Cairo University
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BLOOD LACTATE AS A DETECTOR OF TISSUE HYPOXIA IN HYPOXEMIC CHEST DISEASES

Thesis

Submitted for fulfillment of master degree in pulmonology

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بِسْمِ ٱللَّهِ ٱلرَّحْمَٰنِ ٱلرَّحِيمِ

قَالُوا۟ سُبْحَٰنَكَ لَا عِلْمَ لَنَآ إِلَّا مَا عَلَّمْتَنَآ

إِنَّكَ أَنتَ ٱلْعَلِيمُ ٱلْحَكِيمُ.

صدقَ اللهُ العظيم

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Abbreviations

- **2,3-DPG** : 2,3-diphosphoglycerate.
- **A-a gradient** : Alveolar- arterial gradient.
- **ABGs** : Arterial blood gases.
- **Acetyl CoA** : Acetyl Co-enzyme A.
- **ACPE** : Acute cardiogenic pulmonary edema.
- **ADP** : Adenosine di-phosphate.
- **AE1** : Erythrocyte Cl^-–HCO_3 exchanger 1(anion exchanger 1).
- **ALI** : Acute lung injury.
- **Alt .** : Altitude.
- **AMP** : Adenosine monophosphate .
- **ANOVA** : Analysis of variance.
- **ARDS** : Acute respiratory distress syndrome.
- **ASA** : Acute severe asthma.
- **ATP** : Adenosine tri-phosphate.
- **Ca^{+2}** : Calcium ions.
- **CaO_2** : Oxygen content of the arterial blood.
- **CAs** : Carbonic anhydrases .
- **CB** : Carotid bodies.
- **CBC** : Complete blood count.
- **CHF** : Congestive heart failure.
- **Cl^-** : Chloride ion.

- **cm H_2O** : Centimeter water.
- **CO_2** : Carbon dioxide.
- **COPD** : Chronic obstructive pulmonary disease.
- **COX** : Cyclo-oxygenase enzyme.
- **CPAP** : Continuous positive airway pressure.
- **CSF** : cerebro-spinal fluid.
- **$D_{(u)}O_2$** : useful oxygen delivery.
- **dl** : Deci-liter.
- **DNA** : Deoxyribonucleic acid.
- **DO_2** : oxygen delivery.
- **EPO** : Erythropoietin.
- **ET** : Endothelin.
- **ETT** : Endotracheal tube.
- **$FACO_2$** : Fractional alveolar carbon dioxide concentration.
- **FEV_1** : Forced expiratory volume in the 1st second.
- **FIO_2** : Fractional of inspired oxygen concentration.
- **G.K** : Gluco-kinase enzyme.
- **G6P** : Glucose 6-phosphate.
- **GLUT** : Membrane glucose transporter.
- **H.K** : Hexo-kinase enzyme.
- **H^+** : Hydrogen ion.
- **H_2CO_3** : Carbonic acid.
- **H_2O** : Water.

- **Hb** : Hemoglobin.
- **HCO_3** : Bicarbonate ion.
- **HIF-1** : Hypoxia inducible factor-1.
- **HPV** : Hypoxic pulmonary vasoconstriction.
- **HR** : Heart rate.
- **HVD** : Hypoxic ventilatory drive.
- **ICU** : Intensive care unite.
- **ID** : Inner diameter.
- **IMP** : Inosine monophosphate.
- **IPF** : Interstitial pulmonary fibrosis.
- **K^+** : Potassium ion.
- **kPa** : Kilopascal.
- **L** : Liter.
- **L/P** : Lactate/ pyruvate ratio.
- **LDH** : Lactate dehydrogenase.
- **LTOT** : Long term oxygen therapy.
- **MCH** : Mean corpuscular hemoglobin.
- **MCT** : Monocarboxylate transporter.
- **MCV** : Mean corpuscular volume.
- **mEq** : Milli-equivalent.
- **Mg^{++}** : Magnesium ion.
- **min** : Minute.
- **ml** : Milliliter.
- **mmHg** : Millimeter mercury.

- **mmol** : Milli-mole.
- **mRNA** : Messenger ribonucleic acid.
- **Na_2CO_3** : Sodium bicarbonate.
- **NaCl** : Sodium chloride.
- **NAD** : Necotinamid adinine dinuclutide.
- **$NADH^+$** : Necotinamid adinine dinuclutide reduced form.
- **NBC** : Na^+–HCO_3 co-transporter.
- **NICE** : National Institute for Health and Clinical Excellence.
- **NIPSV** : Noninvasive pressure support ventilation.
- **NPPV** : Noninvasive positive pressure ventilation.
- **O_2** : Oxygen.
- **$P(A\text{-}a)O_2$** : Alveolar to arterial oxygen pressure gradient.
- **P_{50}** : Oxygen tension when hemoglobin is half saturated.
- **$PaCO_2$** : Arterial carbon dioxide tension.
- **PaO_2** : Arterial oxygen tension.
- **PAO_2** : Alveolar oxygen tension.
- **PB** : Barometric pressure.
- **PCO_2** : Carbon dioxide tension.
- **PEEP** : Positive end expiratory pressure.
- **PFK** : Phosphofructokinase.
- **PGI_2** : Prostaglandin I_2.

