

Tartışmalar: Septik Şokta Resüsitasyonu Yönlendirme

SCVO₂'mi Laktatın Temizlenmesi mi?

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GİRİŞ

Septik şok, doğrulanmış ya da şüpheli enfeksiyonu olan hastalarda yeterli sıvı resüsitasyonu rağmen ya da 4 mmol/L'dan daha fazla seviyede bir laktat varlığında (sepsise bağlı doku hipoperfüzyonu adı verilir) hipotansiyonun direnç gösterdiği durum olarak tanımlanmıştır.¹ Bu koşullar altında, Sepsisle Mücadele Kılavuzu ortalama arteriyel basıncın (OAB) 65 mm Hg'nin üzerinde tutulmasını ve laktat seviyelerinin, santral veya karışık venöz hemoglobin satürasyonunun (ScvO₂/ SvO₂) normalleştirilmesini önerir.¹ Bu temelde perfüzyon basıncının eski hale getirilmesi, doku perfüzyonunun iyileştirilmesi ve oksijen alımı ile oksijen ihtiyacı arasındaki dengenin sağlanması anlamına gelir.

Yeni yapılan bir çalışmada, artan laktat seviyeleri ve hipotansiyonu olan septik hastalarda %46'lık bir mortalite oranı tespit edilmiştir.² Ayrıca, resüsitasyonun son noktası olarak ScvO₂ kullanan bir çalışma³ ile resüsitasyonun son noktası olarak hem ScvO₂ hem laktat temizleme kullanan bir diğer çalışma⁴ mortalitede önemli iyileşmeler göstermiştir. Ancak santral venöz basıncı ve OAB'ı ortak hedef seçen ve erken resüsitasyonda ScvO₂ ve laktat temizlemeyi karşılaştıran başka bir çalışma (çoğunlukla septik şok hastalarında) mortalitede fark olmadığını göstermiştir.⁵ Ek olarak, ScvO₂ ölçümlerine dayalı erken hedefe yönelik tedavi ile yatak başında doktor kontrolüne ve genel bakıma dayalı, zorunlu santral venöz kateter yerleşimi olmaksızın sistolik kan basıncı ve kalp atım hızı ölçümlerini esas alan standart terapiyi karşılaştıran yeni bir çalışmada yine mortalitede fark olmadığı gösterilmiştir.⁶

Dolayısıyla, septik şok hastalarının resüsitasyonunda ScvO₂ veya laktat seviyelerinin nasıl kullanılacağı konusu tartışmalıdır. Bu bölümde bu

parametrelerin arka plan fizyolojisi ve septik şok hastalarının tedavisinde klinik kullanımları ele alınmıştır.

VENÖZ OKSİJENASYONUN FİZYOLOJİSİ

Venöz oksimetrenin pek çok yönü yakın zamanlarda incelenmiştir.^{7,8} Dolaşımda bol miktarda oksijen vardır. Kırmızı kan hücreleri, sol ventriküle yaklaşık %100'lük doymuş hemoglobin ile terk edip, mikro dolaşımda oksijen alışverişi yaptıktan sonra sağ ventriküle yaklaşık %75'lik doymuş hemoglobin ile geri dönerler. Dokulara oksijen temini azaldığında, aşamalı oksijen tüketimi bu oksijen fazlasının kullanılmasıyla sağlanır ve bu venöz oksijenasyonun kademeli olarak azalmasına neden olur.⁹ Oksijen teminindeki düşüş kritik bir seviyeye ulaştığında, laktat seviyeleri genellikle artmaya başlar.^{10,11} Bu modellerde, arteriyel oksijen satürasyonu ve hemoglobin seviyeleri çoğunlukla sabit kalırken, venöz oksijenasyon kalp debisiyle (KD) orantılıdır. Dolayısıyla bu koşullarda venöz oksijenasyon, tüm vücudun oksijen talebiyle KD arasındaki dengeyi yansıtır. SvO₂'nin bölgesel venöz oksijenasyon seviyelerini yansıtmadığının bilinmesi önemlidir.¹² Kardiyak fonksiyon normal olduğunda, oksijen içeriğindeki azalmalar KD'deki artışlarla karşılanırken venöz oksijenasyon minimum etkilenir.¹³ Ancak kardiyak fonksiyon sınırlı veya oksijen içeriğindeki azalma aşırı ise, sistemdeki oksijen fazlası esas olarak oksijen talebindeki değişiklikleri telafi etmek için kullanılır ve dolayısıyla venöz oksijenasyon azalır.¹⁴ Klinik koşullarda venöz oksijenasyon pek çok faktöre bağlı olsa da (Şekil 73-1), ana faktör muhtemelen KD'nin oksijen içeriği ve oksijen talebindeki değişikliklere verdiği cevaptır.

