the joint after trauma as well as to optimise intra- and postoperative routines regarding surgery on the joint. It is possible to monitor the metabolism continuously and blood flow in situ in various tissues by microdialysis.⁴ Small catheters are introduced into the tissue and perfused with a neutral solvent. Concentrations of metabolites in the outgoing dialysate reflect their tissue level. By adding a flow marker to the perfusate (usually ethanol) it is also possible to monitor tissue flow. Microdialysis has previously been performed in various tissues in the locomotor system, e.g. bone and tendon,⁵⁻⁷ but never in the synovial membrane.

Basic metabolic compounds such as glucose, lactate, glycerol and pyruvate measured in vivo reflect the metabolic status of a particular tissue when analysed in relation to cir-

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Table I. Details of the 13 patients who underwent arthroscopy

Case	Gender	Age (yrs)	Height (cm)	Weight (kg)	Body mass index (BMI)	Operating time (min)	Diagnosis/injury
1	F	48	176	72	23	47	Osteoarthritis
2	F	29	162	80	30	27	Dislocated patella
3	F	59	169	90	32	35	Osteoarthritis
4	F	54	157	83	34	25	Medial meniscus
5	M	38	173	85	28	25	Medial meniscus
6	M	35	184	88	26	23	Medial meniscus
7	M	31	182	100	30	23	Medial meniscus
8	F	26	162	57	22	41	Medial meniscus
9	M	22	178	79	25	38	ACL
10	F	59	165	74	27	55	Lateral meniscus
11	F	25	169	66	23	35	Pain in the knee
12	F	38	177	87	25	19	Pain in the knee
13	M	28	173	91	30	24	Medial meniscus

culating levels and local blood flow. In situ microdialysis has been shown to be a valuable tool for monitoring tissue metabolism.⁸⁻¹¹

Our aim was to quantify how arthroscopy with saline solution irrigation alters the synovial metabolism and local blood flow after operation. We analysed postoperative levels of lactate, glucose, glycerol and pyruvate using microdialysis in the synovial membrane of the knee after arthroscopy in order to monitor basic carbohydrate metabolism during reperfusion. In order to study tissue-specific effects subcutaneous adipose tissue which has been thoroughly studied^{8,9} was simultaneously monitored in the same way. In a subgroup of the patients, circulating levels of glucose and lactate were also measured. Further, we also studied the course of the local blood flow during this postoperative reperfusion using the ethanol escape method.

Patients and Methods

Thirteen otherwise healthy patients (eight women, five men) undergoing diagnostic arthroscopy or arthroscopic meniscectomy were included in the study after giving their informed consent (Table I). The study was approved by the local Ethics Committee at the Karolinska Institute and Huddinge University Hospital.

Operative procedure. General anaesthesia was induced and maintained with propofol, alfentanil and nitrous oxide. After induction of anaesthesia, a reference dialysis catheter with a pore dimension of 20 kD (CMA 60; CMA Microdialysis AB, Stockholm, Sweden) was inserted into the subcutaneous fat of the contralateral thigh which served as a reference tissue. Arthroscopy was then performed. The joint was irrigated with glucose-free saline and on completion of arthroscopy, a dialysis catheter was introduced into the synovial membrane under arthroscopic control to avoid perforation of the joint. For both catheters CMA 106 pumps were used (CMA Microdialysis AB). The probes were connected to the microinfusion pumps and were continuously perfused with Ringer's solution. In seven patients both tis-

sues were perfused at 0.3 µl/min in order to obtain a high recovery of the measured metabolites (glucose and lactate). In the remaining six patients tissue blood flow was indirectly monitored by adding 50 mmol/l of ethanol to the dialysate solvent.⁴ In these studies the perfusion speed was 2.0 ml/min and ethanol, pyruvate and glycerol were determined. The ethanol escape method has previously been shown to be in excellent agreement with the standard xenon washout method.¹²

After equilibration of the system for 40 minutes, samples were collected every 20 minutes for three hours after operation. Thus fraction 1 monitored the metabolic status 40 minutes after completion of surgery. In the seven patients dialysed at 0.3 µl/min, blood samples were also withdrawn from an antecubital vein before operation (fraction 1) and every 20 minutes for three hours after operation (fractions 2 to 10).

Analysis of compounds. The concentrations of glycerol, pyruvate, glucose and lactate in the dialysate were determined by enzymatic fluorometric methods, using a tissue sample analyser which allowed the use of very small sample volumes (CMA/600; CMA Microdialysis AB). Dialysate ethanol was analysed by an enzymatic spectrophotometric method¹³ and the dialysate *versus* perfusate ethanol ratio was calculated. An increase in ratio is equivalent to a decrease in blood flow and *vice versa*. Blood glucose and lactate were analysed at the Department of Clinical Chemistry at Huddinge University Hospital, which is an accredited laboratory.

Statistical analysis. Data are presented as the means ± SEM. Variations over time were evaluated by one-way ANOVA analysis for repeated measures or repeated measures on ranks according to the type of distribution. The level of significance was set at $p < 0.05$.

Results

Changes in the levels of glucose and lactate in the synovial membrane were analysed in seven patients. Blood samples

Fig. 1

Levels of glucose monitored by microdialysis in synovium and reference tissue over a period of three hours after arthroscopy of the knee. There was a significant decrease in the level of glucose in the dialysate with time (ANOVA, $p < 0.05$), but not in the reference tissue.

