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RESEARCH

Changes in synovial fluid in different knee-joint diseases☆,☆☆

P. Martínez de Albornoz Torrente[a], **F. Forriol**[b,*]

[a] *Servicio de Cirugía Ortopédica y Traumatología, Hospital de Torrejón, Madrid, Spain*
[b] *Facultad de Medicina, Universidad CEU San Pablo, Campus de Montepríncipe, Boadilla del Monte, Madrid, Spain*

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KEYWORDS
Synovial fluid;
Cytokines;
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Joint cartilage

Abstract
Objective: To analyse the changes in synovial fluid (SF) in the most common knees joint diseases, and to establish a relationship according to its concentration.
Material and methods: A total of 62 synovial fluids were analysed from knees with, meniscus disease (32), anterior cruciate ligament (ACL) (17) and isolated chondral injury (13). A quantitative and quality study was performed on each sample, which included cytokines IL-1, IL-2, IL-6, IL-10, TNF-α, and growth factors (IGF-1 and TGF-β).
Results: The SF environment in the ACL injury was mainly anabolic and inflammatory, with increased levels of IL1, IL6, significant levels of TGF-β ($P = .02$ and $P = .004$), IL-10 ($P = .046$ and $P = .047$) and significantly decreased levels of TNF-α ($P = .02$ and $P = .004$). There was mainly a catabolic environment in chondral and meniscal disease, with a significant increase in TNF-α and a significant decrease in TGF-β ($P = .02$ and $P = .004$). The differences were greater in the case of isolated chondral injury.
Conclusion: The changes observed show that, as well as the biomechanical changes, the SF has a negative effect on joint homeostasis, leaving its composition varying depending upon the type of pathology.

PALABRAS CLAVE
Líquido sinovial;
Citocinas;
LCA;
Menisco;
Cartílago articular

Modificación del líquido sinovial en diferentes afecciones articulares de la rodilla

Resumen
Objetivo: Analizar las modificaciones del líquido sinovial (LS) en las afecciones articulares más frecuentes de la rodilla y establecer una relación en función de su concentración.
Material y métodos: Se analizaron 62 muestras de LS de rodillas con afección meniscal (32), rotura del ligamento cruzado anterior (LCA) (17) y lesión condral aislada (13). De cada muestra se realizó un estudio cuantitativo y cualitativo de las citocinas (IL-1, IL-2, IL-6, IL-10, TNF-α) y factores de crecimiento (IGF-1, TGF-β).

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* Corresponding author.
E-mail address: fforriol@gmail.com (F. Forriol).

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Resultados: En la lesión del LCA, el ambiente del LS fue predominantemente anabólico e inflamatorio, con niveles elevados de IL1, IL6, significativos de TGF-β (p = 0,02 y p = 0,004), IL-10 (p = 0,046 y p = 0,047) y significativamente disminuidos de TNF-α (p = 0,02 y p = 0,004). En la afección condral y meniscal, predominó un ambiente catabólico, con elevación significativa del TNF-α y disminución significativa del TGF-β (p = 0,02 y p = 0,004). Las diferencias fueron mayores en el caso de la lesión condral aislada.
Conclusión: Los cambios observados señalan que en la lesión articular, además de la alteración biomecánica, el LS influye negativamente en la homeostasis articular, variando su composición según el tipo de afección.

Introduction

Sokoloff[1] considered joint cartilage, synovial liquid, synovial membrane and subchondral bone as a functional unit to which other aspects should be added, such as the interchange of oxygen and nutrients and the release of hormones and growth factors. There is growing interest in developing techniques that protect and repair joint cartilage lesions. Epidemiological studies indicate that approximately 6% of adults have a degenerative knee problem, a percentage that increases to 10% for individuals who are older than 65.[2]

From a biochemical point of view, joint cartilage is a tissue capable of constantly synthesising and degrading the components of the extracellular matrix. The mechanisms of action of growth factors and interleukins (IL) strengthen or inhibit the synthesis of the extracellular matrix components, as well as favouring the action of molecules that degrade cartilage, such as the proteases or their tissue inhibitors.[3] The mechanical properties of cartilage vary when alterations in the joint structures occur, such as in anterior cruciate ligament (ACL) section, meniscectomy or tibial plateau resection.[4] The synovial liquid (SL) that surrounds the knee joint structures is a dialysed plasma product, secreted by the synovial membrane; under normal conditions, it does not contain coagulation factors, erythrocytes or haemoglobin, but it does present hyaluronate and a lubricating glycoprotein called lubricin, which reduce friction and lubricate the joint.[5]

With the advances in molecular biology, different patterns for protein and cytokine expression in the SL have gradually been defined and these have been linked with joint degradation. Cytokines are implicated in inflammation and joint damage, which is why their concentration in the SL varies according to the state of the joint. The main intra-articular cytokines involved in joint inflammation are the interleukins (IL)-1, 6 and 8, tumour necrosis factor-α (TNF-α) and granulocyte-macrophage colony stimulating factor (GM-CSF). Likewise, there are other anabolic factors, such as insulin-like growth factor (IGF) and transforming growth factor-β (TGF-β) that are also expressed in the SL and can therefore be analysed. The main effects of growth factors on the chondrocytes are accepted to be stimulating the synthesis of cartilage extracellular matrix and inhibiting protease activation.[6]

We accept the idea that mediating SL anabolic–catabolic balance changes the environment and the state of the structures that it bathes and we view SL as the natural cartilage lubricant in the diarthrodial joints, which transports the nutritive elements and the joint residues. Based on this idea, we hypothesised that each type of joint disease should modify SL composition in a different way, changing the metabolic balance and provoking a dominance of catabolic factors; the goals of our study were to analyse SL growth factors and SL cytokines in patients with different knee conditions (ACL tear, meniscus lesion or chondropathy) and to establish a relationship according to their concentrations.

Material and methodology

In a population of patients in a mutual insurance company, after each individual signed an informed consent, we extracted synovial liquid before the knee arthroscopy. All patients were to be operated on for anterior cruciate ligament (ACL) tears, meniscus tears or chondral lesions from tibial plateau fracture, knee osteotomy or joint cleaning.

Table 1 presents the demographic data for the population studied. Knee joint arthrocentesis was performed under sterile conditions, in the operating theatre, with a 10-cm^3 syringe. Once the sample was obtained, it was immediately sent to the laboratory, following preservation protocol. To prevent sample handling and contamination, the samples were kept in the same syringes at 4 °C, for no more than 72 h in the refrigerator.

A total of 62 SL samples were obtained. By knee condition, 32 corresponded to meniscal lesion, 17 were from ACL tear and 13 from chondral lesion as the sole diagnosis. The presence of cytokines (IL-1, IL-2, IL-6, IL-10, TNF-α) and growth factors (IGF-1, TGF-β) were analysed in the SL quantitatively and qualitatively.

We excluded from the study the patients who did not sign the informed consent form, who had any combined knee lesion, presented degenerative alterations, had had previous trauma in either of the two lower limbs, presented varus or valgus angles above 10°, or who had received an operation on the contralateral knee, because of the mechanical overload that might be produced on the study knee.

In the stage of SL reading, each sample was concentrated (1:100) in 5-cm^3 tubes (Centricon®, Millipore) for the quantitative and qualitative molecule study. We used the enzyme-linked immunosorbent assay (ELISA) technique to analyse the growth factors (IGF-1, TGF-β) and the