Scandinavian Journal of Laboratory Animal Science

2021, Volume 47, Number 2
ISSN 2002-0112

Technical report

Blood lactate and glucose concentrations in the femoral artery and three different veins during anaesthesia of healthy laboratory pigs

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Summary

Blood lactate is a parameter used for monitoring pigs during prolonged anaesthesia. Here we compared blood lactate and glucose concentrations in nine anaesthetised laboratory pigs. Seventeen of the samples originated from a liver project and 15 from a kidney project. Mean and standard deviations of arterial blood lactate and glucose were compared with values for portal, renal and femoral veins by using paired Student's t-test, paired Wilcoxon test as well as Spearman rank-order correlation. The study showed that lactate concentration was constant whether measured in blood from the femoral artery, portal vein, renal vein or femoral vein. The study showed that the origin of the blood sampled is not important and that changes in blood lactate concentration are likely to be the same throughout the cardiovascular system in healthy pigs.

Introduction

Pigs are increasingly used as experimental animals in pre-clinical research, and one of the advantages in using pigs is that they can be kept anaesthetised for up to 18 hours (Alstrup et al. 2020). Periods of more than 8 hours of anaesthesia are needed in scan studies and in many intervention studies performed as non-recovery. However, due to scientific and animal welfare reasons it is necessary to monitor their physiology during experimentation (Alstrup et al. 2018). During anaesthesia, blood lactate concentration is measured using conventional laboratory equipment, such as an ABL blood analyser, and it is therefore analysed without extra costs. In humans, blood lactate is used as a marker of hypoxia and as an indicator for poorly performed anaesthesia during surgery (O´Connor and Fraser 2012). In pigs, lactate is also used to evaluate anaesthesia and protocol, as elevated values should give rise to a critical review of procedures (Alstrup et al. 2020). However, relatively few studies with blood lactate measurements have been performed in pigs (Yang et al. 2012; Hofmaier et al. 2013; Alstrup 2016) and, there is still a need for more knowledge about blood lactate in relation to pig anaesthesia. Major differences in blood lactate concentration exist among different breeds of pigs (Hofmaier et al. 2013; Alstrup 2016). Interestingly, a single study has shown that blood lactate concentration is relatively stable during anaesthesia for up to 14 hours in the laboratory, while it increases 5-fold during road transportation of anesthetized pigs (Alstrup et al. 2020). In all these studies, blood lactate was measured in various blood vessels. No pig study has ever investigated the importance of where the blood samples were taken. In human studies, arterial blood is considered to be the gold standard for lactate measurement, but venous blood is often used for practical reasons, and a few studies have shown a good correlation between arterial and central venous lactate concentration in humans (Weil et al. 1987; Mahmoodpoor et al. 2020). Arterial blood is constant in its concentration of lactate, but minor variations may occur in venous blood concentra-

tions (Younger et al. 1996; Cengiz and Tamborlane 2009). Also in resting mice, there is good agreement between arterial and venous measurements of lactate (Felippe et al. 2017). However, a single study performed in anesthetized sheep has shown that blood lactate was higher in venous than in arterial blood (Mathews et al. 2014). We therefore investigated whether differences in blood lactate concentrations exist in blood sampled from a variety of blood vessels (femoral arterial, portal vein, renal vein or femoral vein) in laboratory pigs. For comparison, blood glucose was also measured since these two parameters, lactate and glucose, are closely related. Lactate is the end product of anaerobic glycolysis formed by glucose degradation under hypoxic conditions. Our hypothesis is that lactate measured in blood taken from different blood vessels gives similar values in healthy pigs.

Material and methods

We examined the medical records of nine pigs that underwent anaesthesia and imaging studies in 2016 (kidney project; N = 5) and 2018 (liver project; N = 4); all were approved by the Danish Experimental Animal Inspectorate (Licence number: 2014–15–2934–01026). Blood was sampled from approximately 40 kg (36 kg – 41 kg) female Danish Landrace-Yorkshire crossbreds. They were raised in a specific pathogen free

(SPF) facility and were fed a restricted pellet diet (Svin Foder VAK, Danish Agro, Denmark) with tap-water available *ad libitum*. The pigs were group-housed and acclimatized for at least one week prior to the experiments. The light period was 12:12 hours, the room temperature 20 °C and humidity 51 %. The pigs were fasted overnight before anaesthesia: premedication with 6.3 mg/kg ketamine and 1.3 mg/kg midazolam IM, induction and maintained with infusion of approximately 10 mg/kg/h propofol IV. The pigs were intubated and mechanically ventilated (approximately 15/min x 8 ml/kg) during the procedures.

Catheters were surgically (Ettrup et al. 2011) placed in the femoral artery, portal vein, renal vein and femoral vein. From each pig, 1-6 paired samples were taken from two (liver project) or three blood (kidney project) vessels simultaneously during anaesthesia which lasted for up to 12 hours. The first blood samples were taken after acclimatisation for at least an hour after finishing the surgical placing of catheters. Pulse, oxygen saturation and body temperature were monitored during the scanning as described by Alstrup and Winterdahl (2009). Anaesthesia was adjusted if the pulse suddenly changed, oxygen saturation decreased below 92 % or body temperature was outside the reference range 38.7-40.0 °C. Blood was handled in heparinized syringes according to a previous study performed on porcine blood (Olsen 2003), before being analysed by an automated clinical chemistry unit (ABL 550, Radiometer, Denmark). Only blood lactate and blood glucose concentrations are shown here; blood gases were also measured in order to adjust the anaesthesia (partial pressure of carbon dioxide: 5.3-7.0 kPa and partial pressure of oxygen: 12-25 kPa). At the end of the study, all pigs were euthanised with an overdose of phenobarbital (100 mg/kg, IV).