Fig. 2

Levels of lactate monitored by microdialysis in the synovium and reference tissue over a period of three hours after arthroscopy of the knee. There was a significant increase in the level of lactate in the synovium (ANOVA, $p < 0.05$), but not in the reference tissue.

Fig. 3

Blood levels of glucose and lactate over a period of three hours after arthroscopy of the knee. There were no significant changes in either of the measured compounds with time (ANOVA).

Fig. 4

Ethanol exchange ratio between outgoing/ingoing levels of ethanol monitored by microdialysis in the synovium and reference tissue over a period of three hours after arthroscopy of the knee. There were no significant changes (ANOVA) with time in either tissue.

were also collected but because of technical reasons the level of glucose could only be determined in six and lactate in five. There was a significant decrease in the level of glucose in the dialysate which was indicative of local consumption of glucose in the synovial membrane in the postoperative period (Fig. 1). Simultaneously, there was a significant increase in the level of lactate in the dialysate in the synovial membrane which indicated local production of lactate (Fig. 2). There was, however, no change in the levels of glucose or lactate in the dialysate in the reference tissue

(Figs 1 and 2). During the course of the study, the blood levels of glucose and lactate were stable (Fig. 3).

In six patients blood flow in the synovial membrane and reference tissue was measured by the ethanol escape method. The ethanol ratio was stable in both tissues indicating that there were no changes in local blood flow (Fig. 4). In five of these patients the levels of glycerol and pyruvate were also analysed. The levels of pyruvate in the dialysate increased in the postoperative period in the synovial membrane but did not change throughout the study in the refer-

Fig. 5

Levels of pyruvate monitored by microdialysis in the synovium and reference tissue over a period of three hours after arthroscopy of the knee. There was a significant increase (ANOVA, $p < 0.05$) in the synovium but not in the reference tissue with time.

ence tissue (Fig. 5). There were no significant changes in the levels of dialysate glycerol in either tissue during the experiment (Fig. 6).

The levels of the metabolites in the dialysate in ethanol differed between adipose tissue and the synovial membrane. This could be due to a number of factors besides true differences in tissue concentrations such as recovery and tissue resistance.

Discussion

In this study for the first time we have monitored synovial physiology in vivo using the microdialysis technique to study the effect of supposedly mild surgical trauma on carbohydrate metabolism and blood flow in this tissue. Microdialysis is a well-established method for the continuous monitoring of local metabolism and blood flow.⁵⁻¹² Our study showed a state of reperfusion in the synovial membrane during the postoperative period after arthroscopy of the knee with altered prerequisites concerning metabolism and blood flow. The metabolic findings were in patients undergoing elective arthroscopy because of suspicion of intra-articular pathology such as osteoarthritis or meniscal injury. Since there were no signs of synovial pathology such as swelling or effusion we do not believe that the findings would have been different in normal healthy subjects.

It is clear that the period of ischaemia and the reperfusion-associated events are both involved in tissue injury. Re-establishment of blood flow is essential for the success of a surgical procedure. Quantification of the degree and course of anaerobic metabolism in the synovial membrane after injury to the joint and surgery deserves attention since postoperative effusion and swelling in a joint leads to

Fig. 6

Levels of glycerol monitored by microdialysis in the synovium and reference tissue over a period of three hours after arthroscopy of the knee. There were no significant changes (ANOVA) in either the synovium or reference tissue with time.

impaired function and pain. In the long term, injury to a joint sometimes leads to osteoarthritis. The synovial membrane, which covers the inside of the cavity of the joint except for the cartilaginous areas, controls fluid exchange between the joint and the extra-articular tissues¹⁴ and maintains the lubricating synovial fluid in a proper position. Apart from mechanical properties it is an active organ and has a crucial role in the nutrition and metabolism of the joint since the articular cartilage is avascular and depends on the synovial fluid for both nutrients and oxygen. Monitoring of basic physiological changes in the synovial membrane is therefore of interest.

Local production of lactate and pyruvate in the synovial membrane was found after arthroscopy as was shown by the increase in the levels of lactate and pyruvate in the dialysate of synovial membrane and by no change in the reference tissue or in peripheral blood. In another group of patients blood flow was measured by the ethanol method at a higher perfusion speed than that of the microdialysis fluid. Despite the fact that measurements were performed in another group of patients we conclude, nevertheless, that there was no change in local (or reference tissue) blood flow. There was also a consumption of glucose in the synovial membrane but not in reference tissue or blood.

A hypermetabolic state with an increase in carbohydrate consumption, a decrease in the level of glucose and an increase in pyruvate and anaerobic metabolism with formation of lactate in spite of no change in blood flow occurred during reperfusion after arthroscopy. The synovial membrane plays an important role in the physiology and pathology of the joint. The nutrition of the avascular cartilage depends greatly on the synovial membrane and resulting synovial fluid. In our study, compression of the synovial

blood vessels could be caused by irrigation fluid. In other conditions, such as post-traumatic effusion and bleeding, effusion may also lead to an increased pressure against the synovial membrane with compression of its vessels and relative ischaemia.

Our observations of a reperfusion syndrome in the synovial membrane after intraoperative distension of the synovial membrane with consequent compression of the synovial blood vessels may be of importance for the understanding of the pathological process leading to post-traumatic degeneration of articular cartilage, i.e. osteoarthritis. Our study also suggests that microdialysis is a useful tool for studying metabolism in vivo and blood flow in the synovial membrane.

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