Pilot determination of reference intervals for sorbitol in cattle

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Abstract. A pilot study was conducted to determine reference intervals for sorbitol in cattle. The study determined the level of sorbitol in the urine of cattle. It was found that the endogenous concentration of sorbitol in animals to which it was not administered was below the sensitivity threshold of the spectrophotometer. Extremely close values of sorbitol concentration in males and females were explained. A description of the pharmacokinetics of sorbitol in the body of males and females of cattle is presented. It was found that sex hormones and sex differences in organisms do not have a significant effect on the pharmacokinetics of sorbitol. Further paths for scientific research on the clearance of sorbitol and its use in veterinary medicine are proposed.

1 Introduction

The study of new chemical compounds and their clearance plays a key role in understanding and predicting hepatobiliary pathologies in animals. The hepatobiliary system, which includes the liver, bile ducts, and gallbladder, performs many vital functions, including detoxification, metabolism, and excretion of various substances. Clearance, or the rate of removal of a substance from the body, is an important indicator of the functional state of this system [1-2].

In this context, special attention is paid to the clearance of sorbitol, which serves as a marker of the functional state of the liver and can be used to diagnose and predict pathologies. Sorbitol, or glucitol, is a six-carbon sugar alcohol that is widely used in the food industry and pharmaceuticals. In the body, sorbitol is metabolized in the liver, where it is converted to fructose by the enzyme sorbitol dehydrogenase. This process requires the participation of NAD+ and NADH, which makes sorbitol important for studying metabolic pathways and energy metabolism in the liver [3-4].

Sorbitol clearance reflects the liver's ability to metabolize and eliminate substances, making it a valuable marker for assessing the functional state of the hepatobiliary system. Studying sorbitol clearance allows identifying early signs of liver pathologies such as hepatitis, cirrhosis, and fatty degeneration. In animals with impaired liver function, sorbitol clearance can be significantly reduced, indicating a decrease in metabolic activity and the

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liver's ability to detoxify. This makes sorbitol an important tool for diagnosing and monitoring liver function, as well as for assessing the effectiveness of treatment.

In addition, the study of the clearance of new chemical compounds allows us to identify their potential toxicity and impact on the hepatobiliary system. Many new compounds used in the pharmaceutical and chemical industries can have a negative impact on the liver, causing hepatotoxicity. The study of their clearance allows us to estimate the rate of their metabolism and elimination from the body, which is an important factor in determining the safety and dosage of these compounds. In the context of sorbitol clearance, it is important to note that its metabolism in the liver depends on many factors, including the health of the animal, age, sex and diet. For example, in animals with diabetes or metabolic syndrome, sorbitol metabolism may be impaired, which leads to its accumulation in tissues and the development of complications [5-7].

Therefore, sorbitol clearance can serve not only as a marker of the functional state of the liver, but also as an indicator of metabolic disorders. Various methods are used to study the clearance of sorbitol and other chemical compounds, including pharmacokinetic studies, isotope labeling, and spectrophotometry [8-9]. These methods allow for accurate measurement of the rate of metabolism and excretion of substances, which is important for understanding their effect on the hepatobiliary system. In particular, pharmacokinetic studies allow for the evaluation of parameters such as distribution volume, absorption rate, and excretion rate, which provides a complete picture of the metabolism of the compound in the body. It is also important to note that sorbitol clearance may vary depending on the species of animal. For example, sorbitol clearance may be higher in dogs and cats than in rodents, which is associated with differences in metabolic pathways and functional activity of the liver. This emphasizes the need for species-specific studies to accurately assess clearance and its effect on the hepatobiliary system.

The study of new chemical compounds and their clearance, especially sorbitol clearance, is a relevant and important task for understanding and predicting hepatobiliary pathologies in animals. Sorbitol clearance serves as a valuable marker of liver function and can be used to diagnose and monitor animal health. Understanding the metabolic pathways and factors affecting clearance allows us to develop effective methods for the treatment and prevention of liver diseases, which is important for veterinary medicine and the pharmaceutical industry. The aim of the study is to conduct a pilot study to determine sorbitol reference intervals in cattle.

2 Materials and methods

The studies conducted in 2024 were carried out at one of the livestock farms in the Pskov region specializing in dairy production. The experiments involved Holsteinized cattle, the average productivity of which was up to 5.5 thousand liters of milk per year, and the age of the animals was 1 ± 0.2 years. The animals were divided into two groups based on the principle of pairs of analogues: experimental (n = 20) and intact (n = 20), each of which consisted of individuals of different sexes. The intact group was included in the experiment to exclude false positive results and cross-sensitivity with other methylxanthines. All animals were stratified by live weight, feeding and housing conditions. The main selection criterion was also the absence of various pathologies, which was confirmed by physical examination and clinical and biochemical parameters.