- **PGs** : Prostaglandins.
- **pH** : The logarithm of hydrogen ion concentration.
- **PHD** : Prolyl-hydroxylase protein.
- **PH_2O** : The partial pressure of water vapor at body temperature.
- **Pi** : Phosphate group.
- **Pi/CrP** : Phosphate group/ phospho-creatine ratio.
- **PICU** : Pediatric intensive care unite.
- **PIO_2** : Inspired oxygen partial pressure.
- **PO_2** : Oxygen tension.
- **Qs** : Systemic blood flow.
- **R** : Respiratory quotient.
- **Raw** : Airways resistance.
- **RBC** : Red blood corpuscle.
- **REM sleep** : Rapid eye movement sleep.
- **s** : Second.
- **SaO_2** : Arterial oxygen saturation.
- **Sat Thresh** : Notional threshold in capillary oxygen saturation.
- **SBT** : Spontaneous breathing trial.
- **SD** : Standard deviation.
- **SIMV** : Synchronized intermittent mandatory ventilation.

- **SpO_2** : Pulse oximeter.
- **SPSS** : Statistical package for the social science.
- **SvO_2** : Mixed venous blood saturation.
- **TCA** : Tricarboxilic acid.
- **THAM** : Tromethamine.
- **TTOT** : Trans-tracheal oxygen therapy.
- **TXA_2** : Thromboxan A_2.
- **USA** : United states of America.
- **V/Q** : Ventilation/ perfusion ratio.
- **VO_2** : Oxygen consumption.
- **Δ** : Delta (difference).

List of the contents:

Introduction

Most of the energy deployed in mammalian body is delivered from the oxidation of food fuels, of which the most important is glucose, so biological oxidation proceeds by a large number of stages with phased production of energy. This energy is not released immediately but is stored mainly by means of the reaction of adenosine diphosphate with inorganic phosphate ion to form adenosine triphosphate, which acts as a short-term store of energy. **(Lumb and Pearl $_{(D)}$, 2006)**

In absence of oxygen, the reduced form (NADH) cannot be oxidized to NAD+, and ATP production by the cytochrome system is blocked. Because the carboxylase reaction requires NAD+, pyruvate can no longer enter the mitochondria, and the concentration of both pyruvate and lactate in the cytoplasm increase. Increase in NADH within the cytoplasm result in a disproportionate increase in lactate. **(Effros and Wesson, 2005).**

Most commonly, lactic acidosis occurs as a secondary phenomenon under conditions in which cellular respiration is impaired because of inadequate oxygen delivery. When lack of oxygen compromises ATP generation, the remaining option for the cell is to revert to an anaerobic mode of glucose metabolism. Recall that because fatty acids also must be metabolized under oxidative conditions, they do not represent an auxiliary fuel when oxygen availability is limiting. **(Cohan and Roth, 1996)**

Anaerobic glycolysis results in acid production in the form of H^+. Glycolysis forms pyruvic acid, which is reduced to lactic acid**.** At an intracellular pH of 7.35, lactic acid dissociates to form the carboxylic anion, lactate and H^+. Lactate and the H^+ are both transported on one of the cell into the interstitial fluid by a transporter on the plasma membrane and eventually diffuse into the blood. If the amount of lactate generated exceeds the buffering capacity of the blood, the pH drops below the normal range, resulting in lactic acidosis **(Lieberman et al, 2007)**

At a physiological level, transient lactic acidosis occurs when the persons exercise so vigorously that oxygen dept incurred. But the metabolic capacity of the liver and kidney manage the problem. **(Cohan and Roth, 1996)**

The lactate level can be measured in plasma or whole blood .A lactate level above 2 mmol/L is abnormal but in patient with sepsis a blood lactate level above 4 mmol/L may have more prognostic value **(Marino, 2007).**

The importance of monitoring arterial lactate levels in critically ill patients has been advocated. Lactate is formed from pyruvate by the cytosolic enzyme lactate dehydrogenase. Lactate concentrations >2 mmol/l are generally considered a biochemical indicator of inadequate oxygenation. Circulatory failure with impaired tissue perfusion is the most common. **(Boldt, 2002)**

Aim of the work

The aim of the work:

The aim of this work is to determine the validity of blood lactate level as a detector of tissue hypoxia and as a predictor of deterioration of the condition in hypoxemic pulmonary diseases (including mechanically ventilated and non ventilated patients).