REFERANSLAR

1. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med.* 2013;41(2):580-637.
2. Levy MM, Dellinger RP, Townsend SR, et al. The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. *Crit Care Med.* 2010;38(2):367-374.
3. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med.* 2001;345(19):1368-1377.
4. Jansen TC, van Bommel J, Schoonderbeek FJ, et al. Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. *Am J Respir Crit Care Med.* 2010;182(6):752-761.
5. Jones AE, Shapiro NI, Trzeciak S, et al. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. *JAMA.* 2010;303(8):739-746.
6. The ProCESS Investigators, Yealy DM, Kellum JA, Huang DT, et al. A randomized trial of protocol-based care for early septic shock. *N Engl J Med.* 2014;370(18):1683-1693.
7. Walley KR. Use of central venous oxygen saturation to guide therapy. *Am J Respir Crit Care Med.* 2011;184(5):514-520.
8. van Beest P, Wietasch G, Scheeren T, et al. Clinical review: use of venous oxygen saturations as a goal—a yet unfinished puzzle. *Crit Care.* 2011;15(5):232.
9. Cain SM, Curtis SE. Experimental models of pathologic oxygen supply dependency. *Crit Care Med.* 1991;19(5):603-612.
10. Zhang H, Spapen H, Benlabeled M, et al. Systemic oxygen extraction can be improved during repeated episodes of cardiac tamponade. *J Crit Care.* 1993;8(2):93-99.
11. Cain SM, Curtis SE. Systemic and regional oxygen uptake and delivery and lactate flux in endotoxic dogs infused with dexmedetomidine. *Crit Care Med.* 1991;19(12):1552-1560.
12. Meier-Hellmann A, Hannemann L, Specht M, et al. The relationship between mixed venous and hepatic venous O₂ saturation in patients with septic shock. *Adv Exp Med Biol.* 1994;345:701-707.
13. Weiskopf RB, Viele MK, Feiner J, et al. Human cardiovascular and metabolic response to acute, severe isovolemic anemia. *JAMA.* 1998;279(3):217-221.
14. Silance PG, Simon C, Vincent JL. The relation between cardiac index and oxygen extraction in acutely ill patients. *Chest.* 1994;105(4):1190-1197.
15. van Beest PA, Hofstra JJ, Schultz MJ, et al. The incidence of low venous oxygen saturation on admission to the intensive care unit: a multi-center observational study in The Netherlands. *Crit Care.* 2008;12(2):R33.
16. Reinhart K, Rudolph T, Bredle DL, et al. Comparison of central-venous to mixed-venous oxygen saturation during changes in oxygen supply/demand. *Chest.* 1989;95(6):1216-1221.
17. Kopterides P, Bonovas S, Mavrou I, et al. Venous oxygen saturation and lactate gradient from superior vena cava to pulmonary artery in patients with septic shock. *Shock.* 2009;31(6):561-567.
18. Berridge JC. Influence of cardiac output on the correlation between mixed venous and central venous oxygen saturation. *Br J Anaesth.* 1992;69(4):409-410.
19. Hernandez G, Pena H, Cornejo R, et al. Impact of emergency intubation on central venous oxygen saturation in critically ill patients: a multicenter observational study. *Crit Care.* 2009;13(3):R63.
20. Weissman C, Kemper M. The oxygen uptake-oxygen delivery relationship during ICU interventions. *Chest.* 1991;99:430-435.
21. Podbregar M, Mozina H. Skeletal muscle oxygen saturation does not estimate mixed venous oxygen saturation in patients with severe left heart failure and additional severe sepsis or septic shock. *Crit Care.* 2007;11(1):R6.
22. van Beest PA, van der Schors A, Liefers H, et al. Femoral venous oxygen saturation is no surrogate for central venous oxygen saturation. *Crit Care Med.* 2012;40(12):3196-3201.
23. Ince C, Sinaasappel M. Microcirculatory oxygenation and shunting in sepsis and shock. *Crit Care Med.* 1999;27(7):1369-1377.
24. Chung KP, Chang HT, Huang YT, et al. Central venous oxygen saturation under non-protocolized resuscitation is not related to survival in severe sepsis or septic shock. *Shock.* 2012;38(6):584-591.
25. Velissaris D, Pierrakos C, Scolletta S, et al. High mixed venous oxygen saturation levels do not exclude fluid responsiveness in critically ill septic patients. *Crit Care.* 2011;15(4):R177.
26. Bakker J, Vincent JL, Gris P, et al. Veno-arterial carbon dioxide gradient in human septic shock. *Chest.* 1992;101(2):509-515.
27. Vallee F, Vallet B, Mathe O, et al. Central venous-to-arterial carbon dioxide difference: an additional

