Tribological Monitoring of Drugs Used for the Treatment of Arthropathies

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Lubricating capacity of drugs injected into articular cavity were tested using a pendulum tribometer. The findings indicate that friction coefficient for a pair simulating metallopolymeric articular endoprosthesis is changed under the effect of electromagnetic field after lubrication. Regularities of these changes depend on the nature and mechanism of action of drugs. A method for rapid evaluation of the lubricating characteristics of drugs is proposed for optimizing their therapeutic effect on joints.

Key Words: *friction coefficient; drugs; electromagnetic field; synovial fluid; joint*

Drug injection into articular cavity is now one of the most effective methods for drug therapy of synovial joints. The choice of drug depends on the purpose of treatment. For example, antibiotics and antiinflammatory corticosteroids are used for reducing symptoms of synovitis. Progressive destruction of the cartilage in degenerative diseases can be inhibited with drugs with protective properties and functioning as lubricants similar to natural synovial fluid (SF). Progress in modern pharmacology permits individual choice of drugs [11]. Drugs injected into the articular cavity have targeted therapeutic effects; mixing with SF, they qualitatively modify its biomechanical characteristics. The effects of drugs of the same pharmacological group with the same mechanism of action on friction parameters in the joints can be different. However, drugs are not evaluated from the viewpoint of tribology. No information of this kind can be found in relevant publications [6].

Live tissues forming the joint perceive and generate physical fields, primarily electromagnetic fields (EMF) [1,9]. EMF are characterized by energetic effects on tissue structures and determine biophysical mechanisms, in accordance with which SF in the articular cavity performs its specific functions [3,4].

We evaluated the effects of some drugs on tribological parameters of mobile connections simulating friction centers of articular endoprostheses and the biophysical effects of EMF on friction and lubrication processes intrinsic of the natural joints.

MATERIALS AND METHODS

In order to maximally approximate the experimental conditions to the natural conditions of friction in the joint and optimize the accuracy of measurements, the pendulum type tribometer was used [4,8] containing only one (studied) friction pair (Fig. 1). The philosophy of the device action is based on evaluation of the friction coefficient by the parameters of damped oscillations of the pendulum (method of measuring the logarithmic damping decrement). The friction coefficient values were estimated by computer processing of electrical signals from the tribometer. Five-seven experiments were carried out with each drug and SF specimen.

The studied tribometer friction pair consisted of a base made of superhigh-molecular polyethylene

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and a pendulum-carrying triangular prism (12X18H9 steel) with rounded (2.5 mm radius) basal plane. Trials were carried out with a 2.0-kg pendulum at sliding velocity of 1.0 m/sec, which corresponded to the mean physiological load of human knee joint.

The drugs used for injections into the joints served as lubricants (Table 1). SF specimens collected from involved joints were studied for comparison (Table 2).

Criteria for drug selection were experience gained by Russian physicians using these drugs for the treatment of arthropathies, availability and pronounced clinical effect of the drugs.

SF specimens were aspirated with a syringe from the knee joints of patients under aseptic conditions during diagnostic puncture (before treatment) or interventions (arthroscopy, arthrotomy). Hence, SF was collected from patients with acute synovitis, chronic synovitis during exacerbation in the presence of a degenerative process, chronic synovitis without exacerbation, rheumatoid arthritis, Bechterew disease, and from normal joints (Table 2). At least 5 patients with the same disease were examined. Protein content in SF was evaluated by opalescence forming after addition of sulfosalicylic acid. Quantitative data were obtained by evaluating the degree of opalescence by photoelectrocalorimeter at λ=590-650 nm (red filter). Estimations were carried out using a calibration curve. Mean concentrations of protein in SF in various diseases and their deviations from the means for groups were determined by statistical processing of data corresponding to variation series.

Magnetic field, generated by solenoid (600±2 turns, wire diameter 0.07 mm, coil diameter 21 mm) installed in the pendulum tribometer support (Fig. 2), was created in the studied pair friction zone. Drugs were homogenized by mixing and the sample (0.5 ml) was placed with a syringe into the groove in the tribometer polymeric support and the friction zone was exposed to solenoid EMF during 5-40 min. Current of 0.06 A and 6 V voltage, corresponding to magnetic field tension in the tribometer support (1.2 kA/m), was generated using permanent current source connected to the solenoid through DT-830B multimeter. Such fields are considered effective in therapy of synovial joints [3]. The tribometer pickups were connected to digital gage complex, which permitted automated recording of friction parameters.

Tribological experiments were carried out at 20°C.

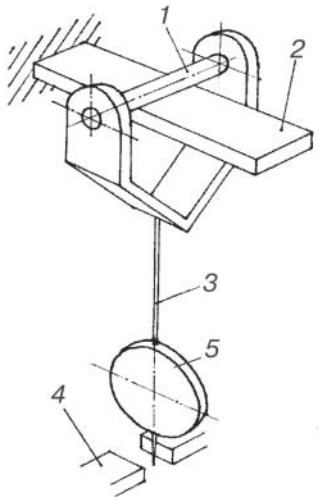

Fig. 1. Pendulum tribometer for evaluating friction in the joints. *1*) indentor; *2*) sample; *3*) pendulum; *4*) fluctuation gauge; *5*) removable load.

