Dynamics of Central Venous Oxygen Saturation and Serum Lactate during Septic Shock Resuscitation

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Background: *Septic shock is a serious condition leading to high mortality and morbidity. Many varieties of attempts aiming toward improving outcomes have been implemented. However, the appropriate therapeutic end point of shock resuscitation is still under investigation. The authors report here the dynamics of commonly used parameters, namely central venous oxygen saturation ($ScvO_2$) and lactate concentration during resuscitation.*

Material and Method: *Adult patients admitted with severe sepsis and septic shock from October 1, 2009 to January 31, 2009 were enrolled. During hemodynamic resuscitation, the central venous blood was drawn for $ScvO_2$ and lactate measurement right after the CVC was placed (T1) and at the point where the blood pressure goal was achieved (T2). The third and the fourth measurements were obtained at 1 and 2 hours thereafter (T3 and T4). These samples were ice chilled and were sent to central laboratory for blood gas analysis and lactate determination.*

Results: *Twenty patients underwent the study. There was no significant change in ScvO2 from T1 to T4. All but five $ScvO_2$ at T1 were above 70%. Lactate level gradually declined during the course of treatment and the clearance from T1 to T3 was calculated as 15.4%. No correlation between $ScvO_2$ and lactate level was noted at any sampling time. When partitioning venous oxygen saturation in to 4 groups, that is $ScvO_2 < 65$, 65-< 75, 75-<85 and ≥ 85, respectively, those with $ScvO_2 \geq 85\%$ had the highest lactate concentration.*

Conclusion: *Central venous oxygen saturation and its changes during treatment were heterogeneous which made this parameter less reliable than others to monitor management. The lactate clearance, although slow, is uniform and may be used alone or in combination with other parameters to monitor resuscitation.*

Keywords: *Sepsis, Septic shock, ScvO2, Lactate, Lactate clearance*

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Septic shock is a serious condition leading to high mortality and morbidity. Numerous attempts consisting of evidence based information and the Surviving Sepsis Campaign[1] have proved to increase outcomes. This includes early stabilization of hemodynamics by rapid restoration of intravascular volume and timely administration of vasopressors adjusted to achieve blood pressure target. Thereafter, inotropes or red blood cell transfusion is administered to render adequate tissue perfusion as judged by global oxygenation parameters[1]. The currently recommended parameters for resuscitation target include the central venous oxygen saturation of more than 70%[1] and later, a measurement of the clearance of serum lactate of more than 10%[2].

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At present, there is no exact parameter indicating the point where adequate oxygenation is restored. Central venous oxygen saturation ($ScvO_2$), which represents amount of venous oxygen left from tissue bed, is low at shock and is satisfactorily high (> 70%) at shock reversal. However, this information may not be applicable in all patients since in some cases, high oxygen saturation is noted despite severe shock[3] and change of lactate level during shock resuscitation is slow. Measurement of tissue oxygen by near infrared spectrometry has been introduced and this has been under investigation. Other measures to quantify regional organ perfusion possess certain limitations.

Hence, the authors conducted a prospective observational study aimed to examine the changes of central venous oxygenation and serum lactate during septic shock resuscitation. This knowledge would render better understanding of the dynamic changes of these parameters from beginning of resuscitation to the end point where tissue perfusion was restored.

Also, the correlation between these parameters would be verified.

Material and Method

Adult patients admitted to the Medical wards or the Medical ICU with severe sepsis and septic shock from October 1, 2009 to January 31, 2010 were enrolled after written informed consents from the patients or their relatives. The diagnostic criteria for sepsis included a suspected infectious source and two of the following: a) temperature > 38°C or < 36°C b) heart rate > 90/minute c) respiratory rate > 20 breaths/minute, or P_aCO_2 32 mmHg or less or d) white blood cell count > 12,000 cell/cu mm^3 or < 4,000 cell/cu mm^3 or > 10% band cells. For septic shock, the patients must have a systolic blood pressure < 90 mmHg after 20 ml/kg fluid challenge. They must be older than 18 year. Patients who underwent cardiopulmonary resuscitation, those who received medications which might cause metabolic acidosis including metformin, stavudine and zidivudine and patients with the diagnosis of cirrhosis and alcoholism were excluded from the present study.

