Zinc Concentrations in Serum during Head and Neck Cancer Progression

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Abstract. *Reduced serum-zinc concentrations are well known as typical laboratory characteristics in advanced head and neck cancer. Our aim was to follow the development of this phenomenon during the disease. Patients and Methods: A total of 21 patients were included in this pilot-study (1 female, 20 male). The median age was 64 years, range 43-80 years. The following tumour localizations were registered: 11 larynx, 4 oropharynx, 2 hypopharynx and 4 other. Serum zinc levels were registered at baseline and during the follow-up investigations using flame atomic absorption spectrometry. Results: The median follow-up time was 17 months, range 6-43 months. During the follow-up, 9/21 patients died tumour-dependently, 2 patients were living with cancer, 8 patients showed NED, and a further 2 patients died of non-cancer related causes. The zinc concentration decreased from 0.76 mmol/l (0.48-1.07 mmol/l) to 0.55 mmol/l (0.32-1.01 mmol/l). Nine of 11 patients with cancer developed extremely low serum zinc concentration 4-6 weeks before dying. Conclusion: The serum zinc concentration may be a marker for definitive palliative situations in head and neck cancer patients.*

Many reports have been made regarding the relations of serum zinc and copper in malignant diseases and their influence on antioxidative systems (1). *In vivo* studies have shown the influence of zinc on the cellular growth of different tissues; a particular role was described in the regulation of apoptosis (2). Increased copper concentrations were also found in patients with solid tumours. The calculated copper-zinc ratio should have prognostic relevance in some cancer types, but as yet it has not been established as a routine clinical parameter (3). Recently we reported the status of trace elements in 100 patients with advanced head and neck cancer prior to therapy (4). Raised serum copper concentrations and reduced serum zinc levels were observed in nearly 40% of the patients studied. During radiochemotherapy no significant changes in the concentrations or the calculated copper-zinc ratio were noted (5). Figure 1 shows the observed serum concentrations before and during radiochemotherapy compared to the reference value. This study investigated the zinc serum concentration as a long-term parameter for head and neck cancer in patients.

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Patients and Methods

A total of 21 patients were included in this pilot-study (1 female, 20 male). The median age was 64 years, range 43-80 years. The following tumour localizations were registered: 11 larynx, 4 oropharynx, 2 hypopharynx, and 4 other. All patients had histologically confirmed squamous cell carcinomas of the head and neck region. Serum zinc levels were registered at baseline and during the follow-up investigations using flame atomic absorption spectrometry (Perkin Elmer Analyst 600). The measurements were performed in the clinical laboratory at the Nordhausen municipal hospital, Nordhausen, Germany.

Table I shows the detailed data for each patient (tumour, TNM, follow-up period, treatment result).

Descriptive statistics were calculated using MS Excel. Statistical differences were analyzed using Student's *t*-test for independent groups with homoscedastic variance.

Table I. *Biometric data for patients included in the study.*

No.	Gender	Age (years)	Follow-up (months)	Localization	T	N	M	Result
1	F	62	41	Glottis	3	2	0	NED
2	M	80	32	Lip	2	0	0	NED
3	M	68	35	Glottis	4	2	0	NED
4	M	43	25	Glottis	3	0	0	NED
5	M	70	17	Oropharynx	2	0	0	NED
6	M	70	17	Palate	3	0	0	NED
7	M	54	17	Glottis	3	0	0	NED
8	M	56	24	Esophagus	4	2	0	NED
9	M	71	17	Supraglottis	2	2	0	TDD
10	M	56	14	Nasopharynx	1	3	0	TDD
11	M	70	7	Hypopharynx	2	0	0	TDD
12	M	64	14	Hypopharynx	4	0	0	TID
13	M	62	18	Glottis	4	0	0	TDD
14	M	62	6	Glottis	3	2	0	TID
15	M	69	10	Glottis	4	0	0	TDD
16	M	53	12	Oropharynx	4	2	0	TDD
17	M	73	9	Oropharynx	3	2	0	TDD
18	M	64	22	Oropharynx	2	2	0	TDD
19	M	56	16	Glottis	3	2	0	TDD
20	M	70	20	Glottis	3	2	0	PD
21	M	66	43	Glottis	3	2	0	PD

TDD: tumour-dependent death, TID: tumour-independent death, PD: progressive disease, NED: no evidence of disease.

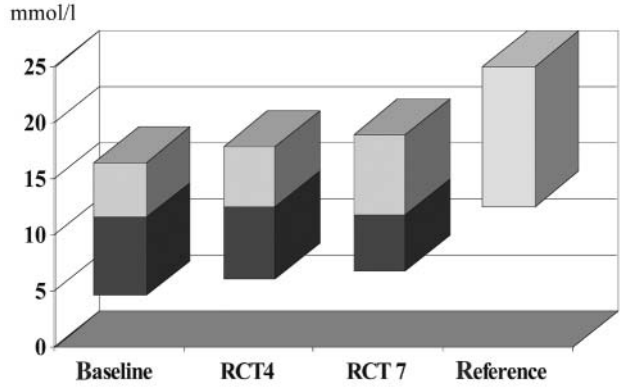

Figure 1. *Serum zinc concentrations during radiochemotherapy (RCT). RCTn: nth week of radiochemotherapy*

