

Scintigraphic studies of the lymphatic articular function in normal and pathological knees

MAMEDE ALBUQUERQUE, JOÃO PEDROSO DE LIMA, ALVES CARDOSO,
NORBERTO CANHA, RODRIGUES BRANCO

Depart. of Orthop. and Traum., University Hosp., Coimbra
Inst. of Nuclear Medicine, Faculty of Med., Coimbra

SUMMARY

The twenty-four hours articular retention and nodal accumulation of ^{99m}Tc labelled dextran (Molecular weight = 70000) injected in the articular cavity of normal (Grp I, n = 68) and pathological (n = 164) knees have been studied by scintigraphic techniques in 115 consecutive patients suffering from initial (Grp II, n = 28 knees) or advanced (Grp III, n = 63 knees) chondropathy or from osteoarthritis (Grp IV, n = 73 knees). Expressed with reference to the injected activity, the pathological joints exhibited an higher retention (decreased lymphatic elimination) of the label in the articulation (Grp II = $84.24 \pm 3.183\%$, Grp III = $85.99 \pm 3.152\%$, Grp IV = $88.72 \pm 3.622\%$) than the normal joints showed (Grp I = $77.44 \pm 4.77\%$, $p < 0.01$ between grp I and II, I and III, I and IV). On the other hand, the nodal accumulation of the labelled molecules appeared greater in the pathological joints (Grp II = $2.41 \pm 0.411\%$, Grp III = $3.05 \pm 0.638\%$, Grp IV = $5.76 \pm 2.197\%$) than in the normal ones (Grp I = $1.88 \pm 0.209\%$, $p < 0.01$ between grp I and II, I and III, I and IV). The present study thus demonstrate in diseased knees and articulations the existence of abnormal lymphatic function that parallels the severity of the disease.

RÉSUMÉ

La rétention articulaire et l'accumulation ganglionnaire de dextran (poids moléculaire = 70000) marqué au ^{99m}Tc Technétium et injecté dans la cavité articulaire de genoux normaux (Groupe I, n = 66) ont été étudiées par technique scintigraphique dans 115 patients consécutifs souffrant soit de chondropathie débutante (Groupe II = 28 genoux) ou avancée (Groupe III = 63 genoux), soit d'ostéoartrites (Groupe IV = 73 genoux).

Exprimée par rapport à l'activité initialement injectée, les genoux pathologiques montrent une rétention articulaire plus élevée (une élimination lymphatique moindre) du traceur (Groupe II = $84.24 \pm 3.18\%$, Groupe III = $85.99 \pm 3.15\%$, Groupe IV = $88.72 \pm 3.62\%$) que les normaux (Groupe I = $77.44 \pm 4.77\%$, $P < 0,01$). A l'opposé, l'accumulation ganglionnaire du traceur apparaît plus grande dans les cas pathologiques (Groupe II = $2.41 \pm 0.41\%$, Groupe III = $3.05 \pm 0.64\%$, Groupe IV = $5.76 \pm 2.20\%$) que dans les cas normaux (Groupe I = $1.88 \pm 0.21\%$, $P < 0,01$).

La présente étude démontre donc, dans le cas de pathologies articulaires, l'existence d'anomalies de la fonction lymphatique dont l'importance apparaît corrélée à la sévérité de l'atteinte articulaire.

KEY WORDS: Articular Lymphoscintigraphy, osteoarthritis of the knee, articular lymphatic dysfunction, ^{99m}Tc -labelled Dextran, degenerative knee arthropathy.

Reprints:

Dr. Mamede Albuquerque
Ortopedia 2
University Hospital
3049 Coimbra - Portugal

INTRODUCTION

In spite of being morphologically described since 1948, by Davies (1), the articular lymphatic system is still a subject with few and vague bibliographical references (2), mainly in what involves its functional exploitation. Nevertheless, in the articular pathology, what really matters is not the morphology of articular lymphatic system but its function. This, that keep the "homeostasis of the articular space" (drainage of fluids and proteins of the chondrosynovial space), is not morphologically objectivable but can be substantiated by quantitative studies.

We thus first studied in dogs the feasibility of the articular lymphatic investigations by scintigraphic techniques and using ^{99m}Tc labelled dextran (3). A standardized method was then obtained and since five years is now routinely used in human patients.

The aim of the present paper is to report the results we obtained in patients with and without osteoarticular diseases of the knees.