The experimental group was orally administered a solution of food sorbitol at a rate of 100 mg/kg in terms of pure D-glucitol. This dosage is considered the most commonly used to determine the level of sorbitol in biofluids after enteral administration [10-11]. The control group was administered an equivalent volume of water for injection. The level of sorbitol was determined by the Corcoran and Page method with a modification [12-13],

using a UV-1100 spectrophotometer (Shanghai Mapada Instruments Co., Ltd., China) 24 hours after administration in the urine of the experimental animals. It is important to note that the study was conducted under conditions as close as possible to the actual conditions of keeping and feeding cattle on this farm. This made it possible to obtain data that can be extrapolated to the entire population of Holsteinized cattle in the region. Animals were carefully selected and checked for the absence of any pathologies, which ensured high reliability of the results. The process of introducing sorbitol and subsequent analysis of its level in urine was organized in compliance with all necessary protocols and standards. The use of the Corcoran and Page method with modification allowed to achieve high accuracy and sensitivity in determining the level of sorbitol. The UV-1100 spectrophotometer used in the study provided reliable and reproducible results. The calculation of the reliability of the difference (p) according to the Student criterion was not carried out due to the exploratory nature of the study and the absence of comparison groups. This means that the main goal of the study was not to compare the results between the groups, but to obtain basic data on the clearance of sorbitol in Holsteinized cattle. These data can be used in further studies to develop methods for the diagnosis and treatment of various pathologies associated with impaired sorbitol metabolism.

3 Results

During the study, it was found that the endogenous concentration of sorbitol in animals that were not administered it was below the sensitivity threshold of the method used, so there are no numerical values for the control group. Data on the concentration of exogenous sorbitol (dosage - 100 mg / kg) in urine per day, as well as the clearance calculated for each animal, are presented in Figures 1 and 2.

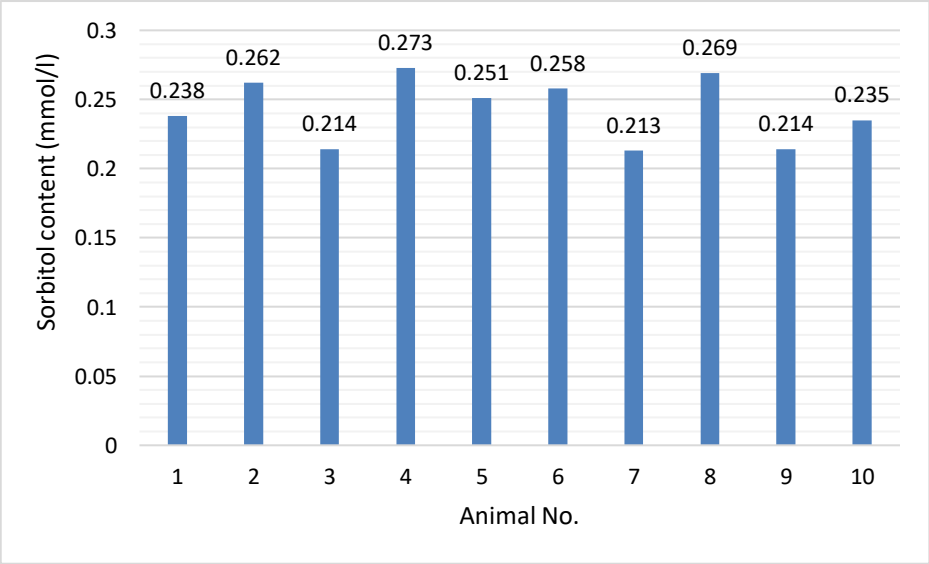

Fig. 1. Sorbitol concentrations in urine (in mmol/l in the experimental group of animals (males, dosage – 100 mg/kg).