All patients underwent our institution's septic shock management guideline. Briefly, after the diagnosis was made, isotonic crystalloid was rapidly given at the rate of 10-20 ml/kg during the first half hour and additional bouts were given to raise mean arterial pressures toward 65 mmHg. Central venous catheter (CVC) was inserted after 1,000-2,000 ml fluid in order to monitor central venous pressures (CVP) and to obtain venous blood samples. Norepinehrine was administered to increase blood pressures when adequate intravascular volume was achieved as judged by a CVP of 8-12 mmHg. When the target pressures were reached, central venous blood was drawn for venous oxygenation measurement ($ScvO_2$) and lactate determination. Dobutamine infusion was added in patients who had venous oxygen saturation of less than 70% and a hematocrit of more than 30%. For venous hypoxic patients with hematocrit less than 30%, red blood cells transfusion would be given. All patients received appropriate empirical antibiotics; which in some cases, were later adjusted according to the culture results.

Study protocol

Four batches of blood were drawn during the study. The first sample was taken right after the CVC (T1) was placed and the second one at the point when the blood pressure goal was achieved (T2). The third and the fourth ones were obtained at 1 and 2 hours thereafter (T3 and T4). These samples were ice chilled and were sent to central laboratory for blood gas analysis and lactate determination.

Statistical analysis

The descriptive data were described as mean $\pm$ SD. The values of $ScvO_2$ and venous lactate in each time frame were plotted. Correlation between $ScvO_2$ and blood lactate at T1, T2, T3 and T4 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).

Ethical considerations

The present study was reviewed and approved by the Siriraj ethics committee, using the Declaration of Helsinki.

Results

Of 20 patients who were included in the study, eight of them (40%) were male. The mean age was 64 years. As shown in Table 1, seven (35%) of them had diabetes mellitus and 6 (30%) had hypertension. As for the site of infection, 6 (30%) were in the respiratory tract, 4 (20%), 3 (15%), 2 (10%) and 2 (10%) were in gastrointestinal tract, urinary tract, bone and joint and soft tissue, respectively. Three of these patients had primary blood stream infection.

Fig. 1 demonstrated scatter plot of $ScvO_2$ and serum lactate in each sampling time. Note that all but 5 $ScvO_2$ values at T1 were above 70%, the point at which denotes the therapeutic endpoint of resuscitation. The venous oxygen saturation remained unchanged throughout treatment period. Serum lactate gradually decreased from T1 to T4. The clearance of serum lactate

Table 1. Baseline characteristics

Variables	No. (%) Total 20 patients
Age (year)	63.9 $\pm$ 17.8
Male (%)	8 (40%)
SAPS II score (mean $\pm$ SD)	60.1 $\pm$ 12.3
Underlying diseases (%)	16 (80%)
Diabetes Mellitus	6 (30%)
Hypertension	7 (35%)
Cardiovascular disease	4 (20%)
Hematologic malignancy	3 (15%)
Kidney disease	2 (10%)
Others	4 (20%)

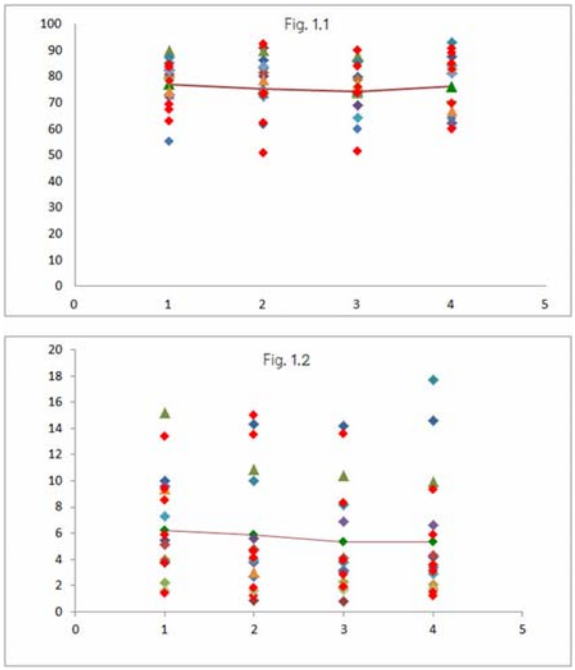

Fig. 1 Venous oxygen saturation and serum lactate during septic shock resuscitation; Fig. 1.1 Dot plots of $ScvO_2$ from T1 (1) to T2, T3 and T4 (2, 3 and 4 respectively). Note that all but 5 $ScvO_2$ at T1 were more than 70%. There was no significant change of mean $ScvO_2$ during septic shock resuscitation; Fig. 1.2 Dot plots of serum lactate from T1 (1) to T2,T3 and T4 (2,3 and 4 respectively). The mean values of serum lactate gradually declined during the course of treatment

at T3 and T4, as calculated from the proportional decrement from the first sample was 14.5%. Fig. 2 discloses the correlation between $ScvO_2$ and serum lactate at T1, T2, T3 and T4 respectively. No significant correlation between these parameters was noted at any time of sampling (T1 r = -0.002, p = 0.995, T2 r = 0.093, p = 0.742, T3 r = -0.018, p = 0.950 and T4 r = -0.003, p = 0.992).

