The effect of oral β-glucan in addition to systemic chemotherapy on the leukocyte values and oral mucositis in the patients with head-neck tumors

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SUMMARY

The effect of oral β-glucan in addition to systemic chemotherapy on the leukocyte values and oral mucositis in the patients with head-neck tumors

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Int. Rev. Allergol. Clin. Immunol., 2004; Vol. 10, No. 2

The major side-effect of most anti-cancer chemotherapeutic drugs is neutropenia, and the administration of these drugs impairs blood-forming functions (e.g. the generation of neutrophils, NK cells, etc.) that are important to maintain the defense systems of the patients. As a result, chemotherapy may accelerate the risk of tumor metastases and fungal infection. An immunomodulating substance, a biological response modifier (BRM) or biotherapy is important for the treatment of cancer and infectious diseases. β-Glucan primes leukocyte CR3 for enhanced cytotoxicity and synergizes with anti-tumor monoclonal antibodies (mAb).
We studied readily the efffect of β-glucan (1,3-1,6 β-glucan) in patients with chemotherapy induced oral mucositis and leucopenia.

Key words: β-glukan, chemotherapy, oral mucositis

STRESZCZENIE

Wpływ doustnego β-glukanu w połączeniu z systemową chemioterapią na stężenie leukocytów i zapalenie śluzówki jamy ustnej u chorych z guzami głowy i szyi

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Najistotniejszym działaniem niepożądanym chemioterapii stosowanej w chorobach nowotworowych jest neutropenia. Leczenie to upośledza funkcje krwiotwórcze w organizmie (np. tworzenie neutrofilów, komórek NK etc.) mające podstawowe znaczenie dla prawidłowego działania układu odpornościowego. Chemioterapia może przyspieszać rozwój zmian przerzutowych oraz sprzyja powstawaniu zakażeń grzybiczych. Stosowanie preparatów immunostymulujących, modyfikatorów odpowiedzi biologicznej (BRM), a także bioterapia mają istotne znaczenie w leczeniu nowotworów i zakażeń. β-glukan zwiększa cytotoksyczność leukocytów CD3, ma też działanie synergistyczne z monoklonalnymi przeciwciałami przeciwnowotworowymi (mAb).
Zbadaliśmy działanie β-glukanu (1,3-1,6 β-glukanu) u chorych z leukopenią i zapaleniem śluzówki jamy ustnej indukowanymi chemioterapią.

Słowa kluczowe: β-glukan, chemioterapia, zapalenie śluzówki jamy ustnej

ß-glucan (1,3-1,6 β-glucan) is a completely natural compound which enhances the immune system. Bread yeast (*Saccharomyces cerevisiae*) which is a structural element of the cell wall is obtained by extraction (2). People under chemotherapy and radiotherapy are individuals prone to infection. Their immune system is weak. β-glucan activates white blood cells such as macrophages, neutrophiles and monocytes which are responsible for defense against infections. It stimulates hemapoetic regeneration, prevents from opportunistic infections and in addition enhances regeneration of the damaged tissues in the body (3). Macrophage proliferation increases phagocytic activity. Reinforces the immune system by increasing the synthesis of lysozymes (4, 5).

MATERIAL AND METHODS

In our study, 40 patients with head-neck tumors treated between 2000-2002 were included. Among the patients 8 had Hodgkin's lymphoma, 10 had non-Hodgkin's lymphoma, 12 had pharyngeal tumor, 5 had maxillary sinus tumor, 5 had nasopharyngeal tumor. Thirty patients underwent radiotherapy.

Equal number of patients were allocated in two groups. There were 4 female and 16 male patients (mean age, 57) in the first group and 6 female and 14 male patients (mean age, 58) in the second group. Leucocytes values were measured before chemotherapy. Three cures of chemotherapy were administered to both of the groups. Second group received oral β-glucan (10 mg/day for the patients weighing up to 60 kg's, 20 mg/day for the patients over 60 kg's) in addition to chemotherapy (Table 1, 2). No side effects was observed in any of the patients during three months.

