Correlation of Arterial, Central Venous and Capillary Lactate Levels in Septic Shock Patients

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Background: *Blood lactate level increases in response to tissue hypoxia and this level is currently used to monitor shock management. To obtain the arterial lactate value in clinical practice is a time consuming process. Our previous study demonstrated good correlation between the capillary lactate determined by a portable lactate analyzer and the standard arterial lactate in critically ill patients. This study was aimed to examine the uses of this capillary lactate in septic shock.*
Material and Method: *A prospective comparison of arterial, venous and capillary lactate level from septic shock patients admitted in the general wards and the Medical ICU, Department of Medicine, Siriraj hospital was performed during October 2009 to February 2010.*
Results: *Thirty patients were included in the study. The mean age was 66 (24-86) years and 16 (53%) were female. The correlation between arterial and central venous was 0.992 and the correlation between arterial and capillary lactate level was 0.945 (p = 0.01 in both comparisons). In addition, there was certain agreement between the arterial and the capillary lactate especially when arterial lactate was below 10 mmol/L.*
Conclusion: *The capillary lactate level determined by the portable lactate analyzer (Accutrend® Plus) correlated well with arterial lactate level. This method, when used cautiously, may be used to monitor septic shock treatment as an alternative to the standard arterial lactate determination.*

Keywords: *Arterial lactate, Central venous lactate, Capillary lactate, Septic shock*

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Lactate is an end product from the reduction of pyruvate during anaerobic metabolism which takes place within the cytosol as a final step of glycolysis. The lactate level is found to increase in 2 conditions. First, in severe illness with tissue hypoxia which results in increased anaerobic metabolism and second, in conditions with altered lactate clearance such as liver and kidney impairment. When carefully excluding patients in the latter group, lactate level can be used as the diagnostic, therapeutic and prognostic marker of global tissue hypoxia in circulatory shock[1-5]. Previous study demonstrated that the level of excess lactate corresponded to severity of circulatory failure and an excess of lactate > 4 mmol/l prognosticates a fatal outcome[6]. The higher lactate clearance in 6 hours after presentation is associated with decreased mortality rate[7]. In addition, apart from venous oxygen saturation, normalizing serum lactate during septic shock resuscitation was proved to be an equivalent alternative monitoring of treatment[8].

In clinical practice, there are limitations in obtaining lactate level since the standard method for lactate determination requires multiple time consuming processes from specimen collection and transportation to biochemical laboratories. In certain areas, such as Thailand, significant time lag between blood collection and laboratory report makes the results not clinically reliable.

The capillary lactate was developed for and used in sport medicine. Previous studies demonstrated good correlation between arterial and capillary lactate both in exercise subjects[9] and in critically ill patients[10].

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However, uses of capillary lactate in septic shock patients may be uncertain because of altered microcirculation during sepsis and vasopressor use[11]. This study, therefore, was performed in septic shock patients to determine the correlation between arterial lactate and capillary lactate measured by the handheld lactate analyzer (Accutrend® Plus). The main purpose was to verify the clinical use of the capillary lactate as a tool to monitor the efficacy of septic shock management.

Material and Method

Patients

Adult patients admitted to the Medical wards or the Medical ICU with septic shock from October 1, 2009 to February 28, 2010, were enrolled after written informed consent from the patients or their relatives. Inclusion criteria consisted of a suspected infectious source and two of the following: a) temperature > 38°C or < 36°C, b) heart rate > 90 beats/min, c) respiratory rate > 20 breaths/min, or PaCO2 32 mm Hg, or d) white blood cell count > 12,000 cells per mm3, < 4,000 cells per mm3, or > 10% band cells) and a systolic blood pressure < 90 mm Hg after a 20 mL/kg fluid challenge. Also, they must have central venous catheter inserted during hemodynamic resuscitation. Patients who underwent cardiopulmonary resuscitation and those who took metformin, stavudine and zidovudine were excluded from the study. During hemodynamic management, their capillary blood was taken and applied to a test strip and attached to the reading device. At the same time, the arterial and central venous blood were taken, ice-chilled and transported to the biochemical laboratory for standard lactate determination.

