International Journal of Veterinary Science and Agriculture Research
Volume 5 Issue 6, November-December 2023
ISSN: 2582-4112, Available at www.ijvsar.com

Piglet hypoglycemia – a comparison of intravenous, intraperitoneal and subcutaneous treatment

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Keywords: *glucose, hypoglycaemia, piglets, therapy, administration*

Abstract: *Hypoglycemia is a decrease in the concentration of glucose in the blood, which can lead to the death of neonatal piglets. In this experimental work, we focused on the evaluation of the techniques, advantages, disadvantages and possible complications of intravenous (i.v.), intraperitoneal (i.p.) and subcutaneous (s.c.) administration of 5% glucose in baby piglets. Infusion therapy was evaluated by examining the application site and comparing changes in blood glucose concentration before administration and subsequently in four fifteen-minute intervals after infusion therapy. By comparing the dynamics of the investigated administrations, we found the highest concentration of glucose in the blood after i.v. administration in 15 minutes – an increase of 36.04%. After s.c. administration, the highest concentration was reached after 30 minutes – an increase of 21.86%. After i.p. administration, we reached the highest average concentration after 45 minutes – an increase of 10.0%.*

I. INTRODUCTION

In pigs, hypoglycemia and dehydration can often occur in the first days of life due to insufficient or limited colostrum and milk intake, low glycogen stores after birth, or enteric infectious pathogens [1]. Hypoglycemia is the term used to describe low blood glucose levels. It usually occurs in the first 12 – 24 hours after the piglets are born. Regarding pathogenesis, during the first days of life, the newborn piglet is unable to mobilize low glycogen stores from the liver to ensure adequate blood glucose levels. It is therefore energetically dependent on the regular intake of lactose from colostrum and sows' milk. If the piglet cannot obtain enough lactose to maintain energy expenditure, it runs out of energy, its body temperature drops, and it eventually falls into a coma and dies [1,2].

Hypoglycemia can also occur due to hypothermia if the ambient temperature in the piglet's bedding area is lower than 30 °C, especially during the first week of life [2,3]. The clinical manifestation of hypoglycemia includes symptoms such as recumbent position, shivering, hypothermia, peddling movements of the limbs, foam around the oral cavity, convulsions, enophthalmos (due to dehydration), and, if the necessary therapy is not provided, coma and death of piglets [4].

The aim of this experimental work was to analyse the metabolic processing of glucose in suckling piglets after intravenous, intraperitoneal and subcutaneous application of 5% glucose solution. Also assess the

technique, advantages, disadvantages and possible complications of the investigated therapies and compare them with each other.

II. Materials and Methods

Animals

We included 20 piglets (Pietrain, Duroc and Landrace crossbreed) at the age of 2 weeks and an average weight of 4.2 kg in the experiment. The piglets were born at the Pig Clinic of the University of Veterinary Medicine and Pharmacy in Košice, where the entire experiment took place. From the first minutes after birth, the piglets were provided with suitable standard conditions, both in terms of housing (separate litter with a temperature of 35 ºC) and nutrition (adequate intake of colostrum and later milk). We handled the animals in accordance with the legislative requirements for animal welfare.

Experimental design

In the experiment, we compared intravenous, intraperitoneal and subcutaneous application of a constant volume (20 ml) of 5% glucose solution. On the beginning, we took blood from the eye sinus (*sinus ophthalmicus*) for the purpose of initial determination of glucose (0 collection). Subsequently, we divided the piglets proportionally into 4 groups and administered a glucose solution at different application sites.

Intravenous application: we administered the solution into the *sinusophthalmicus*. We fixed the piglets in the supine position. The application technique was implemented on the basis of a standard procedure [5], namely under the third eyelid with a ventro-medial direction of a 16 G needle and slow administration of the solution.

Intraperitoneal application: piglets were fixed by the pelvic limbs, head down. The entire volume of the preparation was administered to one place. A 20 G needle was inserted at an acute angle to the surface of the abdominal wall, in the *regiohypogastrica*, paramedially, about a finger's width from the midline, between the last pair of mammary nipples.

Subcutaneous application: we injected 5 ml of glucose 4 times into the skin fold behind the elbow joints of the thoracic limbs and in front of the knee joints of the pelvic limbs (needle 18 G) to piglets that were fixed in a head-down position.

