

To Study the N-Acetylcysteine and Vitamin C Effect on Oxidative Stress in Abdominal Sepsis and Control Patients with Different Weight Range

O Srinivas Kumar¹, M Madan Mohan Rao², G. Obulesu³

¹Assistant Professor, Department of Anesthesiology, ²Associate Professor, Department of General Medicine, Rajiv Gandhi Institute of Medical Sciences, Kadapa, Andhra Pradesh 516002, India. ³Assistant Professor, Department of Microbiology, Karuna Medical College & Hospital, Palakkad, Kerala 678103, India.

Abstract

"Sepsis" was characterized as the foundational reaction to infection, showed by at least 2 of the conditions recorded above for SIRS. "Serious sepsis" was characterized as sepsis related with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may incorporate however are not constrained to lactic acidosis, oliguria, or an intense change in mental status. *Aim:* To Study the N-Acetylcysteine and Vitamin C effect on Oxidative stress in Abdominal sepsis and control Patients with different weight range. *Material and Methods:* The present Study was conducted in the intensive care Unit of the the Dept of Anesthesiology, Rajiv Gandhi Institute of Medical Sciences, Kadapa. *Conclusion:* Along these lines, the sex, age and weight of the patients can impact the dimension of hematological and biochemical markers in patients with sepsis. In any case, since the statistic profile of the patients in our examination was similar between the nominal control and sepsis patients and furthermore between the gatherings, it didn't impact the in general outcome.

Keywords: SOD; GRx; CRP; Catalase.

How to cite this article:

O Srinivas Kumar, M Madan Mohan Rao, G. Obulesu. To Study the N-Acetylcysteine and Vitamin C effect on Oxidative Stress in Abdominal Sepsis and Control Patients with Different Weight Range. *Indian J Anesth Analg.* 2019;6(1):297-302.

Introduction

"Sepsis" has its inception from a Greek word for disintegration or festering, and has been utilized in that setting since before Hippocrates (Geroulanos and Douka, 2006). In any case, in spite of the fact that the word, sepsis, has been utilized for over 2700 years, it is just moderately as of late that we have started to comprehend the pathophysiology of sepsis in any profundity (Vincent and Abraham, 2006).

The rate keeps on expanding, with unsatisfactorily high death rates, not with standing the utilization of particular antibiotics, aggressive agent intercession, healthful help, and calming treatments. Not with standing high mortality, patients with serious sepsis or early septic shock invest drawn out times of energy in the ICU and are altogether more costly to treat than ICU patients without sepsis. It along these lines keeps on having noteworthy clinical and monetary ramifications and remains a zone that pulls in extreme research intrigue.

Corresponding Author: M. Madan Mohan Rao, Associate Professor, Department of General Medicine, Rajiv Gandhi Institute of Medical Sciences, Kadapa, Andhra Pradesh 516002, India.

E-mail: obulesu100@gmail.com

Received on 21.11.2018, **Accepted on** 13.12.2018

“Sepsis” was characterized as the foundational reaction to infection, showed by at least 2 of the conditions recorded above for SIRS. “Serious sepsis” was characterized as sepsis related with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may incorporate, however are not constrained to lactic acidosis, oliguria, or an intense change in mental status. Note that SIRS is a clinical disorder coming about fundamental aggravation, conceivably from a wide assortment of causes. Sepsis is the term utilized when fundamental aggravation is because of an infection. It can grow quickly. The sooner it is analyzed and treated, the better. The most incessant locales of disease prompting sepsis are the lung, urinary tract, midriff, and pelvis.

The digestion of oxygen (i.e., decrease) produces receptive intermediates called free radicals (Halliwell and Gutteridge, 1984). The electronic structure is thermodynamically more steady if electrons are matched with antiparallel spin, bringing about no net spin. In electron orbit terms, a free radical is a particle or a molecule with an unpaired electron in its external shell. By this definition, sub-atomic oxygen itself is a biradical, since it has two unpaired electrons, each arranged at an alternate p orbital. Having a similar spin quantum number, these two electrons are situated in a parallel spin design. This spin confinement makes a circumstance in which a one-electron exchange can happen, permitting the arrangement of a particle or an ion with unpaired electron, a free radical (Halliwell and Gutteridge, 1984). Ions' share of ROS are shaped amid cell breath and by enacted phagocytic cells, including neutrophils, engaged with the fiery reaction. They have physiologically fundamental jobs in mitochondrial breath, prostaglandin generation pathways and have defence. Under typical physiological conditions, a homeostatic parity exists between the arrangement of receptive oxidizing/oxygen species and their expulsion by endogenous cancer prevention agent scavenging compounds. Oxidative pressure happens when this equalization is upset by exorbitant generation of ROS, including superoxide, hydrogen peroxide what's more, hydroxyl radicals, or potentially by lacking cancer prevention agent protections, including SOD, CAT, glutathione peroxidase (GPx), nutrients C and E, and glutathione (GSH). Both may happen in sepsis.