- target for goal-directed therapy in septic shock? *Intensive Care Med.* 2008;34(12):2218-2225.
28. van Beest PA, Lont MC, Holman ND, et al. Central venous-arterial pCO₂ difference as a tool in resuscitation of septic patients. *Intensive Care Med.* 2013;39(6):1034-1039.
 29. Bakker J, Nijsten MW, Jansen TC. Clinical use of lactate monitoring in critically ill patients. *Ann Intensive Care.* 2013;3(1):12.
 30. Brooks GA. Lactate shuttles in nature. *Biochem Soc Trans.* 2002;30(2):258-264.
 31. Cain SM. Appearance of excess lactate in aneshetized dogs during anemic and hypoxic hypoxia. *Am J Physiol.* 1965;209:604-608.
 32. Zhang H, Vincent JL. Oxygen extraction is altered by endotoxin during tamponade-induced stagnant hypoxia in the dog. *Circ Shock.* 1993;40(3):168-176.
 33. Cain SM, Curtis SE. Whole body and regional O₂ uptake/delivery and lactate flux in endotoxic dogs. *Adv Exp Med Biol.* 1992;316:401-408.
 34. Pinsky MR, Schlichtig R. Regional oxygen delivery in oxygen supply-dependent states. *Intensive Care Med.* 1990;16(suppl 2):169-171.
 35. Friedman G, De Backer D, Shahla M, et al. Oxygen supply dependency can characterize septic shock. *Intensive Care Med.* 1998;24(2):118-123.
 36. Bakker J, Vincent J. The oxygen-supply dependency phenomenon is associated with increased blood lactate levels. *J Crit Care.* 1991;6(3):152-159.
 37. Ronco JJ, Fenwick JC, Tweeddale MG, et al. Identification of the critical oxygen delivery for anaerobic metabolism in critically ill septic and nonseptic humans. *JAMA.* 1993;270(14):1724-1730.
 38. van Genderen ME, Klijn E, Lima A, et al. Microvascular perfusion as a target for fluid resuscitation in experimental circulatory shock. *Crit Care Med.* 2014;42(2):E96-E105.
 39. De Backer D, Creteur J, Dubois MJ, et al. The effects of dobutamine on microcirculatory alterations in patients with septic shock are independent of its systemic effects. *Crit Care Med.* 2006;34(2):403-408.
 40. Huckabee WE. Relationships of pyruvate and lactate during anaerobic metabolism. I. Effects of infusion of pyruvate or glucose and of hyperventilation. *J Clin Invest.* 1958;37(2):244-254.
 41. Zborowska-Sluis DT, Dossetor JB. Hyperlactatemia of hyperventilation. *J Appl Physiol.* 1967;22(4):746-755.
 42. Griffith FR, Jr, Lockwood JE, Emery FE. Adrenalin lactacidemia: proportionality with dose. *Am J Physiol.* 1939;127(3):415-421.
 43. Boysen SR, Bozzetti M, Rose L, et al. Effects of prednisone on blood lactate concentrations in healthy dogs. *J Vet Intern Med.* 2009;23(5):1123-1125.
 44. Warburg O. On respiratory impairment in cancer cells. *Science.* 1956;124(3215):269-270.
 45. Levy B, Gibot S, Franck P, et al. Relation between muscle Na⁺+K⁺ ATPase activity and raised lactate concentrations in septic shock: a prospective study. *Lancet.* 2005;365(9462):871-875.
 46. Taylor DJ, Faragher EB, Evanson JM. Inflammatory cytokines stimulate glucose uptake and glycolysis but reduce glucose oxidation in human dermal fibroblasts in vitro. *Circ Shock.* 1992;37(2):105-110.
 47. Brealey D, Brand M, Hargreaves I, et al. Association between mitochondrial dysfunction and severity and outcome of septic shock. *Lancet.* 2002;360(9328):219-223.
 48. Crouser ED, Julian MW, Blaho DV, et al. Endotoxin-induced mitochondrial damage correlates with impaired respiratory activity. *Crit Care Med.* 2002;30(2):276-284.
 49. Didwania A, Miller J, Kassel D, et al. Effect of intravenous lactated Ringer's solution infusion on the circulating lactate concentration: Part 3. Results of a prospective, randomized, double-blind, placebo-controlled trial. *Crit Care Med.* 1997;25(11):1851-1854.
 50. Cole L, Bellomo R, Baldwin I, et al. The impact of lactate-buffered high-volume hemofiltration on acid-base balance. *Intensive Care Med.* 2003;29(7):1113-1120.
 51. Bollmann MD, Revelly JP, Tappy L, et al. Effect of bicarbonate and lactate buffer on glucose and lactate metabolism during hemodiafiltration in patients with multiple organ failure. *Intensive Care Med.* 2004;30(6):1103-1110.
 52. Lalau JD, Lacroix C, Compagnon P, et al. Role of metformin accumulation in metformin-associated lactic acidosis. *Diabetes Care.* 1995;18(6):779-784.
 53. Marinella MA. Lactic acidosis associated with propofol. *Chest.* 1996;109(1):292.
 54. Lonergan JT, Behling C, Pfander H, et al. Hyperlactatemia and hepatic abnormalities in 10 human immunodeficiency virus-infected patients receiving nucleoside analogue combination regimens. *Clin Infect Dis.* 2000;31(1):162-166.
 55. Claessens YE, Cariou A, Monchi M, et al. Detecting life-threatening lactic acidosis related to nucleoside-analog treatment of human immunodeficiency