Portable lactate analyzer

The portable lactate analyzer and the disposable test strips (Accutrend® Plus) were purchased from Roche Diagnostics (Thailand) Ltd. Lactate was determined by using a compact reflectance photometer. Capillary blood was taken from the fingertip and applied on the strip. The strip was then inserted to the reading device. Lactate was determined by reflectance photometry. The results will be shown in 60 seconds. The instrument's range for whole blood lactate analysis is between 0.8-21.7 mmol/L[12]

Arterial and central venous blood lactate determination

The steps of collecting central venous blood were described as follows. Arterial blood was drawn from radial or femoral artery. Venous blood was drawn from internal jugular catheter. Both were collected in tubes containing sodium fluoride and were immediately placed on ice and transported to the biochemical laboratory for standard lactate determination by rapid enzymatic measurement method. The normal range in our laboratory is 0.5-2.0 mmol/L.

Statistical analysis

We expressed our descriptive statistics as mean $\pm$ SD. The extent to which capillary blood lactate could substitute for standard arterial blood lactate was assessed by measures of both correlation and agreement between these values. Correlation between capillary and arterial blood lactate and between central venous and arterial blood lactate were determined by simple linear regression using each value as a variable. The strength of association between the two variables was measured by the Pearson correlation coefficient(r).

Analysis of agreement was performed by using precision-bias matrix as described by Bland and Altman[13]. The method is described as follows. The capillary-arterial lactate difference (Y axis) was plotted against the mean of the arterial and capillary lactate (X axis). The horizontal line labeled "mean" indicates the mean of the capillary and lactate differences which is known as the line of agreement. It is bound by two parallel lines, known as the limits of agreement which are drawn at $\pm$ 1.96 SDs above and below the agreement line. The likelihood that capillary lactate may be used as an alternate to arterial blood lactate in individual patients includes 1) the mean capillary-arterial difference is minimal while the standard deviation is within clinical acceptable range and 2) the mean-difference plots were within the limits of agreement.

Ethical consideration

This study was reviewed and approved by the Siriraj hospital's ethical committee, using the Declaration of Helsinki.

Results

Thirty patients were included in the study. As shown in Table 1, 16 patients (53%) were female and 14 (47%) were male. The average age was 66.2 $\pm$ 16.3 years (mean $\pm$ SD). Twelve patients (40%) had hypertension and 7 (23%) had diabetes mellitus as underlying diseases. Nine patients (30%) had positive blood culture. The infectious sources were as followed: pneumonia (13 patients, 43%), pyelonephritis (2

patients, 7%), peritonitis (2 patients, 7%) and diarrhea (2 patients, 7%). The average values for arterial lactate (A-LAC), venous lactate (V-LAC) and capillary lactate (C-LAC) were 3.9 ± 3.2, 4.02 ± 3.27 and 5.3 ± 2.6 mmol/L respectively. Details of patients' characteristics are listed in Table 1.

Fig. 1A demonstrated correlation between A-LAC and V-LAC, which was 0.992, p = 0.01 and Fig. 1B, the correlation between A-LAC and C-LAC was 0.945, p = 0.01. The average of each pair A-LAC and C-LAC values was plotted against their differences (Bland-Altman plot), as shown in Fig. 2. The mean capillary-arterial lactate difference was 1.317 mmol/L while the standard deviation was 1.136 and the agreement limits ranged from -0.91 to 3.5. All but two paired C-LAC and A-LAC mean and difference plots were in agreement limits. When focusing on each disagreement, it was noticeable that these plots came from the patients with high lactate values (A-LAC 10.9, C-LAC 9.7 mmol/L and A-LAC 15.3, C-LAC 13.6 mmol/L respectively).

Fig. 3 demonstrated a scatterplot between capillary-arterial lactate gradients against the norepinephrine doses. There was no significant correlation between these two parameters, r = -0.156, p = 0.447.