PATIENTS AND METHODS

1. - Patients and materials

230 scintigraphic investigations have been performed in 115 patients (26 women and 89 men, mean age = 44 years old, range = 15 - 74 years) with degenerative knee arthropathy (unilateral: 66 pat. and bilateral: 49). The diagnosis of joint disease was made clinically, radiographically, and verified by notable cartilage damage at time of arthrotomy. According to the clinical and peroperative data (4) the studied knees were classified in four groups: grp I - normal knee (n = 66) — grp II - initial chondropathy (cartilage edeme, n = 28) — grp III - advanced chondropathy (cartilage fissuration, n = 63) — grp IV - osteo-arthritis (cartilage erosion, n = 73).

2. - Scintigraphic methods

2.1. - Miculicities of dextran* (molecular weight = 70000) labelled according to the method of Henze (5) with ^{99m}Tc Technetium pertechnetate (labelling efficiency superior to 95 %) have been injected in each knee after being mixed with 10 ml of physiological saline. The patients deambulation was encouraged throughout the lymphoscintigraphy study.

Scintigraphy pictures of the knees and of subdiaphragmatic nodes (at least 200 to 500 kcounts per picture, matrix registration time for knee = 60 sec and for nodes = 300 sec) were then obtained just after injection and at several different intervals during 24 hours using a Gamma Camera (Maxi Camera GE II, 400 T) equipped with a parallel hole all purpose collimator and connected to a medical computer (Data General Dasher D II).

Areas of interest were drawn for patient and each time post injection on the knees (rectangular area covering all the knee) and subdiaphragmatic nodes (area covering all visualised nodes). Recorded activities were then expressed with reference to the activities recorded in the knees just after injection and the following parameters calculated :

- for each knee, we examined tracer disappearance as a function of time. The represented values were the percentage of radioactivity which remained in the knee as a function of the amount initially injected ;
- for the nodes, we examined the nodal subdiaphragmatic accumulation as a function of time. The represented activity were the percentage of activity accumulated in relation to the tracer activity after first injected in the knee.

For this work, only the 24 values are analysed. Statistical analysis of this values was performed using the Kruskal-Wallis and Mann Whitney U Test.

RESULTS

1. Articular lymphoscintigraphy of the knee - Morphological aspects.

The radiopharmaceutical injected in the knee joint allow not only to delineate the articular spaces (Fig. 1) but also sometimes to visualize the lymphatic vessels (Fig. 2) starting from the injected knees and in all cases the lymph nodes that terminate them (Fig. 3).

2. Articular lymphoscintigraphy of the knee - 24 hours quantifications.

In the articular pathology what really matters is not the morphology of the articular lymphatic system but the knowledge of its function. This function, which is very important to keep the "homeostasis" of the articular ambience (drainage of the fluid and proteins of chondro-synovial space), is not morphologically objectivable but it can only be substantiated by quantitative studies.

For this work, all the 24 hours quantification values are statistically analysed. In contrast to the normal knee, the retention of the radiopharmaceutically are bigger in the pathologic joint (retention of the label in the articulation) : (Grp I = 77,44 % ± 4,77 %, Grp II = 84,24 % ± 3,181 %, Grp III = 85,99 % ± 3,152 %, Grp IV = 88,72 % ± 3,622 % — Table 1). The tracer also accumulated more in the regional nodes draining the pathological knee (Grp I = 1,88 % ± 0,209 %, Grp II = 2,41 % ± 0,411 %, Grp III = 3,05 % ± 0,638 %, Grp IV = 5,76 % ± 2,197 % — Table 2).

For all this values, the Kruskal Wallis Test is statistically demonstrative of significant differences ($p < 0,01$) between the healthy knee and the several groups of pathological knees. The Mann Whitney U Test realized among Grp I / grp II, grp II / grp III, grp III / grp IV is demonstrative that the medias of 24 hours scintigraphic quantifications are significantly different ($pm < 0,01$) in all the several groups tested.

* 0,3 cc.

DISCUSSION

The articulation constitutes a large extracellular liquid space in which the same type of fluid assume different functions as a tissular fluid or a synovial liquid. It represents a real extravascular circulation of water, proteins and other nutrients. This fluid, which is free in the articular cavity and retained in the complex reticulum of the cartilage, is closely related with the tissular liquid of the synovial membrane. The absence of a basal membrane in the synovial tissue facilitates the nutrition of the cartilage, structure without any vessels. In this extravascular reservoir of fluid, two different interfaces may be recognized : the synovial membrane / the articular fluid and the articular fluid / cartilage. The first one has more active and direct exchange, but the second, though quantitatively with less exchanges, has important physical functions. Among them, the hyaluronic acid accomplishes the physical properties of a fluid thick membrane, regulating the permeability and the diffusion of the solutions and may be considered - by its functions - a real biological semiconductor. According to this model, it is easy, in theory, to understand what is the possible role of a normal lymphatic function and its importance to assure a normal nutrition of the articulation. The lymphatic drainage of the articular fluids and proteins also realize a control of the chondrosynovial tissular pression and of the articular fluid volume.

