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Effect of Vitamin C on Hypoxic Index, Length of Stay on Mechanical Ventilation and Mortality rate in patients with Acute Respiratory Distress Syndrome due to sepsis

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Abstract

Background: Sepsis syndrome is a great health problem as it leads to fatal pathological, and biochemical abnormalities. Sepsis is a major cause of death in patients admitted to intensive care units worldwide. Furthermore, survived patients post sepsis syndrome suffered from significant chronic physical and cognitive abnormalities. Recent researches conclude that ascorbic acid has a role in ameliorating vascular response in patients with septic shock.
Objective: was to detect the effect of ascorbic acid on CRP levels, hypoxic index, length of stay on mechanical ventilation and mortality rate in ARDS in critically ill septic patient.
Subjective: This clinical prospective randomized study was carried on 100 septic patients
Results: There was no significant effect of vitamin C treatment on the mortality rate, hospital stay, mechanical ventilation, CRP level and hypoxic index.
Conclusion: The administration of intravenous ascorbic acid in septic patients suffered from ARDS has no effect on improvement of hypoxic index, length of stay on MV and mortality rate.

Keywords: Respiratory distress syndrome – sepsis - vitamin c – mortality - length of stay on mechanical ventilation- hypoxic index

Introduction

Sepsis syndrome is a great health problem as it leads to fatal pathological, and biochemical abnormalities.[1] Sepsis is a major cause of death in patients admitted to intensive care units worldwide.[2] Furthermore, survived patients post sepsis syndrome suffered from significant chronic physical and cognitive abnormalities.[3]

Sepsis is defined according to The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), as life-threatening organ dysfunction caused by a dysregulated host response to infection.[4]

Acute respiratory distress syndrome (ARDS) is rapidly progressive chest condition, characterized by hypoxemia, and patchy lung infiltrates, patients need mechanical ventilation with protective lung strategy to correct severe hypoxia.[5].
The Berlin definition of ARDS: [6]

The onset of ARDS is acute within 7 days of a known clinical cause or recent and/or deteriorating chest symptoms. Chest radiology showed bilateral lung infiltrates not caused by effusions, lobar/lung atelectasis, or nodules. Respiratory insufficiency

occurred in the absence of evidence for heart failure or volume overload. Cardiac evaluation (e.g., echo) to exclude cardiogenic pulmonary edema if no contributing factor is present.[7]

Recent researchers conclude that ascorbic acid has a role in ameliorating vascular response in patients with septic shock. Armour et al. and Wu et al. showed that infusion of ascorbic acid in septic patients enhanced capillary filling and improve the response to vasoactive drugs in septic animals.[8,9]

Furthermore, there is inverse relationship between low level of serum ascorbic acid patients suffered from sepsis and occurrence multiple organ dysfunction and has direct correlation with surviving[10].

Aim of the work:

The aim of the work was to detect the effect of ascorbic acid on CRP levels, hypoxic index, length of stay on mechanical ventilation and mortality rate in ARDS in critically ill septic patient.

Patients and Methods

Patients:

This clinical prospective randomized study was carried on 100 septic patients (sepsis or septic shock) admitted to Critical Care Medicine Departments in Alexandria Main University Hospital and suffering from respiratory failure who fulfill the criteria of ARDS according to BERLIN definition.

Ethical Committee approval (Alexandria Faculty of Medicine) was received. An informed consent was taken from the patients (if conscious before endotracheal intubation) or next of kin.

Methods:

All patients included in this prospective randomized control study were divided randomly in two groups.
Both groups were mechanically ventilated on protective lung strategy, SIMV mode,Tidal volume6-8ml /kg , PEEP more than 5 according to hypoxic index and RR ≤ 35.

Group 1: 50 patients diagnosed as ARDS .They received vitamin C in dose one gram intravenously every 8 hours for 7 days.[11]

Group 2: 50 ARDS patients were the control group not receiving vitamin C.