To battle the danger of oxidative worry, there exist various endogenous cancer prevention agent protections. These incorporate nutrients E and C, professional nutrient A (P-carotene), glutathione peroxidase, glutathione-S-transferase, superoxide

dismutase and catalase, bilirubin, urate, and other plasma proteins. These cancer prevention agents can be partitioned into enzymatic and nonenzymatic gatherings.

The enzymatic cell reinforcements incorporate superoxide dismutase (the essential cancer prevention agent catalyst that follows up on ROS), which catalyzes the transformation of $O_2^{\cdot -}$ to H_2O_2 and sub-atomic oxygen; catalase, which at that point changes over H_2O_2 to H_2O and O_2 , and glutathione peroxidase, which lessens H_2O_2 or different hydroperoxides to H_2O by oxidizing glutathione (GSH). Glutathione-S-transferase like GPX, additionally frees cells of hydroperoxides however does not follow up on H_2O_2 . Re-decrease of the oxidized type of (glutathione disulfide) is then catalyzed by glutathione reductase.

The nonenzymatic cell reinforcements incorporate the lipid solvent nutrients (nutrient E, and nutrient A or P-carotene) and the water-dissolvable nutrients (nutrient C) glutathione. Vitamin E has been depicted as the significant chain-breaking cancer prevention agent in humans. Vitamin C (ascorbic corrosive), acquired principally from citrus natural products, functions as a water-soluble antioxidant able to do comprehensively scavenging ROS, including the real neutrophil oxidants: H_2O_2 , and hypochlorous acid. Vitamin C (ascorbic corrosive) is a powerful electron contributor, responding with both superoxide and hydroxyl radicals. Ex vivo contemplates demonstrated control of cell action by exogenous ascorbic corrosive, in that the expanded adherence of, and superoxide anion generation by, macrophages from mice with endotoxic shock were brought down within the sight of ascorbic corrosive (Victor et al., 2000). In a rodent caecal ligation and cut model, exogenous administration of ascorbic corrosive secured against traded off microvascular perfusion. In vitro contemplates indicated that ascorbic corrosive repressed the replication of microbes and anticipated hydrogen peroxide damage to refined microvascular endothelial cells. In guinea-pigs, which, similar to people, can't integrate their own nutrient C, organization of endotoxin quickly exhausted nutrient C stores; repletion forestalled oxidative harm (Rojas et al., 1996) However, in another investigation utilizing infusion of live microorganisms, mortality was just enhanced in guinea-pigs accepting high dosages of nutrient E; high portions of nutrient C did not enhance survival (Peck and Alexander, 1991). Circling groupings of nutrient C are notably exhausted in patients with sepsis. Extraordinarily extraordinary treatment of imbued ascorbate contrasted and solid subjects was accounted for,

and organization of nutrient C related to different cancer prevention agents neglected to improve free radical-intervened harm (Galley et al., 1997).

Cowley et al., (1996), directed a forthcoming, partner think about containing fifteen patients, who were inside 16 hrs of advancement of serious sepsis and auxiliary organ dysfunction. The mean starting plasma cell reinforcement potential was lower than their range for solid volunteers ($p < 0.05$). Survivors had an underlying plasma cancer prevention agent potential that was more prominent than non-survivors ($p < 0.01$), and sequential subset investigation illustrated that survivors, regardless of having a low beginning plasma cancer prevention agent potential quickly accomplished ordinary or supranormal qualities. While plasma cell reinforcement potential moreover expanded in non-survivors after some time, values in this subset never achieved the ordinary run and stayed beneath qualities in survivors at record-breaking focuses considered ($p < 0.05$). On the premise of their information they were of the sentiment that plasma cancer prevention agent potential at first reductions in patients with sepsis who create organ dysfunction, and it increments after some time.