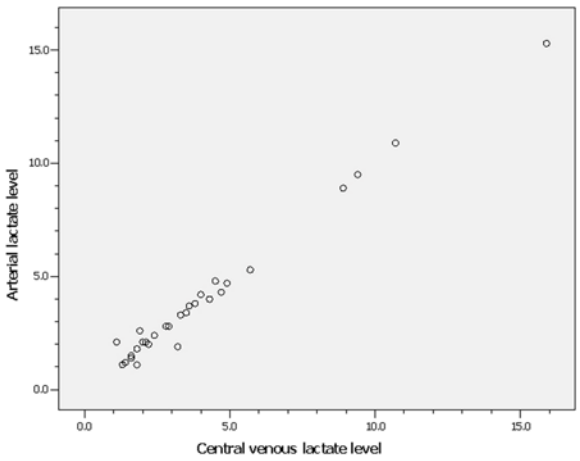
Table 1. Demographic data (n = 30)

Male: female	14: 16
Age (years)	66.2 ± 16.3
Underlying diseases	
Hypertension	12 (40%)
Diabetes	7 (23%)
Arterial lactate level (mmol/L)	
mean ± SD	3.9 ± 3.2
range	1.1-15.3
Venous lactate level (mmol/L)	
mean ± SD	4.02 ± 3.27
range	1.1-15.9
Capillary lactate level (mmol/L)	
mean ± SD	5.3 ± 2.6
range	1.6-13.6
Sites of infection	
Lung (pneumonia)	13 (33%)
GI tract (infectious diarrhea, peritonitis)	5 (16.6%)
Kidney (acute pyelonephritis)	2 (6.6%)
Cellulitis	1 (3.3%)
Sinusitis	1 (3.3%)

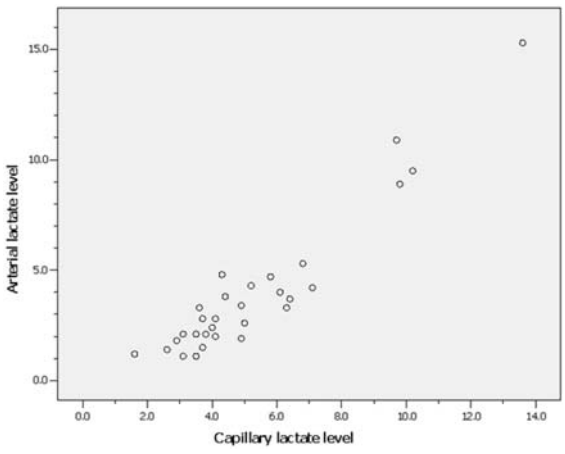
Discussion

The data reported here indicated that, in patients with septic shock, the arterial lactate correlated well with the central venous lactate. Also, the standard arterial lactate and the capillary lactate values determined by the portable lactate analyzer (Accutrend® Plus) correlated well and there was agreement between these methods, especially when the arterial lactate was lower than 10 mmol/L.

These results are parallel with our previous study which reported the good correlation and agreement between arterial and capillary lactate level in critically-ill patients[10]. With the study purpose

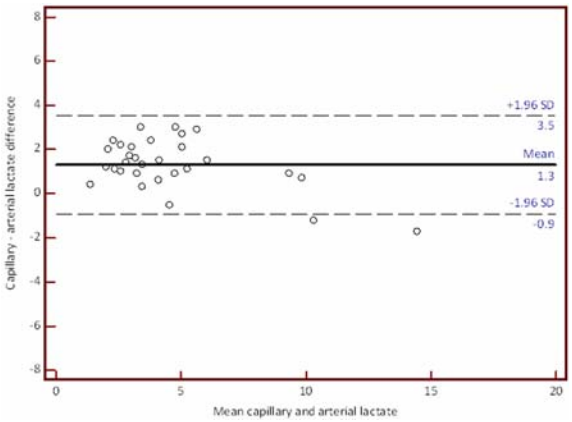


A) Correlation between arterial and central venous lactate, (r = 0.992, p = 0.01)



B) Correlation (r) between arterial and capillary lac tate, (r = 0.945, p = 0.01)

Fig. 1 Correlation between arterial lactate and central venous lactate (A) and arterial lactate and capillary lactate (B)



Note that the mean difference was 1.317 and the standard deviation was 1.136. Thus, 95% limit of agreement lied be tween -0.91 - 3.5. All but two mean - difference plots were within the agreement lines.