When partitioning venous oxygen saturation in to 4 groups, that is $ScvO_2 < 65$, 65-<75, 75-< 85 and ≥ 85 respectively and calculating the corresponding mean lactate concentration, a significant finding is demonstrated. As shown in Table 2, a significantly higher level of lactate was noted at $ScvO_2$ of more than 85%.

Discussion

The above data demonstrated dynamic changes of central venous oxygen saturation and serum lactate during septic shock resuscitation. Interestingly, most venous oxygen saturation were higher than 70% early at the beginning of treatment, then remained unchanged during the treatment course while serum lactate gradually declined. No correlation between venous oxygenation and serum lactate was observed at any time of sampling. Also, when segmenting patients into groups according to venous oxygen saturation, those with the highest $ScvO_2$ had upper most mean serum lactate.

The finding that most $ScvO_2$ values at T1 were greater than 70% was important. It gave rise to the doubt regarding using venous saturation as a parameter indicating therapeutic end point of shock management. T1 is the time at which central venous catheter line were placed. At the moment, most patients were still hypotensive and required further fluid challenge or vasopressors. In addition, subsequent sampling at T2, T3 and T4 disclosed no change in venous saturation. Some explanation for these phenomena might be postulated here. At T1, some patients might receive a significant amount of fluid to raise $ScvO_2$; in the others, mitochondrial dysfunction might be presented and this resulted in high $ScvO_2$ due to cellular failure to use oxygen[3]. Resuscitation improved tissue perfusion but changes in venous saturation varied, resulted in an unchanged mean $ScvO_2$. These findings might also explain the lack of correlation between $ScvO_2$ and lactate. Also these findings, in some part, paralleled with other studies. Puskarich et al[4] recently reported the uses of venous oxygen or lactate clearance as the therapeutic end point of septic shock. The important findings included the initial mean $ScvO_2$ of 80%, which was similar to ours. The achievement of the $ScvO_2$ goal alone in this study was associated with a higher mortality rate as compared with the achievement of only the lactate clearance goal. Pope et al[5] separated the patients with sepsis to 3 groups according to their venous oxygen saturation: those with hypoxia, normoxia and hyperoxia ($ScvO_2 < 70$, 70-90 and > 90%, respectively). They found that the presence of both venous hypoxia and hyperoxia were associated with high mortality and also initial hyperoxia was associated with more fatalities. This concurred with our finding, demonstrated in Table 2, in which patients with $ScvO_2 > 85\%$ had higher lactate level.

As for serum lactate, our data showed that the lactate level gradually declined during sequential follow-up (Fig. 1). The initial level of 6.2 mMol/L dropped to 5.3 mMol/L at T3 and T4 and hence the clearance was 14.5%. This finding clearly demonstrated changes of lactate which were uniform and gradual. It

