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The tissue temperature during injection of drug solution into it as an integral indicator of rheology

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Abstract. The dynamics of local temperature in the area of injection of drug solutions with regard to their physical and chemical properties is studied. It is shown that infrared thermography allows to visualize the processes of intra tissue rheology of drugs both when the temperature of injected drugs differs from the local temperature of tissues in the injection area and when their temperatures are equal. Methods of infrared diagnostics of tissue homogeneity, as well as methods for identifying, specifying the localization, shape and size of tumors, foreign bodies and local inflammations have been developed. It is shown that artificial temperature contrast of veins filled with blood and/or drug solutions in relation to the tissues surrounding them allows to visualize these structures using a thermal imager in real time. It is established that the dynamics of the local temperature of tissues at the injection sites of drug solutions depends not only on the temperature of the injected drugs, but also on the presence and severity of their local irritant effect. It is shown that the local irritating effect of drugs is manifested in the places of their injections by local hyperthermia, hyperemia, swelling and soreness. A direct dependence of the severity of the local irritant effect of drugs on the value of the total concentration of ingredients and the degree of hyperosmotic activity of solutions was established. Therefore, dilution of drugs with water is a way to reduce their local irritant effect.

1. Introduction

Rheological properties of warm-blooded body fluids can change under the influence of various factors of the external and internal environment [1]. Human body temperature determines the intensity of physical, chemical, and biochemical processes simultaneously occurring in his body, and is one of the most important factors determining the properties of biological fluids. Under the conditions of temperature homeostasis in the human body, liquids retain their properties necessary for maintaining the vital activity of the organism and ensuring its needs [2]. It is believed that the body temperature of warm-blooded animals is constant. For example, the core temperature of the human body undergoes slight daily fluctuations in the range of 35.5-37.2 °C, averaging 37.0 °C [3]. In this case, the values of the surface local temperature of the human body are different in different areas. Experimental and clinical application of infrared thermography significantly expanded the understanding of changes in the local temperature of the human body, allowed to establish the ranges and direction of changes in the temperature of the entire object of study [4,5]. So it became clear that human blood circulating through the body can repeatedly change its temperature index, and at the same time change its rheological properties. It is shown that there is an inverse relationship between temperature and blood

viscosity [6]. On average, blood viscosity increases by about 2% for every degree Celsius as the temperature decreases. With a high hematocrit, the effect of temperature is more pronounced [7].

On the other hand, when injecting drug solutions are introduced into the body without heating, so they have a "room" temperature, namely-24-25 ºC. In other words, they are introduced "cold" in relation to the human body. In this regard, of particular interest is the study of changes in local body temperature under the influence of injections of drugs into liquid (blood) and non-liquid soft tissues.

The aim of this study was to study the dynamics of local temperature of tissues at injection sites of drugs, taking into account their physical and chemical properties.

2. Materials and experiments

The study was approved by the Ethics Committee of Izhevsk Medical Academy (approved No.477) on April, 2016. Written informed consent was obtained from all participants. The study included 50 adult patients. The study of the temperature range of the surface of the human body and the temperature of solutions for injection was carried out using infrared thermal imager ThermoTracer TH9100XX (NEC, USA) in the temperature range of 25–36°C. The core temperature was controlled using an esophageal temperature sensor (model MR411, Mindray Bio-Medical Electronics Co., Ltd, China). Acclimatisation time was 15 minutes, the room temperature was 24.0±1°C. Solutions of drugs with viscosity index were used for the study 1.02-1.08 cps at 20 °C. The analysis of osmolality (mmol/kg) of drugs solutions was carried out with the help of Vapor Pressure Osmometer Model 5600 (WESCOR-INC, USA).

3. Results

Thermograms and core temperature value of 30 females (mean age: 51±14 years) and 20 males (Mean age: 47±13 years) were evaluated.

The average core temperature of the body was 37.5±0.2°C (n=50). The difference in skin surface temperatures in different areas reached 10 °C. the Recorded values of surface temperatures in one person in different areas ranged from 24 to 36°C. of Particular interest were the values of skin temperatures in the area of injection of drug solutions. It was found that the average value of skin temperature in the area of intravenous injection before the introduction of drugs was 33.6±0.2°C (n=50). Intravenous solutions with different osmotic activity index were used for observation: 5% glucose solution -280 mmol / kg, 0.9% sodium chloride solution-308 mmol / kg, 5% sodium chloride solution-620 mmol/kg; solutions for intramuscular administration: metamizole sodium 500 mg / ml solution-4520 mmol/kg, ketorolac tromethamine 30 mg / ml solution-2971 mmol/kg.

