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Blood Lactate Concentrations in Göttingen Minipigs Compared with Domestic Pigs

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Measurement of the blood lactate concentration is a useful monitoring tool during anesthesia of animals and people. Recently, blood lactate has been used to monitor anesthetized pigs, but very little is known about variations in blood lactate concentrations in this species. We therefore evaluate the effects of breed (domestic pigs compared with Göttingen minipigs), body weight (domestic pigs of 40 kg compared with 70 kg), type of anesthesia (inhalation compared with infusion) and surgery (minor compared with major surgery) on blood lactate concentrations in pigs. Anesthesia reports from 81 pigs are included. We find significantly higher blood lactate levels in minipigs anesthetized with isofluorane (2.53 ± 1.10 mmol/L) compared with domestic pigs (0.68 ± 0.48 mmol/L). Body weight, type of anesthesia, and type of surgery had no effect on blood lactate levels. Therefore, reference values for blood lactate concentrations in pigs should reflect the breed of interest.

In recent years, pigs have increasingly been used as animal models in biomedical research, and often this use involves anesthesia and surgery.[2] Monitoring of anesthetized pigs is essential for documentation of animal wellbeing and physiology. Blood lactate is an intermediate metabolite, and elevated plasma lactate levels are associated with poor outcome after surgery in humans.[5] Therefore, in human clinical research, blood lactate is often used as an indicator of hypoxia and poor-quality anesthesia and surgery. Recently, blood lactate concentrations in pigs have been measured prior to anesthesia and surgery,[4] and blood lactate has been used for predicting mortality in a porcine hemorrhagic shock model.[7] In the current study we analyzed data from some of our own pig studies. We evaluated the effects of breed (domestic pigs compared with Göttingen minipigs), body weight (40 kg compared with 70 kg), and type of anesthesia (inhalation compared with infusion) and surgery (minor compared with major) on blood lactate concentrations in pigs.

Materials and Methods

All procedures involving animals were approved by the Danish Experimental Animal Inspectorate in accordance with European Directive 86/609/EEC. We examined the medical records of 81 pigs that underwent anesthesia between 2011 to 2014. The study population comprised 19 female Göttingen minipigs (Ellegaard Minipigs ApS, Dalsmose, Denmark) and 62 female Danish Landrace–Yorkshire crossbred domestic pigs from a local farmer. All pigs received a restricted pellet diet (DIA plus FI, DLG, Denmark) and iron (Grynt, DLG, Denmark), and they were acclimated for at least 1 wk before anesthesia. The environmental conditions were 20 °C, 51% relative humidity, uncontrolled light cycles, and 8 air exchanges hourly. The pigs were food-fasted for 16 h prior to anesthesia but had free access to tap water. They were not enrolled in any specific health-monitoring program, but they were clinically evaluated prior to anesthesia. All pigs were premedicated with 1.25 mg/kg midazolam (Dormicum, Roche, Hvidovre, Denmark) and 6.25 mg/kg ketamine (S-Ketamin, Pfizer, Ballerup, Denmark) intramuscularly. Anesthesia was induced with 1.25 mg/kg midazolam and 3.13 mg ketamine intravenously. The pigs were immediately intubated (tube size: 6, 7, or 8), and anesthesia was maintained by infusion of 5 to 10 mg/kg propofol (Propofol Braun, B. Braun Melsungen AG, Melsungen, Germany) intravenously or 2.0% to 2.2% isofluorane (Forene, Abbott, Solna, Sweden) in oxygen and normal air (1:2.2) on a ventilator.

As minor surgery, cortex catheters (Johnson and Johnson, Miami, FL) were placed in a femoral artery and femoral vein in all 81 pigs as described previously.[3] In addition, major surgeries were performed on 22 domestic pigs and included laparotomy (n = 16), liver catheterization (n = 4) ,and craniotomy (n = 2). These pigs were treated with fentanyl or other opiods prior to surgery. Arterial blood gases and blood lactate levels were monitored after surgery, and the samples were handled as described previously[6] and were analyzed by using an automated clinical chemistry unit (ABL 550, Radiometer, Brønshøj, Denmark). Only blood lactate concentration from the first blood sample (obtained approximately 1 h after anesthesia induction) was used in this study. Isotonic saline was infused slowly intravenously to prevent dehydration. Heart rate, body temperature, and reflexes were monitored continuously and used to guide regulation of anesthesia.[1,2] All pigs were later used in positron emission tomographic studies, but those results are not included herein. At the end of the study, the pigs were euthanized with an overdose of pentobarbitone (100 mg/kg; Veterinærapoteket, Frederiksberg, Denmark) intravenously or awakened from anesthesia and returned to the animal facility for further studies. Blood lactate concentrations from the different groups were compared by using the Welch–Satterthwaites t test, as standard deviation values were different between groups, and some group sizes were small. A P value less than 0.01 was defined as statistically significant.

Results

Blood lactate concentrations were significantly ($P < 0.001$) higher in minipigs (2.53 ± 1.10 mmol/L, n = 19) than in domestic pigs (0.68 ± 0.48 mmol/L, n = 16; Table 1). Neither body weight,

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Table 1. Blood lactate concentrations (mean ± 1 SD) in the 81 pigs studied

	Mean body weight/ age	Anesthetic	Type of surgical procedure	No. of pigs	Blood lactate concentration (mmol/L)	*P*
Göttingen minipigs	35 kg/17 mo	Isofluorane	Minor	19	2.53 ± 1.10	<0.001
Domestic pigs	40 kg/3-4 mo	Isofluorane	Minor	16	0.68 ± 0.48	not significant
	40 kg/3-4 mo	Propofol	Minor	16	0.77 ± 0.34	not significant
	40 kg/3-4 mo	Propofol	Major	22	0.88 ± 0.65	not significant
	70 kg/5 mo	Propofol	Minor	8	0.71 ± 0.39	not significant

type of anesthesia, nor type of surgery affected the blood lactate concentration in domestic pigs.