TABLE 1. Drugs for Tribological Studies

Drug	Composition	Manufacturer Firm	Effect
Hydrocortisone	Hydrocortisone acetate 125 mg, lidocaine hydrochloride 25 mg	Gedeon Richter A. O., Hungary	Antiinflammatory
Kenalog-40	Triamcinolonacetonide 40 mg, benzyl alcohol 9.9 mg	Bristol-Myers Squibb SpA, Italy	Antiinflammatory
Diprospan	Betamethasone dipropionate 6.43 mg, betamethasone sodium phosphate 2.63 mg	Schering-Pflau, Germany	Antiinflammatory
Lincomycin hydrochloride	30% lincomycin hydrochloride solution	Drug Factory, Borisov, Russia	Antibacterial
Sinvisk	Gilane A and B (8.0 mg/ml)	Biomatrix, Inc., USA	SF endoprosthesis
Hyalart	Hyaluronic acid, sodium chloride 2 ml	Bayer AG, Germany	SF endoprosthesis

TABLE 2. Physico-Chemical Parameters of SF Specimens

Disease	Transparency	Mucin clot	Changes in hyaluronic acid content	Protein concentration, g/liter
No disease	Transparent	Compact	Normal	10±3
Acute synovitis	Transparent	Loose	Sharply reduced	36±2
Chronic synovitis during exacerbation in the presence of third-degree osteoarthrosis	Transparent	Loose	Reduced	32±4
Chronic synovitis without exacerbation	Transparent	Compact	Normal	24±3
Bechterew's disease	Transparent	Loose	Reduced	35±3
Rheumatoid arthritis	Opalescent	Loose	Reduced	53±5

RESULTS

Initial values of friction coefficient f_0 in the studied friction pair depend on the type of drug, its consistency, and chemical composition, provided all the rest conditions are the same (Table 3).

The minimum f_0 was observed in experiments with hyalart drug intended for the treatment of degenerative diseases of the joints (so-called "endoprosthesis" of SF). Sinvisk belongs to the same group of drugs, but its tribological parameters are inferior to those of hyalart. Visual evaluation of drugs sumples placed in the tribometer support indicates significant differences in their lubricating capacity. Sinvisk is a viscous thick jelly, not flowing over the support during friction. Even after load was over, the drug remained unevenly spread on the groove surface. The consistency of hyalart is more liquid; it evenly wets the surface of the support friction, made from hydrophobic superhigh-molecular polyethylene, creating favorable conditions for the pendulum prism sliding. Presumably, the clinical effect of sinvisk [5] is determined not so much by improvement of sliding in the joint, but mainly by viscous elastic characteristics of the drug, protecting the cartilage from the peak mechanical loading and subsequent improvement of the involved joint function due to stimulation of SF production.

Steroid drugs (kenalog-40, diprospan, hydrocortisone) characterized by a pronounced antiinflammatory effect, being placed into the tribometer groove significantly deteriorated friction. Suspensions of these drugs stratify immediately during their removal from the ampoules. By the time of crystal precipitate formation during droplet sample drying, steroid drugs form the following sequence: hydrocortisone ← kenalog ← diprospan. Hydrocortisone exhibited the highest f; it was characterized by rapid phase stratification, precipitation of crystal suspension on friction surface, and subsiding of the liquid phase from the groove during the friction unit loading. After this the lubricating layer in the tribometer friction unit consisted mainly from hydrocortisone crystal phase acting as an abrasive. A similar picture was observed during lubrication of the tribometer support by kenalog. Significant deviations of the results of measurements of f for

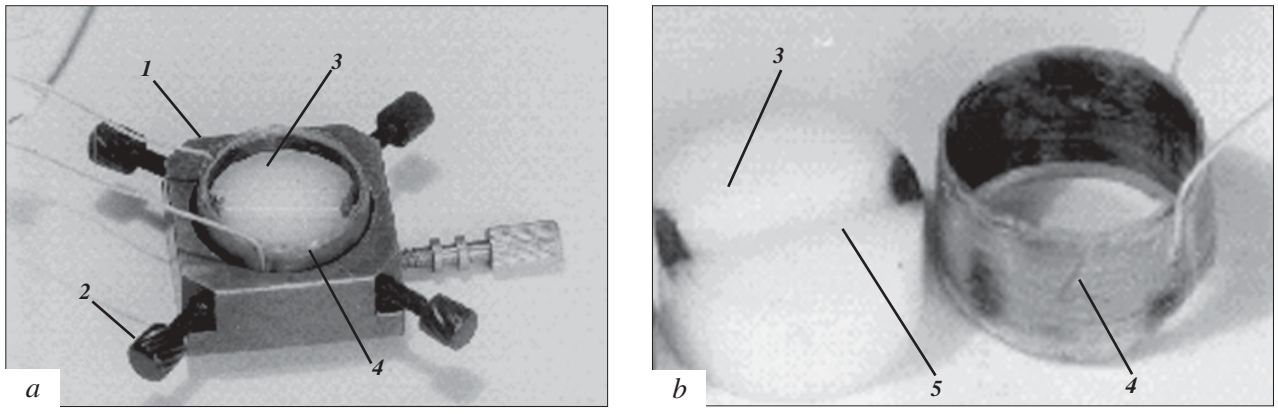

Fig. 2. Supporting unit of pendulum tribometer (*a*) and main elements of friction unit (*b*). *1*) frame; *2*) fixation element; *3*) high-molecular polyethylene support; *4*) solenoid; *5*) groove.

