Assessment of Synovial Fluid *p*H in Osteoarthritis of the HIP and Knee

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Osteoarthritis (OA) is a developing process with a multifactorial causality in which changes of the synovial fluid characteristics occur. Hypothesis: synovial fluid pH in severe OA is correlated with other patient parameters. Synovial fluid pH from 50 patients with severe OA (knee/hip) was determined. The results were assessed and correlations with the patients antropologic data and biological markers were analyzed. 50 patients (26 knee OA and 24 hip OA) were analyzed. The average synovial fluid pH was 7.35 indicating slightly lower levels than in normal joints. Higher pH values were observed in males, under 60 years, secondary OA, Rh+ and Hbg under 13.5g/dL. Lower pH values were obtained in females, age under 60 years, primary OA, Rh-, Hbg over 13.5g/dL, hypertensive and diabetic patients. The synovial fluid pH may not be an appropriate biomarker for severe OA disease. Some patient variables might be correlated with synovial blood pH.

Keywords: osteoarthritis, pH, synovial fluid, knee, hip

Osteoarthritis (OA) is associated with the ageing process and it is an important health problem due to the increased number of patients affected and to its impact in terms of locomotory handicap. The pathophysiological mechanisms of osteoarthritis are multiple. The cartilage degeneration is a major part of this process but the subchondral bone tissue, synovial membrane and synovial liquid are also of critical importance. The cartilage matrix alterations, produced by proteolytic enzymes, releases matrix macromolecule fragments and neo-antigens into the synovial fluid which promotes inflammation in the synovial membrane. As a consequence, mediators which increase cartilage degradation and trigger further inflammation are released [1].

The synovial fluid is an ultra-filtrate of blood plasma which additionally contains glycoproteins, hyaluronic acid, lubricin, collengases and proteinases. Substances pass into and out of the synovial fluid depending upon their molecular size. In particular situations (eg. inflammation) additional components pass into the sinovial fluid [2].

The normal synovial fluid is clear, pale yellow, viscid, and does not clot. It forms a thin film covering surfaces of synovium and cartilage within the joint space with important lubrication capacity. The sinovial fluid temperature is 32 degree Celsius (peripheral joints are cooler than core body temperature). Its viscosity measured by the string sign is 1-2 inches and the normal *p*H is 7.4. [3]

OA understanding usually focuses on the cartilage degradation process where OA is presumed to start, largely neglecting the changes that occur in the synovial membrane and in the synovial fluid. Sinovial fluid *p*H can be a useful marker of local inflammatory activity because changes in *p*H may influence many of the processes involved in inflammation and the transfer of drugs into the joint.

In this study we measured the pH of the sinovial fluid in patients with severe knee and hip OA. A correlation between synovial fluid and some of the parameters of the patients was analysed.

Experimental part

The study was performed in 2016-2017 in the Department of Orthopaedic Surgery and Trauma and the

Department of Biochemistry, University of Sibiu. 50 consecutive patients, with severe OA of hip and knee joints (Kellgren/Lawrence (K/L) stage IV) were enrolled in this study. All the patients were diagnosed and proposed for total joint arthroplasty before admission. A series of preoperative analysis were performed after admission, before surgery.

At surgery, a 3-5 mL sinovial fluid sample was obtained through joint aspiration. Aspiration with a 5mL syringe was performed after the approach was made, both in knee and in hip arthroplasty just before incising the joint capsule. Care was taken not to aspirate other fluids (blood).

The sample was then analysed in the department of biochemistry and the value of the synovial fluid pH was determined. Synovial liquid pH measurements were carried out on an multi-parameter (Seven Excellence, Mettler Toledo, USA) equipped with with an digital pH meter with a single glass electrode (InLab Pro-ISM-IP67, Mettler Toledo, USA). A three point calibration (pH = 4.01; 7.00 and 9.21) was performed, daily, using standard buffer solutions (Mettler Toledo, USA). pH measurements were carried out immediately after samples were collected.

All the data of the patients were extracted from the personal charts at admission. The following data were recorded: gender, age, provenience (rural/urban), OA localisation (hip/knee), OA aetiology (primary/secondary), comorbidities (Hypertension, Ischemic Cardiopathy, Diabetes mellitus, laboratory parameters (Haemoglobin-Hgb, Haematocrit - Hct, Rh, blood type). All the data were saved in a excel sheet. Correlations between patient data and the pH values were analysed.

Results and discussions

The studied group consisted of 50 patients. The mean age was 64.96 years with a male to female ratio of 1/3. Of this group, 26 were undergoing knee and 24 total hip replacements.