After individual administrations, we took blood from the *sinus ophthalmicus* in four equal time intervals to determine the dynamics of glucose changes, after the 15th (1st collection), 30th (2nd collection), 45th (3rd collection) and the 60th minute (4th collection).

Laboratory analysis

Glucose concentration was detected on a Fujifilm Dri-Chem NX600V IC. This analyzer works on the basis of dry chemistry and the time required to measure glucose in a blood sample is approximately 6 minutes.

Statistical processing of results

The significance (P) of differences in the means of corresponding variables were evaluated by One-way analysis of variance and by Tukey's Multiple Comparison Test. We used GraphPad Prism 9 for the statistical process.

III. Results

Average blood glucose values varied dynamically depending on the site of application of the glucose infusion solution. We recorded the highest level of 9.06 mmol/l after 15 minutes of intravenous application with an increase of 36.04% (see figure and table). Subcutaneous application resulted in the highest mean glucose concentration of 8.14 mmol/l after 30 minutes with an increase of 21.86%. Intraperitoneal application reached its highest level of 6.82 mmol/l after 45 minutes with an increase of 10.0%. Statistical analysis did not show any significant changes in glucose concentration.

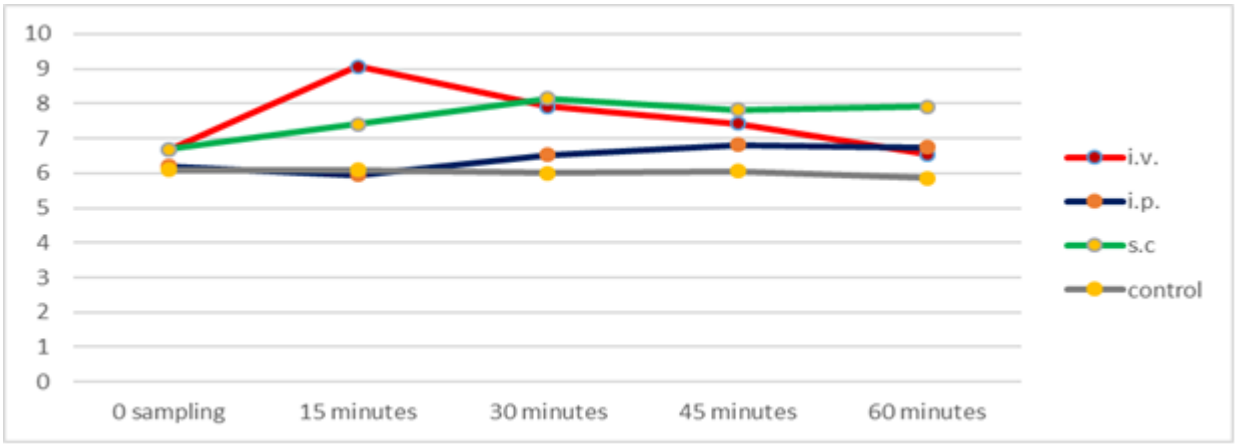

Figure 1 Comparison of different methods of application of 5% glucose(mmol/l)

Table 1 Evaluation of different methods of application of 5% glucose (mmol/l)

	i.v.	***i.p.***	***s.c***	***control***
0 sampling	6.66	6.20	6.68	6.10
15th minute	**9.06**	5.95	7.40	6.10
30th minute	7.92	6.52	**8.14**	6.00
45th minute	7.42	**6.82**	7.82	6.05
60th minute	6.54	6.74	7.92	5.85

IV. Discussion

Due to limited reserves of body fat and lack of brown adipose tissue, newborn piglets have inadequate thermoregulation, therefore they are prone to hypothermia especially in the first week of life [6]. In addition to the predisposition to postnatal hypothermia, piglets are also born with imperfect gluconeogenesis [4]. For this reason, in the first hours after birth, they may not be physiologically able to maintain the glucose concentration at the level of normoglycemia (4.7 – 8.35 mmol/l) [7]. During this period, they are dependent on glycogen reserves and the intake of colostrum or milk. Colostrum is therefore a vital source of energy. If piglets do not receive it, the concentration of glucose in the blood drops to hypoglycemic levels (glycemia < 2.2 mmol/l) within 24 – 36 h [4]. Piglets are born with glycogen reserves sufficient only for the first 16 h after birth [8]. Hypoglycemic piglets are lethargic, weak, and in severe cases, coma or death occurs [4]. Weak, hypoglycemic piglets also have a higher risk of mortality due to trauma after maternal crushing or overlying [9].

