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ELECTROPHORESIS, AS A METHOD OF RATIONAL APPLICATION OF MEDICAMENTS OF CONTEMPORARY MANAGEMENT IN HEALTHCARE

Abstract

Preclinical studies of the intake of drugs in the body by electrophoresis and systemic route (intravenous), we examined the concentrations of drugs and the efficiency of the drug application in both ways. We found high-significance concentrations of drugs in the desired tissue, with multiple smaller amounts of drugs administered by electrophoresis, and high values of Students T-test and significance for all investigated drugs $p < 0.001$. Investigating economic cost-effectiveness, this methodology of drug intake, we observed by evaluating the cost of medicines of significant material savings with drug application with ionophoresis, which is recommended both from the health and material-financial aspect as a rational modern method of drug intake in clinical practice, wherever clinical possibilities allow it.

Key words: drug electrophoresis, material aspect, healthcare marketing.

JEL classification: I1, I10, I18

ЕЛЕКТРОФЕРЕЗА, КАО МЕТОДА РАЦИОНАЛНЕ ПРИМЕНЕ ЛЕКОВА САВРЕМЕНОГ МЕНАЦМЕНТА У ЗДРАВСТВУ

Апстракт

Предклиничким истраживањем уноса лекова у организам електрофорезом и системским путем (интравенски) сагледали смо концентрације лекова и ефикасност апликације медикамената на оба начина. Добили смо висококосигнификантне концентрације лекова у жељеном ткиву, са вишеструко мањим количинама апликованих лекова електрофорезом, те високим вредностима Студентовог т-теста и праговном значајношћу за све испитиване лекове

$n < 0,001$. Истражујући економску исплатљивост, ове методологије уноса лека, запазили смо евалуацијом цена лекова значајне материјалне уштеде јонтофоретском апликацијом лекова, која је препоручује и са здравственог и са материјално-финансијског аспекта као рационалну савремену методу уноса лека у клиничкој пракси, свуда где клиничке могућности то допуштају.

Кључне речи: електрофореза лекова, материјални аспект, здравствени маркетинг.

Introduction

Electrophoresis or ionophoresis of drugs is a safe, painless and effective method to intake the drug into the humans and animals tissue, through the skin by galvanics current (Ђурђевић S, Јездимировић M, et all 2010). The medically important prerequisites for the application of drugs in this way are: that the drug is hydrosolubile, that the drug has a high level of electrolytic dissociation (spontaneous decomposition to ions), that the drug has relatively small ions or dipole molecules, that the patients skin is intact, that there is no metals in the local tissue, that the patients sensibility is preserved, that the chemical structure of the drug is well known as also ionization of its ions, that there is no intolerance to the drug (Kalia YN, Naik A, Garrison J, Guy RH 2004). In this way, many drugs can be intake into the tissues: the adrenocortical hormones, the vasodilators, vitamins, inhibitors of cyclo-oxygenase 2 (coxibs), antibiotics, nonsteroidal antirheumatics (NSAL), and many other drugs. The drug applied in this way is more effective, due to ionic binding to target tissue receptors. Drug is retained longer in the tissue (up to 4 days), systemically distant and side effects are avoided as opposed to systemically distributed drugs peroral (per os) and parenteral (iv) (Ђурђевић S, Јездимировић M, et all 2009.)

Therapeutic dose- the total amount of injection of the drug is lower in the electrophoretic application of the drug compared to the systemic application. The cumulative effects of the drug after succesive electrophoretics application are greater than the systemic (per os and intravenous) intake, thus achieving significant material savings and optimizing the use of drugs in clinical practice, both in human medicine and in veterinary medicine (Ђурђевић S, Јездимировић M, et all. 2010).

Aim of study

The aim study was to investigate and demonstrate the concentrations of the drug being applied (their clinical doses), in the organism of animals or humans by electrophoresis and systemic (iv); as well as the total amount of medicines applied with the goal of saving, from the financial management aspect of the use of drugs in clinical practice and the rationalization of healthcare costs, both in clinical medicine and in veterinary practice.

Materials and methods

In this preclinical and management-financial studies, as sample of experimental animal used species of twenty domestic swine (*Suis domestica*), soybean mixture of Big Yorkshire and Swine Landrace, at the age of 8 weeks, in standard feeding and watering "ad libito" regime, mass in grams $X \pm SD = 24520 \pm 0,34$. The palette of five diferent medicaments applied in inflamed right knee of the last limb joints (inoculation of 0,2 ml of 10% turpentine solution one-time). The swines were divided into two groups: **A** group of 10 individuals swines was systemically-intravenous applied (iv) single clinical dose of drugs in jugularis vein with a five-day successively, while the **B** group of 10 individuals applied the same drugs with electrophoresis (EF) **in one therapeutic dose** (anode surface $4 \times 5 = 20 \text{ cm}^2$, cathode $5 \times 6 = 30 \text{ cm}^2$), with an intensity of galvanic current in the average values $X = 4.5 \text{ mA}$ and the duration of the application 15 min, and biodoses $4.5 \times 20 = 90 \text{ mAmin}$. The following drugs were applied in individual clinical doses, **from anode**: Dihydroergotoxin 9 mg (Redergin®), as vasodilator, Meloxicam 15mg (Movalis®) as inhibitor of cyclooxygenase 2 (coxibs), and **from cathode** Methylprednisolone 40mg (Lemod-Solu®) as a strong steroidal antiinflammatory drug, Acid acethylsalicylicis 500 mg (Aspirin®) as NSAL drug and Metamizol sodium 2.5 g/ 5 ml (Novalgetol®), as a potent analgo-antipiretic. On the seventh day, the aspiration of synovial fluid was performed in the tested individuals of both groups and the high pressure liquid chromatography, as valid world method (HPLC), precisely quantified drug concentration in the micrograms of the drug per gram of tissue. The research was carried out in accordance with the Animal Care Code and the approval of the Ethics Committee and was carried out at the Air Force Medicine of the Military Medical Academy, the National Poison Control Center and the Institute for Scientific Research at the **Military Medical Academy** (Đurđević S, Jezdimirović M et al. 2010).