Nathens et al., (2002), directed a randomized, forthcoming investigation to look at results in patients accepting cancer prevention agent supplementation (alpha-tocopherol and ascorbate) versus those accepting standard consideration. The general danger of pneumonic dismalness was 0.81 (95% certainty interim 0.60-1.1) in patients getting cancer prevention agent supplementation. Different organ disappointment was fundamentally less inclined to happen in patients getting cell reinforcements than in patients accepting standard consideration, with a relative danger of 0.43 (95% certainty interim 0.19-0.96). They inferred that early organization of cell reinforcement supplementation utilizing alpha-tocopherol and ascorbic corrosive lessens the frequency of organ disappointment and abbreviates ICU length of remain.

Aim

To assess

1. the most critical oxidative pressure marker(s) in sepsis
2. the relationship of the dimension of sepsis markers (hematological and biochemical) with that of the seriousness of sepsis
3. the cancer prevention agent operators (N-acetylcysteine and nutrient C) best in

decreasing the dimension of sepsis markers (hematological and biochemical markers) in sepsis.

Material and Methods

The present study was conducted in the intensive care Unit of the the Dept of Anaesthesiology, Rajiv Gandhi Institute of Medical Sciences, Kadapa and the biochemical analyses was performed in the Dept of Biochemistry, Kadapa, Andhra Pradesh.

Sample Size

In the wake of acquiring endorsement from the Board of studies, 50 patients experiencing sepsis, conceded in the ICU and 12 nonnal individuals (as a typical control) (a sum of 62 patients) of either sex, age going between 18-55 years, were enlisted for the examination. Composed educated assent was gotten from the patients or patient's relatives.

Choice Criteria

- Age at least 18 years and not over 55 years of either sex
- Patients analyzed as peritonitis (stomach sepsis)
- Presence of at least two of criteria for fundamental incendiary reaction disorder (SIRS) and
- Presence of unequivocal site of contamination (stomach)
- Post careful septic peritonitis

Note: The criteria for the finding of SIRS is as per the following

1. Temperature more prominent than or equivalent to 38°C or under 36°C ,
2. Pulse more noteworthy than 90 bpm,
3. Respiratory rate more prominent than 20 breaths/min or PaCO_2 in excess of 32 mm Hg, furthermore,
4. WBC tally more noteworthy than 12,000 for each mm or under 4000 for each mm or the nearness of in excess of 10 percent juvenile groups.

Avoidance Criteria

The accompanying patients were excluded in the examination:

- Age under 18 years,
- Glasgow trance like state scale (GCS) under 9,
- patients with un-recordable heartbeat and circulatory strain, with Acute coronary disorder, with medication overdose, with history of harming, with bum damage,

For the biochemical examination the sera were isolated from blood at the earliest opportunity by centrifugation at 2000 x g at 4°C for 10 min in Beckman J2-M1 (Beckman instruments Inc, Palo Alto, C.A. USA) refrigerated axis. The serum got was put away in aliquots at - 20°C until further examination. 50 grown-up patients of both genders with stomach sepsis (septic peritonitis) were enlisted for the investigation. Blood tests of these patients were acquired on confirmation and broke down for assessment of haemato intelligent parameters (Hb_{gm}%, WBC tally, and platelet tally) and serum biochemical parameters (proposed biochemical markers and serum CRP level). The qualities were then contrasted and that of normal control patients (n = 12) to recognize the proposed markers with significant distinction by applying under studies 't' test (unpaired t-test). The markers were then registered to assess the most extreme rate change between the normal control and the sepsis patients. The information has been made reference to as mean ± SD and rate (%). p < 0.01 has been considered factually critical.

Results and Discussion

The present investigation was intended to think about different cancer prevention agents barrier segments (enzymatic and non-enzymatic) for their power as sepsis biomarkers, differentiate them with the conventional sepsis markers and distinguish the most critical of them. The assessment was finished by looking at the dimensions of hematological and biochemical markers (proposed biomarkers and CRP) in all the sepsis patients together (NO = 50) with that of the typical control (NO = 12) subjects.