Fig. 2 Plots of absolute differences between capillary lactate and arterial lactate against their means according to Bland and Altman.

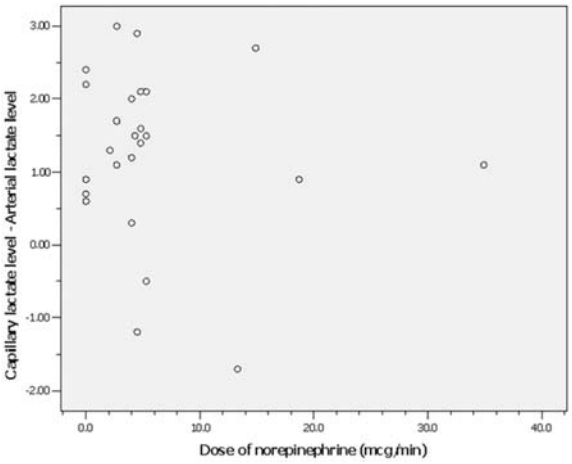


Fig. 3 Correlation between the dose of norepinephrine (mcg/min) and the differences between capillary and arterial blood lactate level, (r = -0.156, p = 0.447).

focused on the septic shock patients, certain differences were disclosed. Although the correlation between A-LAC and C- LAC was high (0.945, p = 0.01; Fig. 1A), the agreement was not perfect. As noted in Fig. 2, the mean difference between C- LAC and A- LAC was 1.317 mmol/L, indicating that most C- LAC values were higher than those of the gold standard A- LAC samples. This can be explained by low flow and stagnant tissue perfusion during septic shock, especially at the peripheral areas at which capillary samples were taken. The standard deviation of the differences, although substantial, was clinically acceptable. When paired C-LAC and A-LAC mean and difference plots were made, all but two were in the agreement lines. Interestingly, the plots outside were from the patients whose arterial lactate levels were extremely high (A- LAC levels 15.3 and 10.9 mmol/L respectively). In addition, these were the only patients in whom the A- LAC levels were higher than the capillary values. In summary, C- LAC correlated well with A-LAC and there were certain agreement between them, especially when the lactate level was not too high (> 10 mmol/L).

To demonstrate the effects of vasopressors on C-LAC and A-LAC gradients, a scatterplot between capillary-arterial lactate gradients and norepinephrine doses were performed in 22 patients. As shown in Fig. 3, no significant correlation between these variables was established. This information may be a useful piece of evidence supporting the position that uses of norepinephrine may not worsen capillary perfusion.

Since there are increasing evidences supporting lactate level monitoring in septic shock[8,14,15], the question which comes up is whether C-LAC obtained by any hand held device or other point of care testing systems could represent the standard A-LAC. This study, as well as our previous work, supported the use of this specific device. Individual testing and validation, however, is need for each hand held and point of care system in order to ensure users optimal diagnostic accuracy and precision.

In conclusion, the capillary lactate level determined by the portable lactate analyzer (Accutrend® Plus) had good correlation and agreement with arterial lactate level. This method or other point of care tests, when used cautiously, may be applicable in monitoring septic shock resuscitation.

Potential conflicts of interest

None.