Results

The results of the study, respectively the comparison of the quantification of the drugs concentrations introduced by systemic intravenous and electrophoresis, were evaluated by the Student t-test for small even samples, and correlation with regression analysis of the price of applied drugs in both ways, with the aim of potential financial savings and economic benefits in human and veterinary medicine. Statistical data processing was done in the DOS statistical package.

Table No. 1 Concentration of drugs in the synovial fluid of the inflamed knee joint of the young swine in the micrograms of the preparation per gram of tissue, or in milliliters of synovial fluid.

Drug concentrations in µg/ml Synovial liquid	Drugs applied iv.	Drugs applied EF	t-test	p
Meloxicam	4.95±0.32	51.12±0.34	12,45	p<0,001
Metamizol natrium	9,81± 1,56	171,66 ± 2,17	19, 44	p<0,001
Acidum acethylsalicyl.	29,6±2,18	216,12±0,35	18,52	p<0,001
Dihidroergotoxin	0,85±1,36	21,34±1,16	15, 12	p<0,001
Methylprednizolon	0,33± 0,15	17,15 ±3,12	14,48	p<0,001

The prices of drugs expressed in dinars of Republic of Serbia (RSD), taken in the first quarter of 2018 in market of Republic of Serbia are:

1 pack. of Meloxicam 0,015g , 10 tablets price: 412,50 RSD,

1 pack. of Dihydroergotoxin 0,0045g, 10 tablets price: 372, 50 RSD

1 ampoule Metamizol natrium 2,5g/5ml: 35,88 RSD x10 amp =358,8 RSD / therapeutic package

1 pack. of Ac.Acethilsalicylici 0,500g , 10 tablets price: 336,60 RSD

1 ampoule Methylprednisolon 40 mg: 126, 82 RSD x 10 lio.amp 1268,2 RSD/ therapeutic package

Putting in the ratio of the current average medicament price to the therapeutic effect and drug concentration of systemic IV and locally introduced EF in RSD, with regression analysis with correlation yields, it gets a high Pearson coefficient of correlation for biomedical investigated phenomena $F=0,768$, indicating high-significance differences in prices spent drugs, according to the quantities in favor of electrophoretic drug intake (Stanišić V. 1994).

Table No. 2 Comparison of the price of the drug package price with the achieved therapeutic dose.

Drugs	Price of drugs applied iv.	Price of drugs applied EF
Meloxicam	83,33 RSD	8,06 RSD
Metamizol natrium	36,57 RSD	2,09 RSD
Acidum acethilsalicyl.	11,37 RSD	1,5 RSD
Dihydroergotoxin	438,23 RSD	17,45 RSD
Methylprednisolon	4226 RSD	72,46 RSD

Discussion

The interest of doctors, patients and veterinarians is to efficiently, safely and in the shortest possible period, with as little side effects as possible, achieve a therapeutic effect on patients and restore functional and work and psychophysical abilities, which in the concrete case of the application of medicines can be achieved in a rational way by iontophoresis, with advantage over systemic intake of drugs intravenously and per os (Jakovljević M. at al. 2014). The prerequisite for such a drug application is the existence of relatively cheap equipment, an electrophoresis device that can be repaid in a very short time by saving significant amounts of drugs applied in this way. This method of drug intake is justified for one region of the body (joint) and the likewise several of them, while it is time required for a greater number of the affected regions of the body, and this limiting factor should also be kept in mind (Đurđević S, Jezdimirović M, et al. 2010) The financial aspect of saving money using application of drugs by electrophoresis is significant because the prices of used drugs in total quantities and therapeutic doses indicate a lower price of medicines introduced in this way. By statistically processing the data obtained in this preclinical study, we note the high significance of the concentration of drugs in the desired tissue, achieved by a multiple dose of drugs, which is from a

large clinical and financial aspect of savings (Tiexira M.G., Zatz J.L, 2017). Republic of Serbia is a country with a modest health budget, and any savings that do not disturb the quality of health services is very important, and the expert public should be aware of modern methodology, which provides significant savings in this important sphere, as evidenced by the modernity Latin quotes “Valetudo bonum optimum” (Jones AM 2006). Therefore, the savings of material resources in the provision of health services would free some of the budgetary funds for priority goals, education of experts, procurement of equipment and medicines, as well as health care funds, in order to achieve better quality health care.

Conclusion

Different types of drugs (vasodilators, cortical preparations, NSAL antirheumatics, analgoantipyretics, coxibes) applied with electrophoresis, compared to systemic (intravenous) intake, achieving statistically significant values of drug concentrations in the target tissue, allowing longer retention in the local target tissue and avoiding systemic and side effects, a clinically significant effect.

Using multiple-dose doses (total and individual amounts) of drugs, in order to achieve multiple-dose therapeutic concentrations of medicaments, achieve high-significance savings with ionophoretic drug administration in comparison with systemic intake, and this method can be proposed as a method of choice in clinical practice, both in human and veterinary medicine, whenever specific health conditions and diagnoses allow it. Introducing a wider medical, professional public with obvious advantages of electrophoretic drug intake method would allow rational material savings in the consumption of medicaments, with significant and useful social and health implications and applicability, enabling massive application of this modern methodology of pharmacokinetics of drugs, illuminated in our research more from the aspect of practiciness and applicability, rather than academism. ”A healthy man has a thousand wishes, and a sick one is only to be healthy”

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