- virus-infected patients, and treatment with L-carnitine. *Crit Care Med.* 2003;31(4):1042-1047.
56. Naidoo DP, Gathiram V, Sadhabiriss A, et al. Clinical diagnosis of cardiac beriberi. *S Afr Med J.* 1990;77(3):125-127.
57. Morgan TJ, Clark C, Clague A. Artifactual elevation of measured plasma L-lactate concentration in the presence of glycolate. *Crit Care Med.* 1999;27(10):2177-2179.
58. Brindley PG, Butler MS, Cembrowski G, et al. Falsely elevated point-of-care lactate measurement after ingestion of ethylene glycol. *CMAJ.* 2007;176(8):1097-1099.
59. Almenoff PL, Leavy J, Weil MH, et al. Prolongation of the half-life of lactate after maximal exercise in patients with hepatic dysfunction. *Crit Care Med.* 1989;17(9):870-873.
60. Mustafa I, Roth H, Hanafiah A, et al. Effect of cardiopulmonary bypass on lactate metabolism. *Intensive Care Med.* 2003;29(8):1279-1285.
61. Stacpoole PW, Wright EC, Baumgartner TG, et al. A controlled clinical trial of dichloroacetate for treatment of lactic acidosis in adults. The Dichloroacetate-Lactic Acidosis Study Group. *N Engl J Med.* 1992;327(22):1564-1569.
62. Vary TC. Sepsis-induced alterations in pyruvate dehydrogenase complex activity in rat skeletal muscle: effects on plasma lactate. *Shock.* 1996;6(2):89-94.
63. Weil MH, Michaels S, Rackow EC. Comparison of blood lactate concentrations in central venous, pulmonary artery, and arterial blood. *Crit Care Med.* 1987;15(5):489-490.
64. Younger JG, Falk JL, Rothrock SG. Relationship between arterial and peripheral venous lactate levels. *Acad Emerg Med.* 1996;3(7):730-734.
65. Fauchere JC, Bauschatz AS, Arlettaz R, et al. Agreement between capillary and arterial lactate in the newborn. *Acta Paediatr.* 2002;91(1):78-81.
66. Aduen J, Bernstein WK, Khastgir T, et al. The use and clinical importance of a substrate-specific electrode for rapid determination of blood lactate concentrations. *JAMA.* 1994;272(21):1678-1685.
67. Brinkert W, Rommes JH, Bakker J. Lactate measurements in critically ill patients with a hand-held analyser. *Intensive Care Med.* 1999;25(9):966-969.
68. Astiz ME, Rackow EC, Kaufman B, et al. Relationship of oxygen delivery and mixed venous oxygenation to lactic acidosis in patients with sepsis and acute myocardial infarction. *Crit Care Med.* 1988;16(7):655-658.
69. Lima A, Jansen TC, Van BOommel J, et al. The prognostic value of the subjective assessment of peripheral perfusion in critically ill patients. *Crit Care Med.* 2009;37(3):934-938.
70. Lima A, van Bommel J, Jansen TC, et al. Low tissue oxygen saturation at the end of early goal-directed therapy is associated with worse outcome in critically ill patients. *Crit Care.* 2009;13(suppl 5):S13.
71. De Backer D. Lactic acidosis. *Intensive Care Med.* 2003;29(5):699-702.
72. Smith I, Kumar P, Molloy S, et al. Base excess and lactate as prognostic indicators for patients admitted to intensive care. *Intensive Care Med.* 2001;27(1):74-83.