Because the ability of the articular lymphatics to remove the labelled particles depend on their size, it may hypotetized that the success obtained with the dextran we used is due to its low molecular weight. Bigger particles could be hardly reabsorbed by the synovial membrane (6) and a large part of the radiopharmaceutical retained in the articulation. Particles of molecular weight inferior to 40 000 can additionally recirculate once again through the blood capilars.

The present study shows an articular lymphatic disfunction in the osteoarthritis. Quantifications made in degenerative arthroses also allowed to distinguish between the lymphatic function of the normal and pathological knees. The values show indeed increased articular retention and nodal accumulation of the label, that paralleled the severity of the osteoarticular disease. The biggest was the retention in the knee and the accumulation in the node, the most advanced is the degenerative arthroses. The represented results thus demonstrate a lymphatic articular dysfunction which coexists with all the other alterations of the articular " ambience " known in this pathologies and that is proportional to the importance of the cartilage lesion.

ACKNOWLEDGEMENTS

The authors are grateful to Dra Lucilia MACEDO of the Department of Maths of University of Coimbra for statistical advice.

REFERENCES

1. DAVIES D.V. (1946) — Lymphatics of the synovial membrane. *J. Anat.*, 80 : 21-23.
2. VITTAS D., REIMANN I., NIELSEN S.L. (1987) — Intra-articular lymphoscintigraphy of the human knee joint : a preliminary study. *Lymphology*, 20 : 98-101.
3. ALBUQUERQUE M., LIMA J.P., CARDOSO A., FERREIRA M., PIRES J., CANHA M., BRANCO J.R. (1990) — Lymphographie articulaire indirecte chez l'animal utilisant le dextran 70 000. *Rev. Chir. Orthop.*, 76 : 80-84.
4. FICAT P. (1979) — Cartilage et arthrose. *Masson*.
5. HENZE E. (1982) — Lymphoscintigraphy with ^{99m}Tc-labelled dextran. *J. Nucl. Med.*, 23 : 923-929.
6. ERCAN M.T., SCHNEIDERREIT M., SENEKOWITSCH R., KRIEGEL H. (1985) — Evaluation of ^{99m}Tc-dextran as a lymphoscintigraphic agent in rabbits. *Eur. J. Nucl. Med.*, 11 : 80-84.

Fig. 1

Articular lymphoscintigraphic study in the arthropathy degenerative of the knee
99 mTc labelled Dextran (PM = 70 000) (Aspect of the injected articulations)
Aspect of the injected articulations (image obtained at 6 hours of lymphoscintigraphic exam) in a patient with unilateral knee degenerative arthropathy (chronic synovitis). Articular space expansion of the suffering knee.
N = normal knee. P = pathological knee.

Etude lymphoscintigraphique articulaire d'une arthropathie dégénérative du genou : aspect des cavités articulaires

Image scintigraphique centrée sur les genoux et obtenue 6 heures après injection chez un patient avec arthropathie dégénérative unilatérale (Synovite chronique du genou droit).

N = genou Normal. P = genou Pathologique.

L'espace articulaire droit apparaît plus grand que le gauche.

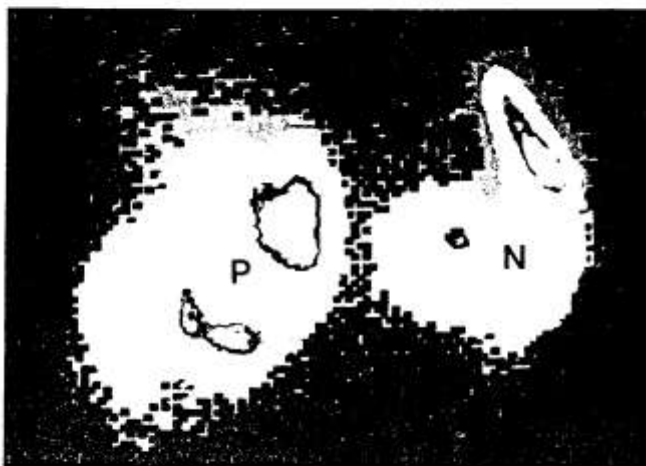


Fig. 3

Articular lymphoscintigraphic study in the arthropathy degenerative in the knee
99 mTc labelled Dextran (PM = 70 000) (Aspect of the active lymph nodes)
Image obtained 6 hours after the articular injection of both knees with 2 mCi of the product in a patient with unilateral knee degenerative arthropathy. A bigger impregnation in inguinal and lomboarctic lymph nodes in the side of the suffering articulation.

