# LEUKEMIA PATIENTS AS AN IMPORTANT MODEL FOR THE TREATMENT OF THE RADIATION SICKNESS

[1]Vladimír MĚRKA, [1]Ladislav JEBAVÝ, [1]Marie VACKOVÁ, [2]Milan BLÁHA
[1]Purkyně Military Medical Academy, Hradec Králové
[2]Clinical Haematology Ward, Teaching Hospital, Hradec Králové

Allow me to make a few historical remarks: When the first nuclear power station in Jaslovské Bohunice was put into operation, the creation of an emergency system was necessary in case of radiation accident or radiation disaster.

Our Military Medical Academy in Hradec Králové was given the task of treating radiation sickness (radiation doses above 1 Gy).

Since 1970 an emergency care center has been developed and improved. As early as 1974 the first reverse isolation system „Life Island" of US and later Czech origin was set into motion. Patients with severe bone marrow aplasia and hemoblastoses have been treated here. Special psychotherapy, artificial nutrition and microbiological surveillance have been introduced (1, 2).

Since 1976 we have been using blood-cell separators for the preparation of thrombocyte and granulocyte concentrates.

In 1976 the first allogenic bone marrow transplantation was performed.

Since 1997 a special unit for blood and bone marrow transplantation has been operating.

It can be said, that radiation sickness and its therapy is more or less connected with leukemia or other malignant diseases all over the world.

Let' s come back to the evaluation of our experiences with supportive therapy.

Protection against life-threatening infection is of essential importance for an immunocompromised patient, for example with leukemia or other malignant diseases (5, 6).

Our conception of prevention of infection is based in the framework of the supportive therapy on:

- Limitation of contact with environment,
  RI - reverse isolation, Life Island,
  Laminar air flow system (1)
- Suppression of potentially pathogenic endogenous microflora of GIT
  SD - selective decontamination (5)
- Stimulation of the hematopoiesis, repair of immune defence mechanisms
  HGF - hematopoietic growth factors,
  hematopoietic stem cells transplantation (3)

With the three above-mentioned methods reverse isolation, selective decontamination and hematopoietic growth factors we have many years experience, which we would like to outline briefly.

The first sample-group of 138 patients, only received reverse isolation (Life Island, laminar air flow system) for the prevention of infection complications. You can see the basic characteristics of this group in table 1.

Table 1

**Basic characteristics, groups of patients RI and RI+SD**

| Basic characteristics Diagnosis | Groups of patients RI (n = 138) | RI + SD (n = 208) |
|---|---|---|
| Number of males<br>females<br>Age $\bar{x}$ (min.-max.) | 83<br>55<br>41 (16-79) | 120<br>88<br>35 (16-73) |
| Acute myelogenic leukemia | 60 | 96 |
| Acute lymphatic leukemia | 13 | 21 |
| Chronic myelogenic leukemia | 5 | 10 |
| Chronic lymphatic leukemia | 3 | 4 |
| Lymphoma | 15 | 36 |
| Bone marrow aplasia | 26 | 21 |
| Myelodysplastic syndrome | 16 | 20 |

In the second group of 208 patients reverse isolation was applied for infection prevention as well as selective decontamination of GIT. In this group there are predominantly patients with acute leukemia as you can see in the table.

Selective decontamination was begun with patients who had no signs of infection in the period in which granulocytopenia below $1.0x10^9xl^{-1}$ arose or was expected and continued during the whole granulocytopenic period.

In the years 1982-1986 the treatment was usually begun with the combination: Nalidixic acid (Nalidixin), dosage 8 g/day. From 1985 instead of Nalidixin we applied Desurol, i.e. oxolinic acid, 2 g/day. As an antimycotic we used nystatin (Fungicidin), 6 mil IU/day. If the decontamination of GIT was not achieved within 10 days we changed the medication. According to the sensitivity we administered a preparation of cotrimoxazol, polymyxin B or E (Colistine), 2 mil. IU/day or neomycin (1 g/day). Fungicidin was replaced by Pimafucin or exceptionally with Nizoral.

Since 1987 we have prefered to apply fluoroquinolones, in most cases ofloxacin, Tarivid in the combination with antimycotic, in most cases fluconazol, Diflucan (4).

In the third group of 96 patients we applied all 3 types of supportive therapy, i.e. RI, SD and hematopoietic growth factors HGF. In 58 patients of this group an autologous stem cell transplantation was performed. You can see, the basic characteristics of this group in table 2.

Table 2

**Group RI + SD + HGF (n = 96)**

| | |
|---|---|
| Number of males<br>females<br>Age $\bar{x}$ (min.-max.) | 51<br>45<br>40 (16-63) |
| Acute myelogenic leukemia | 19 |
| Acute lymphatic leukemia | 8 |
| Chronic myelogenic leukemia | 3 |
| Chronic lymphatic leukemia | 2 |
| Lymphoma | 32 |
| Multiple myeloma | 22 |
| Myelodysplastic syndrome | 4 |
| Solid tumor | 6 |

We used Granulocyte - colony stimulating factor, Neupogen injection or Granulocyte macrophage - colony stimulating factor, Leucomax injection, subcutaneously or in high doses as a continuous infusion. Usual dosage: 5-10 μg/kg/day during the granulocytopenic period below $1.0x10^9xl^{-1}$. Neupogen was administered mainly in cases of acute leukemia and Leucomax in lymphoma and myeloma, myelodysplastic syndrome.