Discussion

Investigation of the effects of pig breed, body weight, and type of anesthesia or surgical procedure on blood lactate concentrations in pigs revealed that Göttingen minipigs had, on average, double the concentration of blood lactate that was found in domestic pigs, even though the exact same anesthesia and surgical procedures were used. This difference may indicate that Göttingen minipigs have a higher blood lactate concentration than domestic pigs or that minipigs are more sensitive to hypoxia. However, I am unaware of any reason why minipigs should be more sensitive to hypoxia. In addition, minipigs typically are easy to anesthetize, even for prolonged periods, and postsurgical complications are rare.[1,2,8] Perhaps the procedures used for pig handling, anesthesia, and surgery were better suited to domestic pigs than minipigs, but complications during anesthesia were rare in both breeds. Therefore the blood lactate concentration likely is truly higher in Göttingen minipigs than in domestic swine. Blood samples obtained from 4 sedated pigs prior to surgery yielded lactate concentrations of 1.8 and 2.7 mmol/L in the 2 female minipigs (27 to 29 kg), compared with 0.7 and 0.8 mmol/L in 2 female domestic pigs (22 to 23 kg). One reason for the different blood lactate concentrations could be differences in the ages of the pigs. For example, a 40-kg animal likely would be an adult minipig (age, 1 to 2 y) but a juvenile (age, 3 to 4 mo) domestic pig.[2] In support of this reasoning, lactate concentration is known to increase with age and muscle mass in humans.[9,10] However, the current results showed no effect of body weight (40 kg compared with 70 kg) or related age-associated differences on blood lactate concentrations in the domestic pigs. Even if the age differences between domestic pigs are small (3 to 4 mo for 40-kg compared with 5 mo for 70-kg domestic pigs), making the difference difficult to detect, it is still unlikely that the higher concentrations in minipigs are only due to their older age (17 mo). Interbreed differences in the blood lactate of pigs are known to exist. For example, blood lactate concentrations were 25% higher in Rheinhybrid–Pietrain pigs than in Landrace–Pietrain crossbreds.[4] In addition, mean plasma lactate acid was 1.52 mmol/L in Erhualian pigs compared with 1.81 mmol/L in Pietrain pigs.[11] These data highlight that breed differences in lactate concentrations probably are common in pigs, in agreement with the genetic influence in pigs reported previously.[12]

Why then are lactate concentration so high in Göttingen minipigs compared with domestic pigs? More data on biochemical metabolites (for example, pyruvate) in minipigs are needed before this question can be answered. In the current study, glucose concentrations were higher ($P = 0.0014$; Student *t* test) in 40-kg domestic pigs (4.8 ± 1.1 mmol/L) than in 35-kg minipigs (mean, 3.4 ± 1.2 mmol/l), both of which groups were anesthetized with isofluorane. The glucose concentrations in the current study were somewhat lower than those reported by the company (4.8 ± 1.2 mmol/L; www.minipigs.dk) for female minipigs and might indicate increased glycolysis, leading to increased pyruvate and lactate levels, in the study population.

An important biologic difference between the groups is their growth rates: whereas 3- to 5-mo-old domestic pigs grow 500 to 700 g daily, the growth rate of 17-mo-old minipigs is less than 50 g daily,[8] indicating a difference in metabolism. In addition, the domestic pigs in the current study had lower lactate concentrations (0.68 to 0.88 mmol/L) than has been published in the literature (1.2 mmol/L).[4] This difference might reflect that Danish Landrace × Yorkshire crossbred pigs actually have lower baseline blood lactate concentrations than do other pig breeds, or they might be less sensitive to hypoxia than are Gottingen minipigs. Alternatively, the anesthesia procedures in the current study might have been more optimal than are those of other laboratories. My laboratory has several years of experience with pig anesthesia and handling techniques, and we believe that a quick intubation after induction of anesthesia is crucial to avoid hypoxia. We also find it important to ventilate the pigs with oxygen-enriched air just after intubation. Only a single study has reported very low blood lactate concentrations (0.89 mmol/L), which were measured in blood sampled from trained gilts with implanted ports.[13]

Blood lactate concentrations after major surgery did not differ from those after minor surgery in the present study. Data from several types of major procedures were pooled to avoid small group sizes. However, high blood lactate concentrations occurred in the 2 pigs that underwent craniotomy (1.2 mmol/L and 1.5 mmol/L), perhaps indicating that this surgical procedure has a greater effect on domestic pigs than do other types of major surgery.

Neither body weight nor type of anesthesia effect blood lactate concentrations. These findings are in agreement with the literature, in which neither body weight nor age influence the blood lactate concentration.[4] Furthermore, these results indicate that both isofluorane and propofol are useful drugs for pig anesthesia, and this opinion is in agreement with the recommendations in several textbooks on pig anesthesia.[1,2,8]

In conclusion, higher blood lactate concentrations were significantly higher in Göttingen minipigs anesthetized with isofluorane compared with similarly anesthetized domestic pigs. Therefore, reference values for blood lactate in pigs should reflect the breed of interest.

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