TABLE 3. Results of Tribological Studies of Drugs and SF Samples in Articular Diseases

Drug/disease	Friction coefficient
Drugs	
Hydrocortisone	0.066-0.106*
Kenalog-40	0.095-0.100*
Diprospan	0.07*
Lincomycin hydrochloride	0.077*
Sinvisk	0.075*
Hyalart	0.0617*
Articular diseases	
no disease	0.0645+
acute synovitis	0.082+
chronic synovitis during exacerbation in the presence of third-degree osteoarthrosis	0.078+
chronic synovitis without exacerbation	0.068+
Bechterew's disease	0.066+
rheumatoid arthritis	0.065+

Note. *Initial and +mean values of friction coefficient are presented.

hydrocortisone and kenalog from the mean values were due to impossibility of providing a constant ratio between the crystal and liquid phases in small volumes of drugs placed into friction zone because of their rapid stratification. Diprospan is a suspension of smaller particles with much slower precipitation than the above drugs, this providing a satisfactory lubricating capacity of this drug.

Lincomycin hydrochloride used for the therapy of bacterial antiinflammatory processes is a saline intensely crystallizing during friction in the air. Presumably, mixing with SF this drug has no abrasive effect on the joint surfaces, because it contains no water-soluble components and easily penetrates through the synovial membrane into the vascular bed.

The initial friction coefficient for diprospan, lincomycin, and sinvisk correspond to chronic synovitis status ($p<0.05$). Friction coefficients characteristic of kenalog-40 and hydrocortisone are higher than of SF maximally changed in acute synovitis. Only hyalart is characterized by friction coefficient comparable with normal SF f_0 ($p<0.05$). Time course of changes in the drug friction coefficients under conditions of exposure to EMF is presented in Fig. 3.

Analysis of the results indicates a high lubricating capacity of SF-replacing drug hyalart, which not only promotes normalization of tribological parameters during injection into the joint, but markedly improves them under the effect of EMF. The same regularities were observed during lubrication of the pendulum tribometer support by normal SF [10]. Diprospan proved to be the most EMF sensitive of the studied steroid antiinflammatory drugs. It was characterized by initial f_0 the lowest for this group of drugs (Table 3), decreasing under the effect of EMF. Statistical processing of the results of hyalart and diprospan testing confirmed with 95.5% reliability the decrease of these drugs' f under the effect of EMF. In a normal joint SF exhibits the characteristics of a quasielectret, reacting to changes in the external biophysical field [7]. This is due to the coordination pattern of SF supramolecular structure bonds. It seems that the best of the studied drugs are also three-dimensional molecular complexes, formed by coordinated and functionally related components structurally sensitive to EMF.

Hence, despite appurtenance to the same pharmacological group, each drug is characterized by specific tribological properties. If all other conditions are equal, the choice of drug with the least friction coefficient seems to be more rational.

The decrease in friction coefficients of some drugs under the effect of EMF prompts combining two therapeutic factors (antiinflammatory and tribological) for amplification of the therapeutic effect of drug injection into involved joint. The method for testing drugs injected into the joints, by pendulum friction device fitted with an EMF source is convenient for tribological express evaluation of the drug efficiency. Any drugs intended for the treatment of joints can be thus studied on very small (about 0.1 ml) samples.

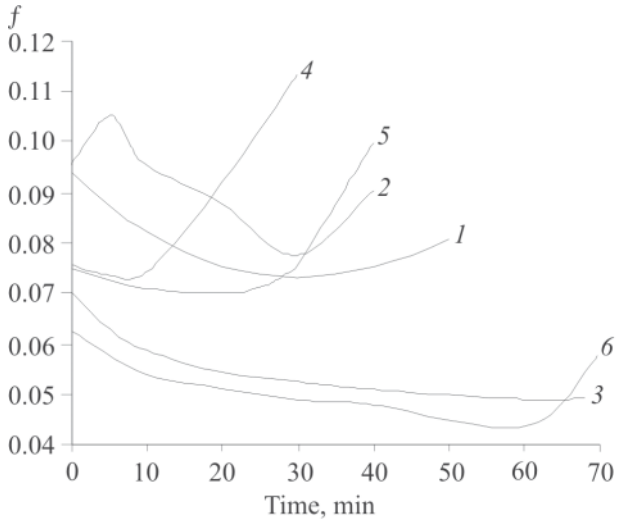

Fig. 3. Relationship between friction coefficient (*f*) and time of drug exposure in the pendulum tribometer support to electromagnetic field. *1*) hydrocortisone; *2*) kenalog-40; *3*) diprospan; *4*) lincomycin; *5*) sinvisk; *6*) hyalart.

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