Table 1: Distribution of the patients in different weight range

Weight (kg)	Normal Control	Sepsis groups
40 - 50 Kg	2(13.3%)	6(10%)
50 - 60 Kg	6(46.6%)	20(43.3%)
60 - 70 Kg	4(40.0%)	24(46.6%)

The appropriation of patients in the scope of 40-50 kg, 50-60 kg and 60-70 kg were 2, 6, and 4, individually in normal control patients. Among stomach sepsis patients the dissemination was 6, 20 and 24 in the weight territory 40-50 kg, 50-60 kg

and 60-70 kg, separately. There are contemplates demonstrating that oxidative harm to lipids increments and cell reinforcementsaves diminish after dietary admission (Cereillo et al., 1998; Mohanty et al., 2000) (Table 1).

Table 2: Comparison of biochemical markers between controls and sepsis patients

Parameters	Controls	Sepsis
SOD (Units/mL)	1.71 ± 0.38	7.18 ± 0.87
Catalase (Units/mL)	1.80 ± 0.60	9.83 ± 1.86
GPX (Units/mL)	0.79 ± 0.03	2.3 ± 0.41
LDH (Units/L)	70.4 ± 8.14	332.55 ± 5.64
CRP (mg/L)	7.6 ± 2.23	236.36 ± 60.40

The expansion in ROS generation after glucose ingestion recommends that dietary admission has a task to carry out in causing expanded receptive oxygen species stack in the hefty in a way like that saw in normal subjects (Mohanty et al., 2000). In this way, wholesome admission is a central point influencing responsive oxygen species age and add up to oxidative load as opposed to overweight or weight. As needs be, the heaviness of the patients in the present investigation did not impact the outcomes since none of our patient was stout or overweight. Further, the mean weight of our patients went between 50 to 69 kg and it was tantamount between the normal control and sepsis patients and between the patients of all the five gatherings (Table 2).

Flawed procedure of blood accumulation can result in false abnormal state of cancer prevention agent. Blood gathered through extremely slender bore needle can cause haemolysis of RBC. Ill-advised division of serum from the cells can likewise impact the outcome. Be that as it may, since a standard and uniform strategy was connected for all the example gathering both in ordinary control and sepsis patients, we accept this did not impact our outcome. From the above outcomes and exchange it very well may be induced that CRP level is the most huge and dominating biochemical marker of sepsis in our investigation.

Conclusion

Along these lines, the sex, age and weight of the patients can impact the dimension of hematological and biochemical markers in patients with sepsis. In any case, since the statistic profile of the patients in our examination was similar between the normal control and sepsis patients and furthermore between the gatherings, it didn't impact the in general outcome.