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ความสัมพันธ์ของระดับแลคเตทในเลือดจากหลอดเลือดแดง, หลอดเลือดดำใหญ่ และปลายนิ้วในผู้ป่วยช็อกจากการติดเชื้อ

ภัทรวิน ภัทรนิธิมา, สุรัตน์ ทองอยู่, รณิษฐา รัตนรัต, วรการ วิไลชนม์, เอกรินทร์ ภูมิพิเชฐ, ไชยรัตน์ เพิ่มพิกุล

ภูมิหลัง: *ระดับแลคเตทที่สูงขึ้นสัมพันธ์กับการขาดออกซิเจนในเนื้อเยื่อ และการตรวจระดับ แลคเตทใช้ในการประเมินผลการรักษาผู้ป่วยช็อกจากการติดเชื้อ การตรวจระดับแลคเตทด้วยวิธีมาตรฐานจากเลือดแดงนั้นใช้เวลามากในการเจาะเลือดและการส่งตรวจ คณะผู้ศึกษาจึงศึกษาการตรวจระดับแลคเตท โดยใช้เลือดจากปลายนิ้ว และอ่านค่าโดยใช้เครื่องตรวจแบบพกพา (Accutrend® Plus) เทียบกับการตรวจแลคเตท ในเลือดแดงโดยวิธีมาตรฐานโดยศึกษาในผู้ป่วยช็อกจากการติดเชื้อ*

วัสดุและวิธีการ: *ทำการศึกษาเปรียบเทียบระดับแลคเตทจากหลอดเลือดแดง หลอดเลือดดำโดยวิธีมาตรฐาน และจากปลายนิ้วผู้ป่วยที่ช็อกจากการติดเชื้อที่เข้ารับการรักษาเป็นผู้ป่วยสามัญในของภาควิชาอายุรศาสตร์ โรงพยาบาลศิริราช ระหว่างเดือนตุลาคม พ.ศ. 2552 ถึง เดือนมีนาคม พ.ศ. 2553*

ผลการศึกษา: *ผู้ป่วย 30 คน เข้าร่วมการศึกษา อายุเฉลี่ย 66 (24-86) ปี เป็นเพศหญิง 16 (53%) คน มีโรคประจำตัว คือ โรคความดันโลหิตสูง 12 (40%) คน และโรคเบาหวาน 7 (23%) คน ตำแหน่งการติดเชื้อ คือ ปอดอักเสบ 13 (43%) คน กรวยไตอักเสบ 2 (7%) คน และเยื่อบุท้องอักเสบ 2 (7%) คน ระดับแลคเตทในหลอดเลือดแดง ระดับแลคเตทในหลอดเลือดดำ และปลายนิ้วเท่ากับ 1.1-15.3 mmol/L, 1.1 -15.9 mmol/L และ 1.6-13.6 mmol/L ตามลำดับ ระดับความสัมพันธ์ของค่าแลคเตทระหว่างหลอดเลือดแดงกับหลอดเลือดดำใหญ่และ หลอดเลือดแดงกับปลายนิ้ว คือ 0.992, 0.945 (p = 0.01) ตามลำดับ เมื่อนำค่าแลคเตทในหลอดเลือดแดง จากการตรวจวิธีมาตรฐาน และค่าแลคเตทที่ได้จากการตรวจจากเลือดที่ปลายนิ้วมาศึกษาความไปด้วยกัน (agreement) โดย Bland Altman plot พบว่าค่าทั้ง 2 มีความไปด้วยกัน โดยเฉพาะอย่างยิ่งเมื่อระดับแลคเตท จากหลอดเลือดแดงน้อยกว่า 10 mmol/L*

สรุป: *ระดับแลคเตทจากหลอดเลือดแดงโดยการตรวจด้วยวิธีมาตรฐานกับระดับแลคเตทจากหลอดเลือดฝอยปลายนิ้วโดยการตรวจด้วยเครื่องตรวจแบบพกพา (Accutrend® Plus) มีความสัมพันธ์กันในระดับที่ดีและมีความไปด้วยกัน (agreement) แพทย์อาจใช้การตรวจระดับแลคเตทจากหลอดเลือดฝอยปลายนิ้วติดตามผลการรักษาผู้ป่วยช็อกจากการติดเชื้อได้*