Measurements:

- Source of sepsis.
- Blood pressure /6 hours and SaO2.
- Vasoactive drugs and doses.
- Daily CRP, CBC, BUN, S. creatinine for 7 days.
- ABG / 6 hours and hypoxic Index.
- Length of stay on MV from day 1 ARDS diagnosis.

Results

The demographic data of the studied groups wasmales in group 1 were 26(52%) and females were 24(48%) while in group 2 were 21(42%) and 29(58%) respectively. Age in group 1 ranged from 23-69 years with mean value 52.30 ± 11.79 and in group 2 ranged from 27-76 years with mean value 56.12 ± 12.57. There was no statistical significant difference between the two studied groups according to demographic data (P>0.05).

As regard the source of sepsis, the most frequent source was chest infection in both groups with 43(86%) and 44(88%) respectively. There was no statistical significant difference between the two studied groups according to source of sepsis (P > 0.05).

Table (1) shows comparison between two studied groups according to mean arterial blood pressure (MABP). There was statistical significant difference between two studied groups according to MABP on day 3, 4 and 5 (P < 0.05) while there was no statistical significant difference according to MABP on admission, day 1,2,6 and 7 (P > 0.05).

Table (1): MABP value in both groups:

MABP	Group 1	Group 2	t	p
On admission	63.36 ± 5.70	61.56 ± 7.74	1.324	0.189
Day 1	63.72 ± 6.61	62.0 ± 8.01	1.171	0.244
Day 2	63.56 ± 7.49	62.48 ± 8.90	0.656	0.513
Day 3	69.15 ± 9.13	64.62 ± 8.86	2.491*	0.014*
Day 4	71.39 ± 8.75	66.71 ± 8.88	2.453*	0.016*
Day 5	73.19 ± 8.08	68.60 ± 6.45	2.579*	0.012*
Day 6	73.03 ± 8.85	69.73 ± 5.06	1.720	0.092
Day 7	74.42 ± 8.98	71.74 ± 7.28	1.120	0.269

Table (2) shows comparison between the two studied groups according to serum CRP level. There was no statistical significant difference between two studied groups according to CRP at all periods (P > 0.05). On the other hand, the level of CRP decreased all over the period of the study.

Table (2): CRP level in both groups:

CRP	Group 1	Group 2	U	p
Day 1	73.69 ± 40.63	70.96 ± 37.48	1203.0	0.746
Day 2	67.42 ± 37.34	70.98 ± 35.79	1180.0	0.629
Day 3	60.45 ± 37.96	73.78 ± 39.95	971.5	0.104
Day 4	56.44 ± 34.57	70.61 ± 38.06	744.5	0.110
Day 5	54.33 ± 34.74	67.23 ± 28.04	436.5	0.121
Day 6	58.89 ± 38.92	65.65 ± 23.17	311.0	0.265
Day 7	56.33 ± 37.91	69.30 ± 31.57	211.0	0.166

U: Mann Whitney test
p: p value for comparing between the studied groups
Group 1: ARDS they will receive vitamin C
Group 2: ARDS patients will be not receiving vitamin C (control group)

Table (3) shows comparison between the two studied groups according to duration of MV. In group 1 ranged from 2-7 days with mean value 4.22 ± 1.61 and in group 2 ranged from 3-7 days with mean value 4.56 ± 1.43. There was no statistical significant difference between the two studied groups according to duration of MV (P > 0.05).

Table (3): Duration of length of stay on mechanical ventilation MV in both groups

	Group 1 (n = 50)	Group 2 (n = 50)	t-test	p
Duration of MV	4.22 ± 1.61	4.56 ± 1.43	1.62	0.093

Table (4) shows comparison between the two studied groups according to mortality at day 7. Survived in group 1 were 41(82%) and died were 9 (18%), while in group 2 were 39(78%) and 11(22%) respectively. There was no statistical significant difference between the two studied groups according to mortality at day 7 (P > 0.05).