References

1. ACCP-SCCM Consensus Conference (1992) Definitions of sepsis and multiple organ failure and guidelines for the use of innovative therapies in sepsis. *Crit Care Med.* 1992;20:864-74.
2. Akca S, Haji Michael P, deMedonca A, Suter PM, Levi M, Vincent JL. The time course of platelet counts in critically ill patients. *Crit Care Med.* 2002;30:753-6.
3. Akinci SB, Erdenl A, Kanbak M, Aypar U. Lack of effect of NAC treatment to ameliorate the progression of MOF. *Saudi Med J.* 2005;26:651-5.
4. Alonso de Vega JM, Diaz J, Serrano E, Carbonell LF. Plasma redox status relates to severity in critically ill patients. *Crit Care Med.* 2000;28:1812-14.
5. Alonso de Vega JM, Diaz J, Serrano E, Carbonell LF. Oxidative stress in critically ill patients with systemic inflammatory response syndrome. *Crit Care Med.* 2002;30:1782-6.
6. Amezcua-Guerra LM, Springaldel Villar R, Bojalil Parra R. Proteina C reactiva aspectos cardiovasculares de unaproteina de faseaguda. *Arch CardiolMex.* 2007;77:58-66.
7. Aminzadeh Z and Parsa E. Relationship between Age and Peripheral White Blood Cell Count in Patients with Sepsis, *hit J Prev Med.* 2011;2:238-42.
8. Andrades ME, Ritter C, Dal-Pizzol F. The role of free radicals in sepsis development. *Front Biosci (Elite Ed).* 2009;1:277-87.
9. Andrades M, Ritter C, de Oliveira MR, Streck EL, Fonseca Moreira JC, Dal-Pizzol F. Antioxidant Treatment Reverses Organ Failure in Rat Model of Sepsis: Role of Antioxidant Enzymes Imbalance, Neutrophil Infiltration, and Oxidative Stress. *J Surg Res.* 2011;167:307-13.
10. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care. *Crit Care Med.* 2001;29:1303-10.
11. Anup R, Apama V, Pulimood A, Balasubramanian KA. Surgical stress and the small intestine: role of oxygen free radicals. *Surgery.* 1999;125:560-9;174.
12. Bakker J, Zhang H, Depierreux M, van Asbeck S, Vincent JL. Effects of Nacetylcysteine inendotoxic shock. *J Crit Care.* 1994;9:236-43.
13. Balaban RS, Nemoto S, Finkel T. Mitochondria, oxidants, and aging. *Cell.* 2005;120:483-95.
14. Batra S, Kumar R, Seema, Kapoor AK, Ray G. Alterations in antioxidant status during neonatal sepsis. *Aim Trop Paediatr.* 2000;20:27-33.
15. Becker KL, Nyle'n ES, White JC, MuUer B, Snider RH Jr. Clinical review 167: procalcitonina and the calcitonin gene family to peptides inflammation, infection and sepsis: a journey from calcitonin back to its precursors. *J Clin Endocrinol Metab.* 2004; 89:1512-25.
16. Bellary SSKW, Anderson WA, Arden DA, Butterfield. Effect of lypopolysaccharide on the physical conformation of the erythrocyte cytoskeletal proteins. *Life Sci.* 1994;56:91-98.
17. Calandra T, Baumgartner JD, Grau GE, Wu MM, Lambert PH, Schellekens J, et al. Prognostic values of tumor necrosis factor/cachectin, interleukin-1, interferon-alpha, and interferon-gamma in the serum of patients with septic shock. *J Infect Dis.* 1990;161:982-7.
18. Carbonell LF, Nadal J A, Llanos MC, Hema Andez I, Nava E, DoAaz .T. Depletion of liver glutathione potentiates the oxidative stress and decreases nitric oxide synthesisi in a rat endotoxin shock model. *Crit Care Med.* 2000;28:2002-6.
19. Dai CH, Krantz SB, Kollar K, Price JO. Stem cell factor can overcome inhibition of highly purified human burst-forming units-erythroid by interferon gamma. *J Cell Physiol.* 1995;165:323-32.
20. Davies KJ, Goldberg AL. Oxygen radicals stimulate intracellular proteolysis and lipid peroxidation by independent mechanisms in erythrocytes. *J BiolChem.* 1987;262:8220-6.
21. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Intensive Care Med.* 2008;34:17-60.
22. Espat NJ, Helton WS. Oxygen free radicals, oxidative stress, and antioxidants in critical illness. *Support Line.* 2000;22:11-20.
23. Flohe L, Gunzler W. Assays of glutathione peroxidase, in: S.P. Colowick, N.O. Kaplan (Ed.), *Methods Enzymology*, Academic Press, New York, 1984,pp.114-121.
24. Fox ES, Brower JS, Bellezzo JM, Leingang KA. N-acetylcysteine and alphatocopherol reverse the inflammatory response in activated rat Kupffer cells. *J Immunol.* 1997;158:5418-23.
25. Galley HF, Davies MJ, Webster NR. Xanthine oxidase activity and free radical generation in patients with sepsis syndrome. *Crit Care Med.* 1996 a;24:1649-53.
26. Harman LS, Mottley C, Mason RP. Free radical metabolites of L-cysteine oxidation. *J BiolChem* 1984;259:5606-611.
27. Lagranha CJ, Deschamps A, Aponte A, Steenbergen C, Murphy E. Sex differences in the phosphorylation of mitochondrial proteins result in reduced production of reactive oxygen species and cardioprotection in females. *Circ Res.* 2010;106:1681-91.
28. Macdonald J, Galley HF, Webster NR. Oxidative stress and gene expression in sepsis. *Brit J Anaesth* 2003;90:221-32.

29. Noctor G, Foyer CH. Ascorbate and glutathione: keeping active oxygen under control. *Annual Rev Plant Physiol Plant Mol Biol* 1998;49:249-79.