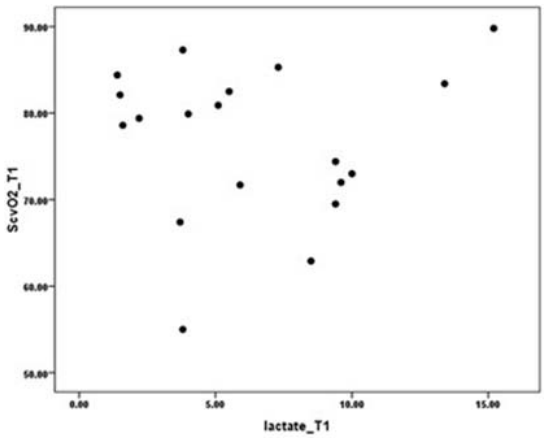

Fig. 2a

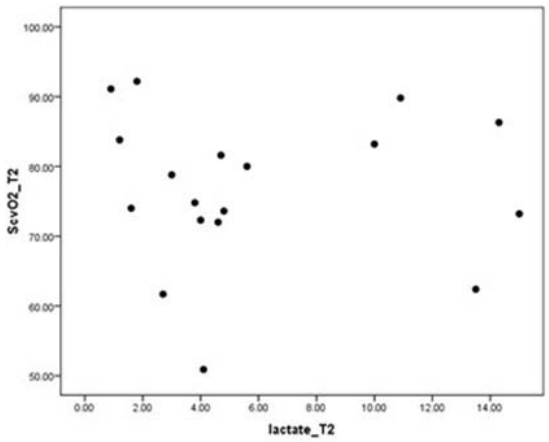

Fig. 2b

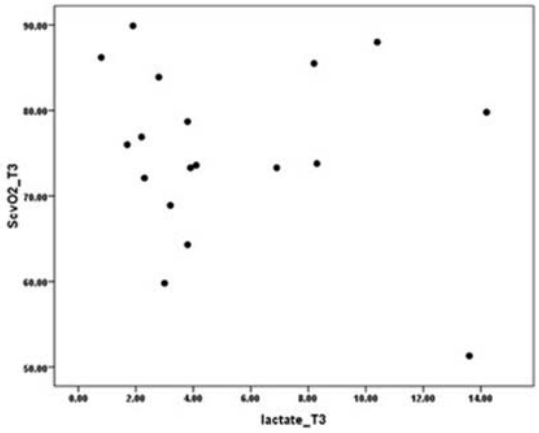

Fig. 2c

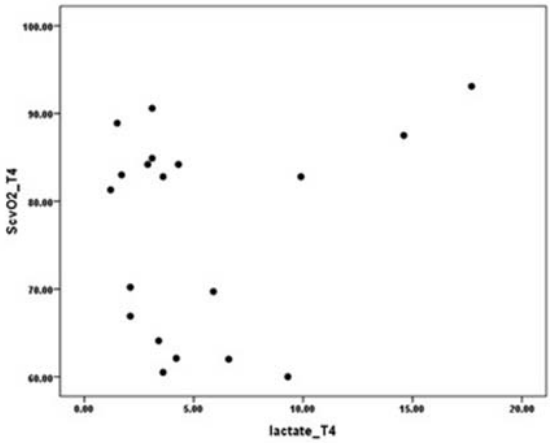

Fig. 2d

Fig. 2 Correlation between $ScvO_2$ and serum lactateduring septic shock resuscitation. The venous oxygen saturation ($ScvO_2$) and serum lactateduring septic shock resuscitation at T1, T2, T3 and T4 were plotted as shown in figures 2a, 2b, 2c and 2d respectively. No significant correlation between these parameters was noted at any time of sampling (T1 r = -0.002, p = 0.995, T2 r = .093, p = 0.742, T3 r = -0.018, p = 0.950 and T4 r = -0.003, p = 0.992)

Table 2. The average of serum lactate concentration in each $ScvO_2$ range. Note that the mean serum lactate at $ScvO_2 \geq 85\%$ was higher than other 3 subgroups (p = 0.042)

$ScvO_2$ (%)	< 65	65-<75	75-<85	≥ 85
Sample size (total = 74)	13	20	26	15
$ScvO_2$ (%)	59.8 ± 4.5	71.9 ± 2.3	81.1 ± 3.0	88.80 ± 2.4
Serum lactate (mmol/L)	6.16 ± 3.87	5.94 ± 3.44	4.3 ± 3.61	7.49 ± 5.99

was comparable to other studies which demonstrated the benefit of using lactate clearance to identify reversal of tissue hypoxia. Jansen et al[6] reported a randomized control studyaiming to examine the efficacy of lactate clearance in critically ill patients, in whom 38% had diagnoses of sepsis. They allocated patients into 2 groups. One underwent routine protocol aimed to restore hemodynamics without knowing lactate level, while the other underwent the algorithm focusing on reducing lactate level of at least 20% every 2 hours for

the first 8 hours. The latter group had better survival. This supported the superiority of using lactate clearance to define the end point of shock resuscitation. At present, abundant studies disclosed similar results[7,8]. Hence, more resuscitative algorithms using lactate as a primary parameter indicating tissue perfusion would be expected. At the same time, alternative parameters, namely near infrared spectroscopy[9], microvascular blood flow determination[10] and etc. have been tested in order to better identify the reversal of tissue hypoxia. In conclusion, the present study demonstrated the dynamics of central venous oxygen saturation and serum lactate during septic shock resuscitation. The heterogeniety of $ScvO_2$ and its changes during treatment course made this parameter less reliable than expected to monitor septic shock management. The lactate clearance, although slow, but uniform and may be use alone or in combination with other parameters to monitor resuscitation. Further studies are necessary to examine and discover an effective tool to better monitor the treatment of this serious disease.

Potential conflicts of interest

None.