As a criterion of efficacy we used the duration of granulocytopenia and the occurrence of infection complications.

As you can see in table 3 the longest period of monitoring (=hospitalisation) and of granulocytopenia is in the group RI+SD. This can be explained by the fact that cytostatic cures were in this group almost two times more frequently given than in other groups. The lowest number of days with granulocytopenia was observed statistically significantly in the group with HGF.

As far as the infection complications are concerned one of the basic signs of the beginning of infection is usually fever. The lowest number of days with fever is in the group with HGF (tab. 4).

As for infection the best results are observed in the group with HGF. The number of infection episodes and their duration decreases in combined supportive therapy by one third to one half. The decreased occurrence of infection complications in the group with HGF is accompanied by a reduced number of days with systemic administered antibiotics (tab. 4).

Table 3

**Characteristics of patients during granulocytopenia <1.0 x $10^9$x $l^{-1}$**

| Basic characteristics | Groups of patients | | |
|---|---|---|---|
| | RI (n = 138) | RI+SD (n = 208) | RI + SD + HGF (n = 96) |
| Total period of monitoring (days) | 4693 | 10 192 | x)2208 |
| $\bar{x}$ (min.-max.) | 34 (8-83) | 49 (13-260) | 23 (8-68) |
| Duration of granulocytopenia < 1.0x$10^9$x$l^{-1}$ total days | 3174 | 7072 | x)1056 |
| $\bar{x}$ (min.-max.) | 23 (5-77) | 34 (4-249) | 11 (5-26) |
| Number of days with granulocytopenia /100 days | 68 | 69 | 48 |

x) p<0.001

Table 4

**Occurrence of infection complications**

| Evaluated characteristics | Groups of patients | | |
|---|---|---|---|
| | RI (n = 138) | RI + SD (n = 208) | RI + SD + HGF (n = 96) |
| Number of days with fever >38 °C/100 days, $\bar{x}$ SEM | 39 ± 29 | 23 ± 22 | 17 ± 14 |
| | p < 0.01 | | |
| Number of patients with infection | 72 (52%) | 79 (38%) | 28 (29%) |
| Number of infection episodes/100 days, $\bar{x}$, SEM | 7 ± 4 | 5 ± 3 | 2.5 ± 1.0 |
| Number of days with infection/100 days, $\bar{x}$, SEM | 66 ± 29 | 40 ± 21 | 26 ± 11 |
| | p < 0.001 | | |
| Number of days with ATB /100 days, $\bar{x}$, SEM | 63 ± 31 | 30 ± 19 | 27 ± 12 |
| | p < 0.001 | | |

## Conclusion

Our results show the advantages of the supportive therapy combination:

- Reverse isolation protects the patient against potentially pathogenic exogenous microflora.
- Selective decontamination suppresses potentially pathogenic endogenous microflora.
- Hematopoietic growth factors stimulate hematopoiesis and the functional state of mature phagocytic cells.
- Occurrence of infection complications decreases.
- A better clinical state allows for a more intensive treatment of the basic disease.

Our experiences obtained during the treatment of some malignant diseases can be successfully used in the therapy of victims of a radiation accident. In a case of a total war it would be hardly possible.

### Literature


1. BLÁHA, M. - MĚRKA, V.: Prevention of infection complications in immunocompromised patients. Part I. Reverse isolation. In *Sbor. věd. Prací LF UK HK*. Hradec Králové, LF UK HK, 1988, vol. 31, no. 4, p. 299-341.
2. BLÁHA, M., et al.: Metoda odwrotnej izolacji w srodowisku aseptycznym w leczeniu osób napromienionych Probl. Med. nukl., 1989, vol. 3, no. 1, p. 1-7.
3. FILIP, S. - BLÁHA, M.: Monitorování terapeutického efektu hemopoetických růstových faktorů u nemocných po cytostatické léčbě. Voj. zdrav. Listy, 1994, roč. 63, č. 3/4, s. 83-92.
4. JEBAVÝ, L., et al.: Selektive Dekontamination mit Chinolonen zur Infektionsverhütung bei Patienten mit Granulozytopenie. Hyg. Med., 1993, vol. 18, no. 10, p. 439-446.
5. MĚRKA, V. - BLÁHA, M.: Prevention of infection complications in immunocompromised patients. Part II. Selective decontamination. In *Sbor. věd. Prací LF UK HK*. Hradec Králové, LF UK HK, 1989, vol. 32, no. 4, p. 357-384.
6. MĚRKA, V. - JEBAVÝ, L.: Opyt selektivnoj dekontaminacii kišečnika. Ž. Mikrobiol. (Moskva), 1991, no. 2, p. 30-32.


Correspondence: Doc. RNDr. Vladimír Měrka, CSc.
Vojenská lékařská akademie J. E. Purkyně
Třebešská 1575
500 01 Hradec Králové

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