RESULTS

Leucocytes levels were measured by cell detection by laser beam method with a Beckman Coulter Hmx hemogram device. Values between 3500-10000/mm^3 were accepted as normal. Leucocytes count (2750±631,20) after chemotherapy was significantly ($p<0.001$) lower than before chemotherapy (4305±1139). However, more limited downfall was observed (6185±1549.96 and 5820±1859.99, significance at the level of $p=0.05$) in the second group following the treatment. In comparison of the two groups, significant reduction of leucocyte s counts was observed in the group which received chemotherapy ($p<0.001$). In addition, oral mucositis secondary to chemotherapy and radiotherapy was seen more seldom in the patients who received β-glucan (grade 2 in 5 cases and grade 1 in 6 cases in group 1; grade 2 in 2 cases and grade 1 in 3 cases in group 1).

DISCUSSION AND CONCLUSION

Vervicka et al. have performed studies on the nutritional stimulation of the immune system against cancer and infection. Yeast welded 1-3 β-glucan was tested in the rats infected with bacillus anthracis. Bacillus of the anthrax has two types: edema forming and lethal toxin. Lethal toxin inhibits the phagocytosis of the neutrophils and the release of IL-1, IL-2, interferon-γ and TNF-α (6). Researchers have observed the activation of TNF-α from the macrophages and elimination of the lethal effect of the toxin following oral intake of 1-3 β-glucan (7). *Carswell* et al. have shown that 1-3 β-glucan inhibits the tumor development by increasing the proliferation of the lymphocytes, activation of the natural killer cells and

Table 1. Leucocyte values and the degree of mucositis in the patients with head-neck tumors receiving chemotherapy only

Patient's No.	Patient's age	Leucocytes values before chemotherapy	Leucocytes values after chemotherapy	Degree of mucositis
1	63	4000	2900	+
2	52	3600	2500	+
3	59	5200	3400	–
4	61	6500	4000	–
5	60	6000	3000	–
6	55	5400	3200	
7	52	4800	2600	+
8	57	3000	2000	++
9	59	2800	1500	++
10	64	3400	2600	–
11	47	3100	1900	++
12	54	5400	2800	–
13	56	3800	2600	+
14	73	4500	3000	–
15	70	4000	2800	+
16	59	3000	2200	++
17	49	4200	2100	++
18	54	4400	3200	+
19	56	6000	3900	–
20	47	3000	2800	–

Table 2. Leucocytes values and the degree of mucositis in the patients with head-neck tumors receiving chemotherapy + β-glucan (Immuneks)

Patient's No.	Patient's age	Leucocytes values before chemotherapy + β-glucan	Leucocytes values after chemotherapy + β-glucan	Degree of mucositis
1	65	5800	5000	–
2	57	4700	3200	++
3	52	6700	6000	–
4	49	7200	6700	–
5	44	3800	3500	+
6	52	4600	4000	+
7	50	7400	6800	–
8	63	9200	8000	–
9	69	7400	8500	–
10	71	5300	5000	–
11	60	5400	6200	–
12	59	6200	5000	–
13	64	8000	7200	–
14	52	3900	2500	++
15	49	3800	3200	+
16	56	5700	6000	–
17	61	6200	5700	–
18	71	6800	7500	–
19	67	8200	7800	–
20	43	7400	8600	–

macrophages and particularly synthesis of TNF-α (8). In addition, β-glucan also increases the synthesis of IL-1β. IL-1β increases the mobilization of the polymorphonuclear leucocytes from the bone marrow and their chemotactic abilities. It expedites hematopoetic recovery in the rats underwent radiation and protects against the infections during the treatment. *Sugavaza* et al. have reported stimulation of the immune system, decreased septic morbidity and increased antiviral activity in the HIV (+) patients after addition of 1-3 β-glucan to the diet (9). *Mitoni* et al. have demonstrated inhibition of tumor development, enhancement of the tumor killer activity of the macrophages, neutrophils and natural killer cells and increased release of cytokins from the Peyer's plates in the intestinal mucosa by oral β-glucan in the preclinical colonic cancer model (10). Reported studies are in accordance with ours.

In conclusion, in our opinion oral administration of β-glucan in addition to chemotherapy strengthens the immune system and improves the life quality.

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