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การเปลี่ยนแปลงของค่าความอิ่มตัวของออกซิเจนในเลือดและระดับแลคเตทในหลอดเลือดดำส่วนกลางในผู้ป่วยช็อคจากการติดเชื้อ

ไชยรัตน์ เพิ่มพิกุล, กิตติมา นพเก้ารัตนมณี, สุรัตน์ ทองอยู่, รณิษฐา รัตนะรัต, เอกรินทร์ ภูมิพิเชฐ

ภูมิหลัง: *ภาวะช็อกจากการติดเชื้อ(Septic shock) เป็นภาวะที่พบได้บ่อยและมีอัตราตายสูง การรักษาตามแนวทาง Surviving Sepsis Campaign ซึ่งรวบรวมองค์ความรู้จากการศึกษาต่างๆ สามารถลดอัตราตายได้ จุดหมายของการรักษาการจัดการให้ออกซิเจนที่ไปสู่เนื้อเยื่อต่างๆ กลับมาเป็นปกติ โดยใช้ค่า central venous oxygen saturation ($ScvO_2$) ซึ่งการศึกษาต่อๆ มาพบว่ามีข้อจำกัด อีกทั้งมีข้อมูลการใช้ระดับแลคเตทและการลดลงของค่าดังกล่าวระหว่างการรักษา (lactate clearance) เป็นการประเมินจุดหมายการรักษา*

วัตถุประสงค์: *เพื่อศึกษาการเปลี่ยนแปลงระหว่าง $ScvO_2$ กับ serum lactate ในผู้ป่วยช็อกจากการติดเชื้อระหว่างการรักษา*

วัสดุและวิธีการ: *เป็นการศึกษาแบบเก็บข้อมูลไปข้างหน้า (prospective cohort study) โดยการคัดเลือกผู้ป่วยที่มีภาวะช็อกจากการติดเชื้อในกระแสเลือด (Septic shock)ที่ได้รับไว้ในโรงพยาบาลศิริราช ตั้งแต่วันที่ 1 ตุลาคม พ.ศ. 2552 ถึง 31 มกราคม พ.ศ. 2553 ผู้ป่วยดังกล่าวได้รับการรักษาตาม septic shock guideline โดยผู้ศึกษาจะส่งเลือดจากเลือดจากเส้นเลือดดำใหญ่ที่คอ (central venous blood) ตรวจหา $ScvO_2$ กับ serum lactate ที่เวลาได้รับการใส่สายสวนหลอดเลือดดำ (T1) เมื่อผู้ป่วยมีความดันเลือดกลับเข้าสู่ตามเป้าหมาย (target blood pressure) (T2)และ เมื่อ 1 ชั่วโมง 2 ชั่วโมงหลังจากนั้นตามลำดับ (T3, T4)*

ผลการศึกษา: *ผู้ป่วยจำนวน 20 คนที่เข้าร่วมการศึกษา ค่า$ScvO_2$ ตั้งต้นส่วนใหญ่มีค่ามากกว่า 70% และค่าเฉลี่ยของ$ScvO_2$ไม่มีการเปลี่ยนแปลงตลอดช่วงการรักษา (T1 – T4) ขณะที่ค่าเฉลี่ยของระดับแลคเตทลดลงช้าๆ พบว่า lactate clearance จาก T1 ถึง T3 มีค่า 14.5% ไม่พบความสัมพันธ์ระหว่างค่า $ScvO_2$ กับ serum lactate ในทุกช่วงเวลา (T1 –T4) และเมื่อแบ่งกลุ่มข้อมูลเป็น 4 กลุ่ม คือ กลุ่มที่มีค่า $ScvO_2$< 65%, 65 - <75%, 75 - <85% และกลุ่มที่มี $ScvO_2$> 85% จะพบว่า ค่า lactate ลดลงเมื่อ $ScvO_2$เพิ่มขึ้นตามลำดับ ยกเว้นเมื่อ $ScvO_2$> 85% จะพบว่า ค่า lactate เพิ่มขึ้น อย่างมีนัยสำคัญ*

สรุป: *ในระหว่างการรักษาภาวะช็อกจากการติดเชื้อ ค่า$ScvO_2$ ในผู้ป่วยขณะช็อกส่วนใหญ่มีค่าสูงมากกว่า 70%และมีการเปลี่ยนแปลงไม่แน่นอนในแต่ละราย ทำให้ค่าเฉลี่ยตลอดช่วงการรักษาไม่เปลี่ยนแปลง ส่วนค่าแลคเตทมีการเปลี่ยนแปลงช้าแต่เป็นในทางเดียวกัน ข้อมูลนี้จึงสนับสนุนการใช้ lactate clearance ในการประเมินการรักษา*