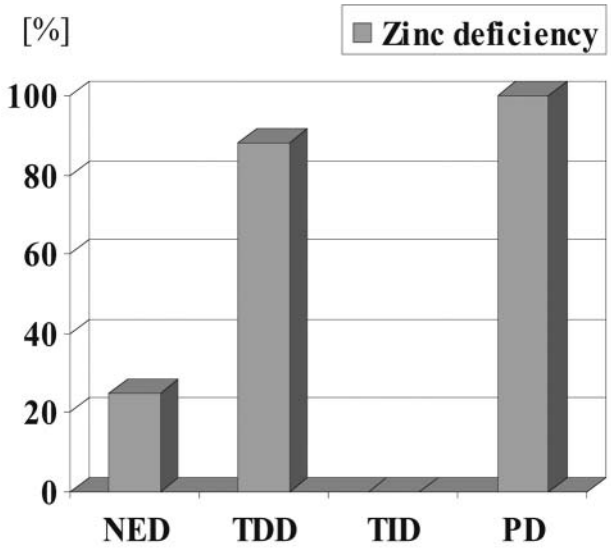

Figure 2. *The relationship between reduced serum zinc concentration and tumour status.*

Results

At the time of analysis patients 1-8 were living without any sign of tumour. Patients 9-19 died during the follow-up period, and Patients 20-21 were living with tumour and antineoplastic chemotherapy. Reduced zinc levels were found in only 2/8 patients living without cancer. In contrast, 7/11 patients who died exhibited significant reductions of endogenous serum zinc during the last weeks of their life. Patients 20 and 21 (living with cancer) were also categorized as having reduced zinc levels. These different developments are summarized in Figure 2. Overall a reduction of serum zinc concentration from an initial median of 0.765 μg/l (range 0.48-1.07 μg/l) to 0.55 μg/l (0.32-1.01 μg/l) at the end of follow-up was found. Significant reductions in serum zinc concentrations were measured in median 4 weeks before the patient's death (range 3-6 weeks).

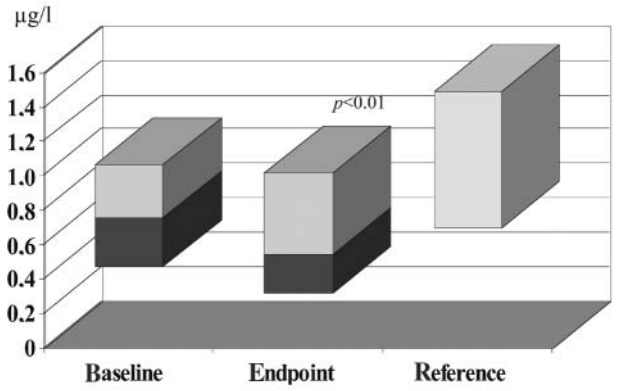

Figure 3. *Development of serum zinc concentration during the disease.*

Figure 3 shows the development of serum zinc concentration during the follow-up compared to the actual reference values used for our hospital.

Discussion

Tumors of the upper aerodigestive tract include a number of rare tumour types that account for just 3%-4% of all cancer mortality in males and about 1% in females. Viewing the statistics over time, a substantially lower mortality rate was seen in the early 1950s which began to rise sharply in the mid-1960s. This development was similar in both West and East Germany. The cancer registers for the former West and East Germany calculated similar 5-year survival rates: 36% and 41.3% for males, and 53.2% and 53.2% for females respectively (6). The situation for laryngeal cancer is completely different. It is also a rare cause of cancer mortality, accounting for only 1.5% of male cancer death. The male mortality increased, starting in the mid-1950s, and then leveled off in the early 1990s, whereas female mortality has remained almost constant during the same period. Five-year survival rates were reported of 65.4% and 55.5% for males and 75.8% and 66.4% for females for the former West and East Germany respectively (6).

Interpreting these data, we will be faced with nearly one third of our patients entering a palliative situation. It is one of the most difficult questions to decide whether no antitumour treatment should be performed in an individual. This is one of the reasons to look for parameters indicating the development of the disease or the forthcoming changes in the general apperance of individual patients. To date, there is no ideal tumour marker for patients with advanced head and neck cancer(7). SCC antigen (8, 9), CYFRA 21-1 (10) and some other markers are established and are able to detect recurrent diseases, providing they were already elevated at baseline, but we have no typical marker to help us in a palliative treatment decision. Our earlier results showed that the copper/zinc ratio is not able to give additional information about the genesis of an advanced head and neck tumour (5). Nevertheless, serum zinc levels are reduced in nearly one third of all patients suffering from cancer in this region (4). The presented preliminary data reflect a tight relationship between the rapidly decreasing serum zinc concentration and the terminal situation of our cancer patients. A patient's time-window is limited and so any additional information may be essential for both him and for the palliative care team. Additional antitumoural treatment options should be used very restrictively during this period and the main attention will be focused on symptomatic palliative care. More data are necessary to investigate this problem better and to test the described hypothesis.

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