N = lymph nodes of the side of the normal knee

P = lymph nodes of the side of the pathological knee

B = bladder.

Etude lymphoscintigraphique articulaire d'une arthropathie dégénérative du genou : image des ganglions.

Image scintigraphique centrée sur les structures ganglionnaires drainant les genoux injectés (N = côté Normal, P = côté Pathologique) et obtenue 8 heures après injection chez un patient avec arthropathie dégénérative unilatérale. Les ganglions inguinaux et lomboarctiques du côté pathologique montrent une activité, une captation plus élevée que celle du côté normal.

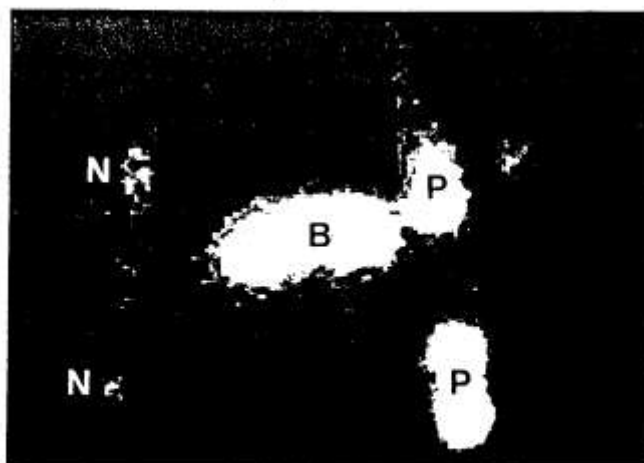


Fig. 2

Articular lymphoscintigraphic study in the arthropathy degenerative of the knee
99 mTc labelled Dextran (PM = 70 000)
(Aspect of the lymphatic channels)

Image obtained two hours after the injection of the product in both knees in a patient with unilateral chondroarthry. Starting in the pathological knee we can see the lymphatic vessels.

N = injected normal knee

P = injected pathological knee

LC = lymphatic channels

LN = impregnation of lymph nodes of pathological knee side.

Etude lymphoscintigraphique articulaire d'une arthropathie dégénérative du genou : image des vaisseaux lymphatiques.

Image scintigraphique centrée sur les vaisseaux lymphatiques (LC) et les structures ganglionnaires (LN) sus-jacents aux genoux injectés (N = genou Normal, P = genou Pathologique) et obtenue 2 heures après injection chez un patient avec chondroarthry unilatérale.



Table 1

*Articular lymphoscintigraphic study
in the arthropathy degenerative of the knee
Statistical analysis of the 24 hours quantification values
obtained in an area of interest including the whole knee joint.*

*Résultats de rétention articulaire après 24 heures
obtenus dans les différents groupes étudiés.*

	Normal	Initial Chondr.	Advanc. Chondr.	Ostheo Arthr.
MEAN	77,44	84,24	85,99	88,72
St dev.	4,77	3,188	3,152	3,622
Minima	64,61	75,11	78,48	77,19
Maxima	96,94	89,95	97,20	96,45
Limits :				
Minima	76,267	83,000	85,201	87,874
Maxima	78,612	85,473	86,789	89,564

Table 2

*Articular lymphoscintigraphic study
in the arthropathy degenerative of the knee
Statistical analysis of the 24 hours quantification values
obtained in an area of interest including all the active lymph nodes
draining the knee.*

*Résultats de l'accumulation ganglionnaire après 24 heures
obtenus dans les différents groupes étudiés.*

	Normal	Initial Chondr.	Advanc. Chondr.	Ostheo Arthr.
MEAN	1,88	2,41	3,05	5,76
St dev.	0,209	0,411	0,638	2,197
Minima	1,12	1,76	1,92	2,56
Maxima	2,5	3,11	5,56	12,19
Limits :				
Minima	1,826	2,246	2,889	5,251
Maxima	1,928	2,565	3,210	6,277