The average *p*H value of the sinovial fluid was 7.35 with a maximum of 7.68 and a minimum of 6.8. This shows only a minor difference to the normal joint *p*H. The majority (76.9%) of the results were clustered between the values of 7.24 and 7.5. Other studies showed that the *p*H of the

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OA synovial fluid shift to more acidic zone (from normal 7.4 to 6.85 in OA) suggesting this as a trigger of OA exacerbation. [4] Lower *p*H of diseased synovial fluid disrupts normal hydrogen bonding and partially denatures synovial fluid proteins altering the hyaluronic acid structure and concentration, leading to decreased viscosity [5]. This is detrimental to the function of the joints enhancing the evolution of arthritic changes [6]. It is well known that synovial pathology plays an important role in osteoarthritis and there is a direct relationship between the synovial reaction and the clinical symptoms. This suggests that the synovial membrane is involved in the disease progression [7, 8]. Correlations between the synovial fluid *p*H and the recorded data were performed.

pH vs gender

66.6% were females and only 33.3% were males. Medium synovial fluid *p*H was 7.319 for the female population and 7.488 for the male population. The male population had a significant higher synovial fluid *p*H then the female population.

pH vs age

We divided all the patients in two groups - group one with ages over 60 years (average 70.76 years) and group two with ages under 60 years (average 50 years). The average value of the synovial fluid *p*H was 7.35 for the first group and 7.45 for second suggesting that at higher ages (over 60 years), are associated with lower synovial fluid pH values.

pH vs localisation (Hip/Knee)

The hip arthritis patients had a average synovial fluid value of 7.399 whereas the knee arthritic patients the average *p*H value was of 7.322. A slightly increased *p*H value was observed in the hip population. Our data does not demonstrate statistically significant differences in synovial fluid pH between osteoarthritic knee joints and hip joints. Because all patients were in advanced OA stages (Kellgren-Laurens), a correlation with the stage of the disease was not possible.

pH vs provenience (rural/urban)

66% from all patients were of urban provenience while only 34% came from the rural areas. Medium synovial fluid *p*H was 7.351 for the urban population and 7.357 for the rural population. No correlation with the medium of provenience was found.

pH vs aetiology of arthritis (primary/secondary)

The majority of the patients had primary arthritis (60%) and their mean synovial fluid pH was 7.322. 40% of the patients were of secondary origin (AVN, Fracture) and their average *p*H value was of 7.44 showing a significantly higher range in comparison with the primary arthritis cases. No explanation of this correlation could be found.

pH vs RH (positive/negative)

There was a higher number of Rh-positive patients (68%) and their average pH was 7.6 whereas the Rh-negative patiens (32%) had a mean value of 7.315, suggesting that there might be a correlation between Rh and synovial fluid pH.

pH vs HGB

We divided all the patients in two groups - group one with HGB values over 13.5g/dL and group 2 with Hgb values under 13.5g/dL. The average value of the synovial fluid *p*H

was 7.14 for the first group and 7.32 for second sugesting that higher Hgb values are associated with lower *p*H values.

pH vs blood group

Regarding the blood group, the patients distribution and the mean synovial fluid pH were: group A – 41.66% - 7.42; group B – 4.16% - 7.32, group AB – 4.16% - 7.45, group O -50% - 7.339. Although group A and AB patients had slightly higher *p*H values in comparison with O and B, there was no statistical difference. The relatively low number of patients is a bias in this regard.

pH vs comorbidity

Because of their higher prevalence, we studied the potential influence of cardiovascular diseases and diabetes on the synovial fluid pH. We found that the diabetes patients (62.5%) and the hypertensive patients (70.8%) had lower pH values while in the patients with ischaemic heart desease group there was no influence on the pH value was noted. The relatively low number of patients could influence our result.

The presented results show higher *p*H values in males, under 60 years, secondary OA, Rh+ and Hbg under 13.5g/ dL and lower pH values in females, age under 60 years, primary OA, Rh-, Hbg over 13.5g/dL, hypertensive and diabetic population. There was no correlation between the synovial fluid *p*H and the following parameters: the localization of OA (knee, hip), origin of the population (rural/ urban), ischemic heart disease or blood group.

The relative low number of the patients enrolled in this study can be considered as a limitation of this study.

No correlation of synovial fluid *p*H with blood \dot{p} H was performed. Other studies revealed that the mean values for blood and synovial fluid differ significantly, in OA patients the synovial fluid *p*H being significantly less than the blood *p*H. [6]

Joints are complex structures that allow repetitive, pain free, frictionless movements because of their very specialised structure. The synovial membrane is very important due to its role in producing the synovial fluid which nourishes the chondrocytes due to its role in removing metabolites and matrix degradation products from the synovial space. [1] Our results can be compared with the results of other studies in which more sophisticated techniques were applied. However, analysis of synovial fluid *p*H has not been shown to be useful in terms of evaluating patients with severe joint OA.

Conclusions

The synovial fluid pH may not be an appropriate biomarker for severe OA disease. Some patient variables might be correlated with synovial blood pH (gender, Rh, Hgb, some comorbidities).

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