JOURNAL OF SURGICAL RESEARCH • DECEMBER 2016 (206) 325–336

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Appropriate timing of blood sampling for blood gas analysis in the ventilated rabbit

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ARTICLE INFO

Article history:
Received 15 March 2016
Received in revised form
20 June 2016
Accepted 2 August 2016
Available online 9 August 2016

Keywords:
Arterial sample
Blood gas analysis
Oxygen saturation
Rabbit
Sample timing
Venous sample

ABSTRACT

Background: Arterial and venous blood gas analyses (BGAs) are essential to evaluate devices that measure biological oxygenation. The appropriate timing of blood sampling for BGA after respiratory rate (RR) change in animal experiments has not been reported. This study investigated the appropriate timing of blood sampling for BGA in ventilated rabbits and whether venous samples are an alternative to arterial samples.

Materials and methods: Under general anesthesia, 14 rabbits (body weight, 3.02 ± 0.09 kg) were ventilated and their RR was changed (40/min, 30/min, and 20/min). Blood was sampled through cervical arterial and venous catheters. Experiment 1: in seven rabbits, arterial BGA was measured at 0, 0.5, 1, 2, 3, 5, 10, 15, and 20 min after the RR change. Experiment 2: in seven different rabbits, simultaneous arterial and venous BGA were measured at 0, 2, 5, 10, 15, and 20 min after the RR change.

Results: Oxygen partial pressure (PO_2) and saturation (SO_2) of the arterial blood stabilized 0.5 min after the RR changed. In venous BGA, no index stabilized during observation. The arterial and venous values of the carbon dioxide partial pressure (PCO_2) and pH had significant correlations (arterial $PCO_2 = 0.9316 \times$ venous $PCO_2 - 4.4425$ [$r = 0.9178$]; arterial pH $= 1.0835 \times$ venous pH-0.5795 [$r = 0.9453$]).

Conclusions: In ventilated rabbits, arterial PO_2 and SO_2 stabilized in 0.5 min. No venous value stabilized after the RR change. Only the PCO_2 and pH of venous samples may be an alternative to arterial samples under the defined formula.

Introduction

The development of new medical devices has driven the progress of intensive medicine.[1] Medical monitoring devices such as the electrocardiograph and pulse oximeter are broadly used to assess a patient's condition noninvasively and to decide whether medical treatments are needed. In clinical settings, the pulse oximeter is widely used. This

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http://dx.doi.org/10.1016/j.jss.2016.08.007

simple device monitors oxygen saturation in arterial blood and provides information about the respiratory state. However, some studies[2–4] show limitations in the accuracy of the pulse oximeter, and blood gas analysis (BGA) is recognized as the most reliable index for respiratory condition.

Pulse oximeter and real-time monitoring of oxygenation using similar technology (i.e., near-infrared spectroscopy [NIRS])[5,6] are also used in intensive care for neonates with congenital or peculiar diseases.[7] Relative to the blood gas analyzer, these devices sometimes cause improper readings because of hemodynamic collapse due to hypothermia, hypoxia, or acute anemia; skin color; and brightness around the sensor. A dramatic change in circulation occurs in neonates because of hypothermia, hypoxia, or subsequent oxygen therapy.[2] In these specific conditions, the accuracy of a pulse oximeter and NIRS may be unreliable.[5,6,8–10] To assess accuracy of these devices, *in vivo* experiments are an important step to prove the utility of these devices, although experiments in humans are sometimes unacceptable for ethical reasons. Therefore, animal experiments remain important.[11]

BGAs in experimental animals are essential to improve oxygenation monitoring systems[11]; however, no study exists concerning the appropriate timing after the change in the settings of a ventilator. In several studies that used pulse oximetry in rabbits,[12–14] arterial blood gas was sampled at 2 min after the setting of artificial ventilation. The investigators confirmed that the values of the pulse oximeter were stabilized at this point, but they did not confirm that the values of arterial blood gas were stabilized.