In our experimental work, we point out the advantages and disadvantages of three possible ways of hypoglycemia treatment in piglets. According to our results, intravenous application has proven to be the fastest and most effective way to raise blood glucose. We recommend its use when dealing with comatose states of baby pigs. However, the disadvantage is mastering the technique of application to the eye sinus. There is a risk of damage and inflammation of the conjunctiva and eyelid. In case of incorrect intravenous administration, accidental, unwanted application outside the vein (venous sinus), so-called extravasation [10]. In terms of disadvantages in newborn piglets, the insufficiently ossified bony structures of the orbit and the risk of piercing them must also be taken into account [4].

Fixation of animals is very important for intraperitoneal application. In our case, we fixed the piglets upside down in order to avoid injury to the internal organs (effect of gravity). The needle insertion angle is also important, it must be sharp. After penetrating the skin, subcutaneous tissue, muscles and peritoneum, aspiration is very important in order to exclude puncture of abdominal organs such as intestines, urinary bladder, etc. The advantage of this administration is the relatively quick application of a larger volume of the drug. The

disadvantage is the risk of damage to internal organs and the formation of adhesions, which can complicate the reproduction of sows in the later period. For this reason, we do not recommend this method of application to animals intended for breeding [10].

For the subcutaneous method of application, we used the same method of fixation of piglets as for i.p. application, which allows easy administration of the drug into the skin fold behind the elbow joints and/or in front of the knee joints. A great advantage of subcutaneous application is high bioavailability and rapid onset of effect [11]. In general, it is often used in cases where continuous treatment and low-dose therapy are preferred. There is a lower proportion of blood vessels in the subcutaneous tissue, and therefore drugs administered in this way are released into the bloodstream slowly but continuously [12]. Potential local adverse reactions following subcutaneous application include edema, erythema, pain, and ecchymosis. Local edema usually subsides within a few hours [13]. The disadvantage is also the necessity of applications to several places, to which piglets react sensitively. From this point of view, the recommended maximum injection volume per application site should be taken into account. Literature sources generally agree that in humans the maximum volume that can be applied per site is approximately 1.5 mL [14]. In pigs, a maximum of 1 to 2 ml can be applied to one place for the smallest categories and 3 ml for adult pigs [1]. In our experiment, we applied 5 ml of glucose to one place without any problems in piglets weighing an average of 4.2 kg. For this method of application, we recommend using 18G thick needles, as using thinner needles increases the application time. When using thicker needles, the drug will flow out of the injection site. Subcutaneous application can be used alone or in combination with other methods of rehydration therapy in pigs.

In case of hypoglycemia, there is also the possibility of oral administration of glucose by adding it to milk. However, not very vital and lethargic piglets at an early age very often do not accept or, due to the disappearance of the sucking reflex, cannot accept milk from a bottle. In some cases, the piglets take a long time to get used to the bottle and it is often necessary to respond immediately to hypoglycemia. Therefore, one of the options is feeding colostrum or milk through a tube directly into the stomach [15].

However, in the treatment of hypoglycemia in piglets, it is necessary to remember that it requires repeated application of glucose and ensuring the optimal temperature of the piglets' bedding in the range of 30 – 35 °C.

V. Conclusion

The application of a 5% glucose solution intravenously through the eye sinus is the most effective and fastest way to increase the blood glucose concentration of piglets. We recommend its use in dealing with severe, comatose states of hypoglycemia. Subcutaneous administration is a relatively safe form of administration of solutions. In practical conditions, we can combine it with other methods of therapy. The intraperitoneal route of drug administration is the least effective in terms of rapid replenishment of glucose in the blood serum, but it can be used when larger volumes of drugs are applied.

VI. Acknowledgements

This work was supported by the Slovak Research and Development Agency under the Contract no. APVV-22-0457 and VEGA no. 1-0162-23.

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