

LETTER

Open Access



The adrenal-vitamin C axis: from fish to guinea pigs and primates

Michael H. Hooper¹, Anitra Carr² and Paul E. Marik^{1*}

Keywords: Vitamin C, Cortisol, Stress response

Primates and guinea pigs are unable to synthesize vitamin C. In contrast, almost all other mammals produce vitamin C in their livers with production increasing during stress. Furthermore, largely to metabolic consumption, a high percentage of critically ill patients are deficient in vitamin C. In an observational study, Carr et al. found that 75% of critically ill patients had plasma levels of vitamin C that were abnormally low [1]. The degree and incidence of deficiency were most pronounced in those patients with sepsis. Several trials have shown that administration of vitamin C to patients with sepsis is associated with better patient outcomes, suggesting a causal relationship between vitamin C deficiency and outcome. The mechanism(s) by which vitamin C administration may improve outcomes is unclear. Observations of very high vitamin C levels in the adrenal gland as well as its release in response to ACTH suggest that vitamin C plays a role in the stress response [2]. Release of cortisol in response to stress is well documented in humans and throughout the animal kingdom. However, there is marked inter-species variation in the amount of cortisol released in response to a stressor. Interestingly, there is a strong inverse correlation between the ability of an animal to endogenously produce vitamin C and the cortisol response when stressed. Barton et al. reported the baseline cortisol and response of numerous fish species to handling [3]. Those fish species which synthesized vitamin C had a 1.6-fold increase in cortisol levels after stress as compared to a 20.2-fold increase in those fish species that were unable to produce vitamin C, with the non-producers having a significantly higher baseline

cortisol level. Additional evidence supports the concept of an inverse correlation between vitamin C and cortisol levels. Guinea pigs that are made deficient in vitamin C hyper-secrete cortisol [4]. Supplementation of ascorbic acid in humans and animal models is associated with a decreased cortisol response after a psychological or physical stressor [5]. High serum levels of cortisol in patients with sepsis are associated with a poor prognosis. Traditionally, this association has been explained on the assumption that higher cortisol responses are due to a more intense physiological stress and a higher severity of illness. However, the inverse relationship of cortisol levels with vitamin C status would suggest an alternative hypothesis, namely, that high levels of cortisol and the associated poorer outcomes of patients are a function of vitamin C deficiency.

Acknowledgements

None

Funding

None

Availability of data and materials

Available on request

Authors' contributions

MHH drafted the original version of the manuscript. PEM and AC reviewed and revised the manuscript. All authors read and approved the final manuscript.

Authors' information

Not applicable

Ethics approval and consent to participate

Not applicable

Consent for publication

All authors have reviewed the final version of the manuscript and approve the manuscript for publication.

Competing interests

The authors declare that they have no competing interests.

* Correspondence: marikpe@evms.edu

¹Division of Pulmonary and Critical Care Medicine, Eastern Virginia Medical School, 825 Fairfax Av, Suite 410, Norfolk, VA 23507, USA

Full list of author information is available at the end of the article



Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details

¹Division of Pulmonary and Critical Care Medicine, Eastern Virginia Medical School, 825 Fairfax Av, Suite 410, Norfolk, VA 23507, USA. ²Department of Pathology, University of Otago, Christchurch, PO Box 4345, Christchurch 8140, New Zealand.

Received: 11 January 2019 Accepted: 22 January 2019

Published online: 28 January 2019

References

1. Carr AC, Rosengrave PC, Bayer S, Chambers S, Mehrtens J, Shaw GM. Hypovitaminosis C and vitamin C deficiency in critically ill patients despite recommended enteral and parenteral intakes. *Crit Care*. 2017;21:300.
2. Padayatty SJ. Human adrenal glands secrete vitamin C in response to adrenocorticotrophic hormone. *Am J Clin Nutr*. 2007;86:145–9.
3. Barton BA. Stress in fishes: a diversity of responses with particular reference to changes in circulating corticosteroids. *Integr Comp Biol*. 2002;42:517–25.
4. Enwonwu CO, Sawiris P, Chanaud N. Effect of marginal ascorbic acid deficiency on saliva level of cortisol in the guinea pig. *Arch Oral Biol*. 1995; 40:737–42.
5. Brody S, Preut R, Schommer K, Schurmeyer TH. A randomized controlled trial of high dose ascorbic acid for reduction of blood pressure, cortisol, and subjective responses to psychological stress. *Psychopharmacology*. 2002; 159:319–24.