Table (4): Mortality rate at day 7 in both groups

	Group 1 (n = 50)		Group 2 (n = 50)		χ^2	p
	No.	%	No.	%		
Mortality at day 7						
Survived	41	82.0	39	78.0	0.250	0.617
Died	9	18.0	11	22.0		

Discussion

In our study, both groups were matched as regard age and sex with no significant difference between them. The results was in agreement with study carried out by Zabet M. et al., 2016, they study the role of vitamin C on septic patients, they found that age and sex had no significant effect on the net result of their study.[12]

We found that, the majority of the source of sepsis in patients in the two groups was chest infection (86.0 and 88.0%) respectively, with no statistical significant difference between both groups (p> 0.05). This results was in concordance with ***Shin et al., (2019)*** study, they study the effect of vitamin C on patients with septic shock, the source of sepsis in the two groups was matched without significant difference.[13]

MABP values on day 3, 4 and 5 (P < 0.05) were statically different between both studied groups, while on admission, day 1,2,6 and 7, there was no difference (p> 0.05). In contrast to our study, ***Ried et al., (2016).*** They study the effect of high dose intravenous ascorbic acid , they concluded that ascorbic acid decreased the MABP up to 8-9 mmHg in prehypertensive patients.[14]

As regard serum CRP level, there was no difference in both group of patients (p>0.05). On the other hand, the level of CRP decrease all over the period of follow up, this results was agreement with Fowler A., et al., 2014, they study the effect of intravenous vitamin C in patients with severe sepsis where patients were divided into 3groups according to dose of viamin C given, placebo, low and high dose of vitamin C. At start of the study,[15] CRP levels across the three groups were nearly the same. Follow up CRP level showed slowly improvement over the study period in the placebo group.[16] and this could be explained by the role of CRP as an inflammatory marker.

We concluded the kidney function show no significant difference between the two studied groups, no change in the renal function all over the period of follow up, high dose of vitamin C show insignificant effect on renal function, this result was in agreement with meta analysis done by ***Lin J. et al., (2018)***.[17]This is an important result as one of the adverse effect of high dose ascorbic acid is stone formation and renal dysfunction. Our result could be explained by short duration of administration in the study (7 days).

The duration of mechanical ventilation in group 1 ranged from 2-7 days with mean value 4.22±1.61 and in group 2 ranged from 3-7 days with mean value 4.56±1.43. Although the duration of mechanical ventilation in group I less than group II but there was no statistical significant difference between the two studied groups according to duration of MV (P> 0.05).

These results were in contrast with Zhang et al., 2018, who concluded that the infusion of ascorbic acid was linked to less days spent on mechanical ventilation.[18] Also Tyml et al. demonstrated an increase in the hypoxic index (increased PaO2/FiO2 ratio in the treatment group), but the length of stay on mechanical ventilation receiving vitamin C was 12.1 days with no statistically significant difference between both group of the study.[19,20]

In our study the mortality at day 7, show that the survived in group 1 were 41(82%) and died were 9(18%), while in group 2 were 39(78%) and 11(22%) respectively. There was no statistical significant difference between the two studied groups according to mortality at day 7 (P > 0.05).

In a double-blinded randomized clinical trial, 28 adult surgical patients with septic shock had a significantly decreased in 28-day mortality was lower in the patients receiving intravenous vitamin C, compared with the placebo group. This results disagreement with our finding may be explained by different duration (28 day) of follow up versus (7 days) in our study.[21]

Conclusion

The administration of intravenous ascorbic acid in septic patients suffered from ARDS has no effect on improvement of hypoxic index, length of stay on MV and mortality rate.

