Trace element in Total Pareteral Nutrition with special references to zinc

A.Okada[1], R. Nezu[2] and Y. Takagi[1]

[1]*Dept. of Pediatric Surgery and* [2]*First Dept. of Surgery, Osaka Univ. Medical School, Osaka 553, Japan*

The recent development of artificial nutritional support induced dramatic improvement of prognosis in patients with various catastrophic disordors. Particularly, total parenteral nutrition (TPN) has made it possible to provide adequate nutrition to patients via central vein for prolonged period of time,[1] hence reduced mortality rate in those patients who would otherwise have died because of starvation.

In a way, there has been an increasing number of clinical cases that are solely depending on TPN. This has posed various unforseen problems. Among them, supply of trace elements has been paid particular attention.

In the early 1970', a very small number of patients on prolonged TPN in our institution developed characteristic skin lesions on the face, scrotum and perianal area.

These lesions were progressive and later they extended to the extremities, particularly in joints and nails. Accessory symptoms including stomatitis, glossitis and loss of hair were observed.

Enteritis-like symptoms such as vomiting, abdominal pain and diarrhea, very much resembling symptoms in acrodermatitis enteropathica, which had been known to be a rare inheritant disease, has also been accompanied. Searching for the etiologic factor, we first demonstrated that zinc deficiency was responsible for those characteristic lesions.[2,3] Since then, many papers supporting this have been published.[4]

At present, a series of those symptoms is understood as a new disease entily and is well recognized as "acute zinc deficiency".

However, much remains unclear about several points, i.e., (1) How is systemic zinc level reflected in such condition? (2) Is there any difference among primary diseases as to the incidence of zinc deficiency? (3) What is an adequate amount of zinc to prevent deficiency or to maintain normal serum level? and (4) Are the any abnormal distribution of zinc in the body induced by TPN? To answer these questions, the following clinical studies were designed.[5]

In 99 adult patients receiving TPN without any supplementation of zinc, a study on the time course of the level of zinc in plasma, erythrocytes and urine in relation to the development of zinc deficiency was performed. As a result, zinc deficiency developed in 11 cases. In all cases the administration of zinc induced a dramatic symptomatic relief. The plasma zinc level was significantly lower at the time of onset of zinc deficiency than that in normal subjects, before TPN, or at the time of symptomatic relief. The urinary zinc level at the time of onset of zinc deficiency was significantly lower than that

in normal subjects or at the time of symptomatic relief but not significantly lower than that before TPN. A comparison between patients developing and those not developing zinc deficiency within 4 weeks of the onset of TPN showed that only plasma zinc level was significantly lower in the former than the latter group. The urinary zinc level also tended to be lower, although not significantly, in the former than the latter group but varied widely. No difference was present between the group as to the erythrocyte zinc level.

Zinc deficiency developed in none of those patients who had a plasma zinc level of 50 μg/dl or more but in five of 10(50%) patients with less than 30 μg/dl of zinc in plasma. Zinc deficiency was frequent in patients with benign gastrointestinal diseases, particularly in inflammatory bowel diseases. During the course of TPN with solutions not containing zinc a steady fall occurred only in plasma zinc level. Administration of daily dose of 60 μmol (3.9mg) was found to be adequate to prevent plasma zinc level from falling and maintain it essentially within normal range. None of the patients receiving zinc in daily dose of 60 μmol (3.9mg) developed signs of zinc deficiency or showed an abnormally elevated plasma zinc level throughout the period of observation. From this finding, one might, therefore, recommend a daily dose of 60 μmol (3.9mg) for the amount of maintaining zinc level on the patients receiving TPN.

Now, another question rises; why does zinc dificiency occur so often during the course of TPN? There are several possible reasons. In Japan, the standard TPN solutions currently have a low zinc content as compared to those in the other countries.[6,7] TPN prepatation in Japan contains only 20–30 μg of zinc per day for adult patients, which is less than about 1/100 of daily requirement. Secondly, there is an increased urinary excretion of zinc during TPN, since urine is known to be the main source for excretion during TPN. There are several reports describing an increased urinary excretion of zinc during TPN possibly caused by sugar-amine-complex as a zinc-chelating agent.[8] Thirdly, there is an increased demand for zinc during TPN since most of patients who need TPN are usually more or less malnourished, and repletion by TPN accelerates anabolism, resulting in an increase demand of zinc.[9]

As described before, TPN involves a number of factors predisposing to zinc deficiency. Therefore, it is advisable to add zinc to TPN solutions routinely in the therapy of the patients, especially those predisposed to malabsorption. At present, in our institution, we routinely use trace element ampules containing 60 μmol of zinc and 4 other elements such as copper, iron, manganese and iodide.

There exists the possibility that, with the recent increasing popularization of parenteral or enteral nutritional support, disease states caused by the deficiency of trace elements such as this may be produced increasingly. Zinc deficiency might constitute only a small visible part of the problem and therefore, it would be important in the prectice of TPN to attend to it with an adequate knowledge and with caution against development of deficiency.

Recently, the deficiency of selenium[11,12] and chromium[13] in patients on prolonged TPN over a year are reported. In keeping with the advanves in TPN, the physiological roles of zinc and various other

trace elements in man will be made increasingly clear, thus opening up, we believe, an area where both clinical and basic medical sciences can powerfully contribute to the further progress in clinical medicine.

REFERENCES

1. Dudrick, S. J., Wilmore D. W., Vars H. M. (1986): Long term total parenteral nutrition with growth in puppies and positive nitrogen balance in patients. Surg. Forum, 18, 356.
2. Okada, A., Takagi, Y., Itakura, T. *et al.* (1975): Zinc deficiency during intravenous hyperlimentation. Igaku No Ayumi (Jpn. ed.), 92, 436.
3. Okada, A., Takagi, Y., Itakura, T. *et al.* (1976): Skin lesions during intravenous hyperalimentation. Zinc deficiency. Surgery, 80, 692.
4. Kay R. G. and Tasman-Jones C. (1975): Acute zinc deficiency in man during intravenous alimentation. Aust. NZ J. Surg., 45, 325.
5. Takagi, Y. (1982): Zinc metabolism and deficiency in total parenteral nutrition. J. Jpen Surg. Soc., 83, 163.
6. Yamaji, A., Kurata, Y., Fujii, Y. *et al.* (1978): Trace elements in total parenteral nutrition solution. Igaku No Ayumi (Jpn. ed.), 105, 934.
7. Okada, A. and Takagi, Y. (1976): An importance of zinc in total parenteral nutrition solution. Jpn. J. Surg., 6, 189.
8. Freeman J. B., Steginк L. D. and Meyer P. D. (1975): Excessive urinary zinc losses during parenteral alimentation. J. Surg. Res., 18, 463.
9. O'Dell, B. L. (1974): Role of zinc protein synthesis (Introduction). in: Clinical Application of Zinc Metabolism, ed. by Pories W. J., Charles C Thomas, Springfield, IL., pp. 5.
10. Van Rij, A. M., Thomson, C. D. DcKenzie J. M. *et al.*: Selenium (1979): deficiency in total parenteral nutrition. Am. J. Clin. Nutr., 32. 2076.
11. Fleming C. R., Lie J. T., McCall, J. T. *et al.* (1982): Selenium deficiency and fatal cardiomyopathy in a patient on home parenteral nutrition. Gastroenterology, 83, 689.
12. Jeejeebhoy, K. N., Chu, R. C., Marliss, E. B. *et al.* (1977): Chromium deficiency, glucose intolerance, and neuropathy reserved by chromium supplementation, in a patient receiving longterm total parenteral nutrition. Am. J. Clin. Nutr., 30, 531.