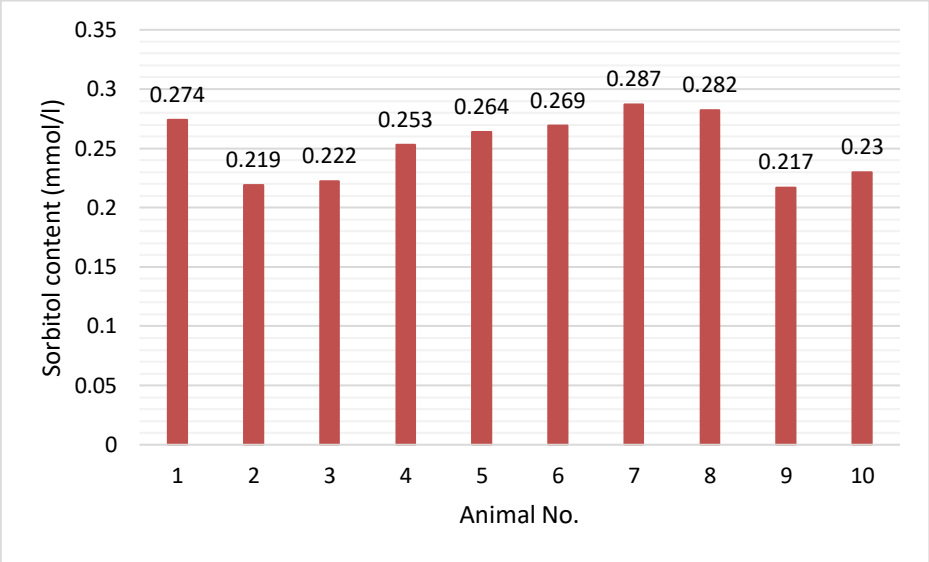

Fig. 2. Sorbitol concentrations in urine (in mmol/l in the experimental group of animals (females, dosage – 100 mg/kg).

The very similar values of sorbitol concentration in males and females can be explained by the peculiarity of its biotransformation.

Sorbitol, also known as D-glucitol, is a hexahydric alcohol that is widely used in medicine and the food industry as a sweetener and osmotic diuretic. The pharmacokinetics of sorbitol include the processes of absorption, distribution, metabolism and excretion, which can vary depending on various factors, including the sex of the animal. However, despite these differences, the pharmacokinetics of sorbitol in males and females are equivalent.

The pharmacokinetics and biotransformation of sorbitol in the body of animals are complex processes that include absorption, distribution, metabolism and excretion of this polyol. Sorbitol, also known as D-glucitol, is a six-carbon sugar alcohol that is widely used in the food industry and medicine as a sweetener and osmotic diuretic.

Sorbitol is absorbed in the small intestine of animals by passive diffusion. However, its absorption is slower than glucose, due to its low solubility and the absence of specific transport systems. As a result, a significant portion of sorbitol may remain in the intestine, causing an osmotic effect and contributing to an increase in the volume of intestinal contents.

After absorption, sorbitol is distributed to various tissues and organs of the animal. It can penetrate cells through membranes, but its distribution is mainly limited to the extracellular space due to its polarity and molecular size. Sorbitol does not bind to plasma proteins, which facilitates its free distribution.

Sorbitol is metabolized in animals primarily in the liver. It is metabolized via the polyol pathway, which includes two main enzymes: polyol dehydrogenase and sorbitol dehydrogenase. Polyol dehydrogenase catalyzes the conversion of glucose to sorbitol, and sorbitol dehydrogenase converts sorbitol to fructose. This pathway plays an important role in sugar metabolism and maintaining osmotic balance in cells. In the liver, sorbitol can also be oxidized to fructose, which can then be metabolized to glucose or glycogen. This process provides energy for cells and maintains glucose homeostasis.

Thus, the pharmacokinetics of sorbitol in male and female animals demonstrate similarity. This can be explained by the fact that the processes of absorption, distribution,

metabolism and excretion of sorbitol are not dependent on sex. In addition, sex hormones and sex differences in body composition and organ function do not significantly affect the pharmacokinetics of sorbitol. These data are important for the clinical use of sorbitol, since they allow the use of the same dosages and administration regimens for male and female animals.

4 Discussion

The use of sorbitol clearance as a predictor of hepatobiliary pathologies in animals opens up new prospects for veterinary diagnostics. Early detection of liver and biliary tract dysfunction allows timely treatment and prevention of severe complications. It is important to note that for the successful use of sorbitol clearance in veterinary practice, additional studies are required on various animal species and with various hepatobiliary pathologies. It is also necessary to develop standardized methods for determining the concentration and clearance of sorbitol, which will be available for widespread use in veterinary laboratories.

5 Conclusion

The established values of sorbitol concentration will be the starting point for studying its clearance in the context of using the clearance indicator as a predictor of hepatobiliary pathologies in animals.

The established values of sorbitol concentration in animal biological fluids are an important starting point for further studying its clearance. Sorbitol clearance can serve as a reliable predictor of hepatobiliary pathologies, which opens up new opportunities for early diagnosis and treatment of these conditions. Continued research in this area will allow the development of effective methods for diagnosing and monitoring the functional state of the liver and biliary tract in animals, which will contribute to improving their health and well-being.

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