Journal of Critical Care (2012) **27**, 102.e1–102.e6

ELSEVIER

Journal of Critical Care

Zinc supplementation in intensive care: Results of a UK survey☆

Andrew Duncan PhD[a,*], Pamela Dean MB, ChB[b], Malcolm Simm MB, ChB[b], Denis StJ. O'Reilly MB, ChB[a], John Kinsella MB, ChB[b]

[a]*Scottish Trace Element and Micronutrient Reference Laboratory, G4 0SF Glasgow, United Kingdom*
[b]*Intensive Care Unit, Glasgow Royal Infirmary, G4 0SF Glasgow, United Kingdom*

Keywords:
Zinc;
Supplementation;
Critical care medicine

Abstract

Purpose: Our laboratory receives many routine requests for plasma zinc analysis from intensive care units (ICUs) throughout Scotland. However, such requests are inappropriate because plasma zinc concentrations fall independently of nutritional deficiency during the systemic inflammatory response and, therefore, in critically ill patients. This survey was performed to investigate how widespread this practice was and if low plasma zinc concentrations were interpreted as zinc deficiency so triggering inappropriate initiation of zinc supplementation.

Materials and Methods: A questionnaire was sent to ICUs throughout the UK; nonresponders were contacted by telephone, and the questionnaire details were recorded. The questionnaire asked if plasma zinc was routinely requested, the frequency of requests, whether patients were supplemented with zinc, and if so, the grounds for supplementation and the dose given.

Results: Plasma measurement of zinc was routinely performed in 18% of UK ICUs. Zinc supplementation was given in 10%, usually as a result of finding low plasma zinc concentrations. Dosages of supplementation varied widely between ICUs: from 0.4 to 135 mg zinc per day. Approximately 6% of ICUs gave very high supplements of zinc of 90 and 135 mg/d.

Conclusions: The finding of a low plasma zinc concentration in Intensive Therapy Unit patients is often misinterpreted as indicating zinc deficiency and inappropriately prompts zinc supplementation. There is no evidence base to support high-dose zinc supplementation in ICU patients. This practice is justifiable only if future randomized trials demonstrate a benefit.

1. Introduction

Zinc plays a crucial role in many metabolic processes, and because of its involvement in the immune response and wound healing, it is considered to be of importance in critically ill patients. Such patients have an increased metabolic rate [1], often against a background of recent inadequate dietary intake and ongoing feeding difficulties. The low plasma concentrations of zinc that are often found might seem to reflect poor nutrition. However, this does not necessarily indicate deficiency because plasma zinc concentrations fall as part of the systemic inflammatory response [2]. This decrease in plasma zinc is partially caused by redistribution of carrier proteins because of increased

☆ There are no conflicts of interest to declare.

* Corresponding author. Tel.: +41 41 211 4494; fax: +41 41 552 3324.
E-mail address: Andrew.duncan@ggc.scot.nhs.uk (A. Duncan).

0883-9441/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.jcrc.2011.07.083

vascular permeability; sequestration into tissues [3]; and losses in urine, drains [4], and mucosal secretions [5]. Plasma zinc is predominantly bound to albumin, and so, the low concentrations of albumin found during the systemic inflammatory response also partially explain low plasma zinc concentrations. Consequently, plasma zinc measurement during the systemic inflammatory response and, therefore, in critically ill patients is uninformative and may be misleading.

A recent Scottish survey demonstrated that during routine clinical care of patients on total parenteral nutrition, the existence of an acute inflammatory response is often not considered when interpreting plasma trace element concentrations (personal findings). This laboratory receives significant numbers of plasma zinc requests from intensive care units (ICUs) throughout Scotland, suggesting that this is also the case in this setting. This prompted the current survey, by questionnaire and telephone inquiry, of UK ICUs to investigate whether zinc was measured routinely, if low results were inappropriately considered to indicate deficiency, if this prompted zinc supplementation, and if so, the doses used.

2. Methods

A list of adult ICUs in the UK was compiled from the ICU directory. A questionnaire (see Supplemental Material) was addressed to the first named consultant in the units and sent to all 263 ICUs throughout the UK. Nonresponders were contacted by telephone, and responses to the questionnaire were recorded.

Intensive care units were asked if zinc supplementation was administered in addition to Additrace (Fresenius Kabi, Bad Homburg, Germany) or any of the standard proprietary enteral or parenteral feeds. If supplementation was given, the preparation and dose were ascertained. Three choices were given as criteria for commencing supplementation: given routinely, on clinical grounds, and/or if plasma concentration was low. Finally, the responder was asked how frequently trace elements were measured.

3. Results

A total of 92 (35%) of 263 questionnaires were returned by post. The response rate increased to 259 (99%) by contacting nonresponders by telephone and recording questionnaire details. Two questionnaires, which were completed irrationally, were discarded.

Plasma zinc was routinely measured in 40 (18%) of 227 ICUs (36 ICUs did not reply to this question). When plasma zinc is measured, the frequency was daily in 6 ICUs (2.6%), twice-weekly in 10 (4.4%), weekly in 18 (7.9%), and fortnightly in 6 (2.6%).

The criteria for starting zinc supplementation were as follows: given routinely (in 3/24, or 12.5%) if plasma concentration is low (in 13, or 54%), on clinical grounds (in 6, or 25%), and low plasma concentration and clinical grounds (in 1, or 4%).

Table 1 Dose and form of zinc administered

Form	No. of ICUs	Zinc dose (mg/d)
Zinc sulfate	1	0.4
Zinc sulfate	2	6.5
Not stated	1	9.5
Zinc gluconate	1	10
Multitrace 2+	1	13
Solvazinc	1	90
Solvazinc	7	135

Solvazinc: Galen Ltd, Craigavon, UK; Multitrace: American Regent, New York, NY.

Most ICUs do not measure zinc (82%) or administer supplements (90%). However, a significant minority of ICUs, 26 (10%) of 263, supplement patients with zinc. Table 1 details the doses and forms in which zinc is given; 12 ICUs gave no details regarding the form or dose of zinc given. Of the 14 ICUs that replied, equivalent to 4.2% of UK ICUs, 6 (43%) administer doses similar to or less than recommended dietary intakes. Of the 14 ICUs, equivalent to 5.6% of UK ICUs, 8 (57%) administer doses of zinc of 90 mg/d or 135 mg/d[1], which is many times greater than the recommended dietary intake.

4. Discussion

Zinc is an essential trace element having important structural roles and as a cofactor in many enzyme reactions. It is required in the immune system for normal T-cell function [6,7]; for pancreatic synthesis, storage, and secretion of insulin [8]; as an antioxidant in superoxide dismutase [9]; and in wound healing by stimulation of keratinocytes, fibroblasts, and collagen synthesis [10]. As a result of its wide-ranging biologic effects, the rationale for its replacement in zinc deficiency is apparently sound. Measurement of zinc in plasma or serum is considered to be the most useful and most widely used indicator of deficiency [11,12]. However, in patients with a systemic inflammatory response, plasma zinc concentrations decrease independently of nutritional status [2]. For example, in nutritionally replete patients admitted for elective surgery, plasma concentrations fall rapidly postoperatively and return to normal levels without supplementation [13]. This fall in plasma zinc is proportional to the rise in the concentration of C-reactive protein. Consequently, the measurement of plasma zinc in patients with an inflammatory response, typical in ICU patients, is of no value in assessing zinc status and should not be taken to indicate deficiency.

[1] To avoid confusion, the mass dose of elemental zinc rather molecular zinc is quoted throughout.