References

1. Torio CM, Moore BJ. National Inpatient Hospital Costs: The Most Expensive Conditions by Payer, 2013: Statistical Brief #204. Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Rockville (MD)2006.
2. Vincent JL, Marshall JC, Namendys-Silva SA, Francois B, Martin-Loeches I, Lipman J, et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. The Lancet Respiratory medicine 2014;2(5):380-6.
3. Iwashyna TJ, Ely EW, Smith DM, Langa KM. Long-term cognitive impairment and functional disability among survivors of severe sepsis. Jama 2010;304(16):1787-94.
4. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). Jama 2016;315(8):801-10.
5. Guest W. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. Internal Medicine 2015;342(18):1301-1308.
6. Ferguson ND, Kacmarek RM, Chiche J-D, Singh JM, Hallett DC, Mehta S, et al. Screening of ARDS patients using standardized ventilator settings: influence on enrollment in a clinical trial. Intensive care medicine 2004;30(6):1111-6.
7. Karbing DS, Kjærgaard S, Smith BW, Espersen K, Allerød C, Andreassen S, et al. Variation in the PaO 2/FiO 2 ratio with FiO 2: mathematical and experimental description, and clinical relevance. Critical care 2007;11(6):R118.
8. Armour J, Tyml K, Lidington D, Wilson JX. Ascorbate prevents microvascular dysfunction in the skeletal muscle of the septic rat. Journal of applied physiology 2001;90(3):795-803.
9. Wu F, Wilson JX, Tyml K. Ascorbate protects against impaired arteriolar constriction in sepsis by inhibiting inducible nitric oxide synthase expression. Free radical biology & medicine 2004;37(8):1282-9.
10. Borrelli E, Roux-Lombard P, Grau GE, Girardin E, Ricou B, Dayer J, et al. Plasma concentrations ofcytokines, their soluble receptors, and antioxidant vitamins can predict the development of multiple organ failure in patients at risk. Crit Care Med 1996;24(3):392-7.
11. Marik P. Vitamin C for the treatment of Sepsis: The Scientific Rationale. J.pharmthera.2018.04.007.
12. Zabet M., Mohammadi M, Ramezani M and Khalili H. Effect of high‐dose Ascorbic acid on vasopressor's requirement in septic shock. J Res Pharm Pract 2016;5:94-100.
13. Shin T, Kim Y, Ryoo S, Hwang S, Jo I, Chung S, Choi S, Such G. and Kim W. Early Vitamin C and Thiamine Administration to Patients with Septic Shock in Emergency Departments: Propensity Score-Based Analysis of a Before-and-After Cohort Study. J. Clin. Med. 2019, 8, 102.
14. Juraschek SP, Guallar E, Appel LJ, Miller ER 3rd. Effects of vitamin C supplementation on blood pressure: a meta-analysis of randomized controlled trials. Am J Clin Nutr 2012; 95:1079–1088.
15. Fowler A., Syed A., Knowlson S., Sculthorpe R. Farthing D., DeWilde C., Farthing C., Larus T., Martin E, Brophy D and Gupta S. Phase I safety trial of intravenous ascorbic acid in patients with severe sepsis. Journal of Translational Medicine 2014, 12:32.
16. Lobo SM, Lobo FR, Bota DP, Lopes-Ferreira F, Soliman HM, Melot C, Vincent JL: C-reactive protein levels correlate with mortality and organ failure in critically ill patients. Chest 2003, 123(6):2043–2049.
17. Lin J. Li H. Wen Y and Zhang M. Adjuvant Administration of Vitamin C Improves Mortality of Patients with Sepsis and Septic Shock: A Systems Review and Meta-Analysis. Journal of Internal Medicine, 2018, 8, 146-159.
18. Zhang M, Jativa D. Vitamin C supplementation in the critically ill: A systematic review and meta-analysis. SAGE Open Medicine Volume 6: 1–12. 2018.
19. Tyml K. Vitamin C and microvascular dysfunction in systemic inflammation. Antioxidants 2017; 6: E49.
20. Sadeghpour A, Alizadehasl A, Kyavar M, et al. Impact of vitamin C supplementation on post-cardiac surgery ICU and hospital length of stay. Anesthesiol Pain Med 2015; 5: e25337.

21. Zabet MH, Mohammadi M, Ramezani M, Khalili H. Effect of high-dose Ascorbic acid on vasopressor's requirement in septic shock. J Res Pharm Pract 2016; 5:94–100.

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