73. Sladen RN. Oliguria in the ICU. Systematic approach to diagnosis and treatment. *Anesthesiol Clin North America.* 2000;18(4):739-752, viii.
74. Hernandez G, Bruhn A, Castro R, et al. Persistent sepsis-induced hypotension without hyperlactatemia: a distinct clinical and physiological profile within the spectrum of septic shock. *Crit Care Res Pract.* 2012;2012:536852.
75. Ait-Oufella H, Lemoine S, Boelle PY, et al. Mottling score predicts survival in septic shock. *Intensive Care Med.* 2011;37(5):801-807.
76. Kajbaf F, Lalau JD. The prognostic value of blood pH and lactate and metformin concentrations in severe metformin-associated lactic acidosis. *BMC Pharmacol Toxicol.* 2013;14:22.
77. Guyette F, Suffoletto B, Castillo JL, et al. Prehospital serum lactate as a predictor of outcomes in trauma patients: a retrospective observational study. *J Trauma.* 2011;70(4):782-786.
78. Parsikia A, Bones K, Kaplan M, et al. The predictive value of initial serum lactate in trauma patients. *Shock.* 2014;42(3):199-204.
79. Bakker J, Vincent JL. The effects of norepinephrine and dobutamine on oxygen transport and consumption in a dog model of endotoxic shock. *Crit Care Med.* 1993;21:425-432.
80. Vincent JL, Dufaye P, Berre J, et al. Serial lactate determinations during circulatory shock. *Crit Care Med.* 1983;11(6):449-451.
81. Arnold RC, Shapiro NI, Jones AE, et al. Multicenter study of early lactate clearance as a determinant of survival in patients with presumed sepsis. *Shock.* 2009;32(1):35-39.
82. Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med.* 2013;39(2):165-228.
83. Cecconi M, De Backer D, Antonelli M, et al. Consensus on circulatory shock and hemodynamic

- monitoring. Task force of the European Society of Intensive Care Medicine. *Intensive Care Med.* 2014;40(12):1795-1815.
84. Jansen TC, van Bommel J, Schoonderbeek FJ, et al. Early lactate-guided therapy in intensive care unit patients a multicenter, open-label, randomized controlled trial. *Am J Respir Crit Care Med.* 2010;182(6):752-761.
85. Lima A, van Genderen ME, van Bommel J, et al. Nitroglycerin reverts clinical manifestations of poor peripheral perfusion in patients with circulatory shock. *Critical Care.* 2014;18(3):R126.
86. Atasever B, van der Kuil M, Boer C, et al. Red blood cell transfusion compared with gelatin solution and no infusion after cardiac surgery: effect on microvascular perfusion, vascular density, hemoglobin, and oxygen saturation. *Transfusion.* 2012;52(11):2452-2458.
87. Hernandez G, Luengo C, Bruhn A, et al. When to stop septic shock resuscitation: clues from a dynamic perfusion monitoring. *Ann Intensive Care.* 2014;4:30.
88. Bakker J, Coffernils M, Leon M, et al. Blood lactate levels are superior to oxygen-derived variables in predicting outcome in human septic shock. *Chest.* 1991;99(4):956-962.