It was found that intravenous administration of 0.9% sodium chloride solution with a viscosity index of 1.03 cps and a temperature of +24.0°C led to a decrease in local skin temperature in the injection area. At the same time, it was found that the intensity of cooling of the skin at the site of intramuscular injection of the drug depends on the speed of administration of the drug solution. Thus, at the rate of introduction of a solution of 0.9% sodium chloride 1 ml/min. the local skin temperature at the injection site after 2 and 4 minutes decreased to 31.9±0.4 °C and 31.3±0.2 °C (respectively), and at the introduction of this solution at a rate of 10 ml / min. - local temperature decreased up to 29.1±0.1 °C and 27.5±0.3 °C (respectively).

With the help of infrared thermography, it was found that with an increase in the rate of intravenous administration of cold solutions of drugs, the size of the local hypothermia zone increased. It was found that in this case the localization of the local hypothermia zone corresponded to the projection area of the cooled vein. Moreover, it turned out that the zone of local hypothermia, which appears when a solution of "room" temperature is injected into the vein, provides temperature contrast of the vein, which, in turn, provides its visualization in the infrared range of the radiation spectrum.

The revealed regularities formed the basis of the following inventions "Method for infrared phlebography" and "Method of subcutaneous veins imaging in infrared radiation spectrum range according to A.A.Kasatkin" [8,9]. In addition, it turned out that an artificial increase in the local

temperature inside the vein due to intravenous administration of a solution with a temperature of 38-42°C causes the appearance of a zone of local hyperthermia in the area of the vein projection, which also allows to visualize the vein in the infrared spectrum of radiation [10].

On the other hand, injection into skeletal muscle of a solution of 50% sodium Metamizole, a solution of 3% ketorol trometamine or a solution of 0.9% sodium chloride (control) with a "room" temperature also led to cooling of the skin in the injection area. The duration of local hypothermia after injection averaged 5-7 minutes. Further monitoring of the local temperature revealed the appearance of a zone of local hyperthermia of the skin at the site of intramuscular injections of some drugs. It turned out that a qualitative solution of Ketorolac trometamine and a qualitative solution of sodium Metamizole cause the appearance of local hyperthermia at the injection site due to local irritant action. The skin temperature at the site of administration of these solutions increased by 0.3-0.6°C compared to the initial values.

Analysis of the results showed that the local irritant effect of these drugs causes their high osmotic activity. It was found that the high osmolality of these solutions of drugs leads to the appearance of local hyperthermia of the skin at the injection site because these drugs cause dehydration of cells, the severity of which determines the severity of all symptoms of local inflammation of tissues in the injection area, as well as the possibility of reversibility of the inflammation process and the probability of necrosis of inflamed tissues. These results coincided with the data obtained earlier in similar studies on awake 2-month-old pigs [11]. In particular, it was shown that intramuscular and subcutaneous injections of antibiotic solutions with high osmotic activity (namely, hypertonic solutions of lactam antibiotics) are manifested by the creation of a local hyperthermia zone at the injection site [12].

It is shown that osmolality along with acidity, viscosity, hardness (for tablets) is an important indicator of drug quality, determining the rheology of drug solutions inside tissues at the injection site [13,14]. Due to this, it was found that the decrease in the osmotic activity of the drug solution due to its dilution with water up to the isoosmotic level (up to 280 – 300 mosmol/l of water), which corresponds to the osmolality level of less than 1000 mmol/kg, eliminates the local irritant effect of the drug, the development of necrosis and abscess at the injection sites.

Thus, infrared monitoring of local skin surface temperature at injection sites of drug solutions can serve as an integral indicator of their rheology and safety when taking into account the physico-chemical properties of drugs.

4. Conclusions

The dynamics of local temperature in the surface of the human body, recorded by infrared thermography taking into account the physical and chemical properties of drugs, can under certain conditions serve as an integral indicator of the intra tissue rheology of drugs. This, in turn, can be used for infrared assessment of tissue structure homogeneity in order to detect tumors, foreign bodies and local inflammatory processes, as well as to assess the safety of drugs and their injections.

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