Arterial blood is considered the gold standard for lactate measurement as it is constant irrespective of the arterial sampling site (Younger et al. 1996). Therefore, mean and standard deviations of arterial blood lactate and glucose were calculated as a baseline with which measurements from each of the three venous vessels (portal, renal and femoral veins) were compared using the paired Student's t-test and Wilcoxon Signed-Rank Test. We also calculated Spearman rank-order correlations. All data were consistent with a normal distribution based on a graphical distribution. The level of statistical significance was set as $p < 0.05$.

Results

Results are shown in Table 1. Blood lactate and glucose were measured in 32 paired blood samples from the femoral artery, portal vein, renal vein and femoral vein from the nine pigs. In the femoral artery, all blood lactate and glucose concentrations were within the reference range seen in previous studies on domestic pigs (Alstrup 2016). For both the blood lactate and glucose concentrations, none of the three venous blood vessels (portal, renal and femoral) differed from the femoral artery values, with all p-values being very high ($p > 0.5$). Spearman rank-order correlations were between 0.97 and 1.00 for lactate and over 0.70 for glucose.

Discussion

Our findings showed that both blood lactate and blood glucose concentrations sampled from three different veins reflected the general lactate and glucose concentrations in arterial blood during anaesthesia of healthy adult pigs. In particular, the correlation (0.97 or higher) was high for lactate concentration.

Table 1: Blood lactate and blood glucose concentrations in pigs during anaesthesia.

Sampling site	Parameter	Liver project (4 pigs, 17 samples)	Kidney project (5 pigs, 15 samples)
Femoral artery - Mean ± SD	Lactate Glucose	**0.8 ± 0.2 mmol/l** **4.2 ± 0.6 mmol/l**	**0.6 ± 0.2 mmol/l** **6.1 ± 1.1 mmol/l**
Portal vein - Mean ± SD	Lactate Glucose	**0.8 ± 0.2 mmol/l** C_s=0.97 **4.2 ± 1.4 mmol/l** C_s=0.93	ND ND
Renal vein - Mean ± SD	Lactate Glucose	ND ND	**0.6 ± 0.3 mmol/l** C_s=0.99 **6.0 ± 0.7 mmol/l** C_s=0.71
Femoral vein - Mean ± SD	Lactate Glucose	ND ND	**0.6 ± 0.5 mmol/l** C_s>0.99 **6.4 ± 1.3 mmol/l** C_s=0.94

ND: not done. No significant ($p<0.05$) differences from femoral artery were found based on paired Student´s t-tests and Wilcoxon Signed-Rank Test. C_s: Spearman rank order correlation.

It is therefore not necessary, in practice, to measure blood lactate from several catheters simultaneously during many surgical procedures. This is similar to clinical studies, despite slight differences indicating marginally higher venous lactate values in humans (Younger et al. 1996). Also, as mentioned earlier, similar concentrations of blood lactate are measured in arterial and venous blood from resting mice, while in anesthetized sheep higher venous values are seen (Mathews et al. 2014; Felippe et al. 2017). The pig therefore appears to resemble the mouse and man in this respect. We did not find a difference in glucose between arterial and venous blood in our pig measurements, which is surprising as venous blood usually contains 0.17-0.28 mmol/l less glucose than arterial blood in humans (Cengiz and Tamborlane 2009). This could be explained by the fact that for at least 16 hours prior to anaesthesia the pigs were fasting, which is known to stabilize blood glucose (Cengiz and Tamborlane 2009). The correlation between venous and arterial blood was lower (0.71-0.94) for glucose concentration than for lactate. It could be speculated that blood glucose would have been higher in the portal blood post prandially, but this was not tested in our pigs. None of the pigs had lactate measured in blood samples taken from the ear vein. Ear vein blood is easier to measure in pigs when no catheters have been surgically inserted into the blood vessels.

Limitations: The study was only performed on healthy pigs that had a normal blood lactate concentration. Therefore, this limits the use of the results for studies with elevated lactate values, for example, in disease models. However, it is still possible that elevated levels of lactate could be observed simultaneously in central and peripheral blood vessels, as shown for patients with sepsis (Velissaris et al. 2019). As a concluding comment, it should also be mentioned that we used all available data from our laboratory in this study. The number of animals was therefore not determined from power calculations, but still represents typical numbers of pigs used for surgery and scanning studies. Thus, the study cannot document that there are no differences in arterial and venous blood lactate concentration in pigs, but simply shows that during typical experimental setups the measurements will be comparable.

Conclusion

Based on the above results we conclude that in healthy adult pigs there was no significant difference in concentrations of lactate or glucose whether measured from central arterial or venous blood.

Conflict of interest

The authors declared no potential conflict of interest.

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