In human arterial BGA, the time to reach oxygenation equilibrium after changing respiratory conditions is reportedly 7-20 min.[15,16] In general, cardiac output is a linear factor of oxygen delivery in tissues.[17] Edwards *et al.*[18] report that the average cardiac output of adult rabbits weighing 2.0 kg is 350 mL/min. The average human cardiac output in male adults weighing 70 kg is 5 L/min.[19] Rabbits have 2.39 times larger cardiac output per kilogram of body weight. Therefore, we set a hypothesis that the time to reach oxygenation equilibrium in rabbits are 3-8.4 min because of the difference of cardiac output between human and rabbits.

Venous blood gas seemed to be an important factor to discuss oxygenation and oxygen consumption; however, the behavior of venous blood oxygenation is unclear. The effect of arterial and venous blood gas values of tissue oxygen saturation, as measured by NIRS in medical practice, is controversial.[20] Arterial and venous BGA is essential for further research. To the best of our knowledge, there has been no study on simultaneous arterial and venous gas analysis.

In this study, we therefore used rabbits, which have a similar body weight as a human neonate and are widely used as models of acute respiratory disease and validation of pulse oximeters.[12–16,21] The aim of the study was to investigate the appropriate timing of blood sampling for BGA in a ventilated rabbit model and to investigate whether venous samples are an alternative to arterial samples.

Materials and methods

Ethical approval

All animal experiments were approved by the Animal Experimentation Committee at the National Defense Medical College (Tokorozawa, Saitama, Japan). The approval number is 13091.

Animal preparation

Fourteen adult 15-wk to 21-wk-old female Japanese White rabbits weighing 3.02 ± 0.089 kg (mean ± standard deviation) were used for the experiment.[22] The animals were purchased from a laboratory animal supplier (Kitayama Labes Co, Ltd, Nagano, Japan) and housed singly in a cage in our animal facility more than 1 wk before the experiments to acclimate them to the environment. Constant room temperature (25°C) and humidity (50% ± 5%) were maintained with 12 h of light-dark cycle. They had *ad libitum* access to pellet food and water.

Anesthesia and monitoring

Anesthesia was induced by an intramuscular injection of mixture of 35 mg/kg ketamine (Ketalar; Daiichi Sankyo Co, Ltd, Tokyo, Japan) and 5 mg/kg xylazine (Sederac; Nippon Zenyaku Kogyo Co, Ltd, Fukushima, Japan) in the gluteal region.[23] Figure 1 shows the experimental setup. After the eyelash reflex and pinch reflex disappeared, the rabbits were placed supine on a heating table (KN303-B; Natsume Seisakusho Co, Ltd, Tokyo, Japan), and the hair in the neck and left hindlimb were shaved. All surgical procedures were performed under sterile conditions. The rabbits were monitored by a pulse oximeter, a noninvasive manometer, and an electrocardiograph with three needle-type subcutaneous electrodes (Life Scope BSM-5192; Nihon Kohden Corp, Tokyo, Japan). The subcutaneous electrodes were placed at the right and left upper chest and left upper abdomen. A lead II electrocardiogram monitored the animals throughout the experiment. Blood pressure in the right lower thigh was noninvasively measured every 2.5 min by the manometer (Life Scope BSM-5192; Nihon Kohden Corp). The rabbits' bodies were covered by a heating blanket (Homeothermic Monitor K020917; Harvard Apparatus, Holliston, MA) and their rectal temperature was maintained at 39.5°C ± 1.0°C.[24]

A 23-gauge venous catheter (Surflo, SR-OT2419C; Terumo, Tokyo, Japan) was inserted in the left auricular vein, and physiological saline (Otsuka Pharmaceutical Co, Ltd, Tokushima, Japan) was infused at a rate of 6 mL/kg/h.[25] An L-shaped incision was created in the neck region. A midline incision was made through the jaw to the jugular notch of the sternum and extended 3-cm horizontally to the right. A tracheotomy was performed 1-cm dorsal from the cricoid and a tracheal tube with a 4-mm internal diameter (RUSCH Safety Clear; Teleflex Medical OEM, Gurnee, IL) and a 5.3-mm external diameter was cut to 11 cm length and distal 4 cm of tube was inserted into trachea (Fig. 2A). Tracheal tube was connected to