

AUTOLOGOUS STEM-CELL TRANSPLANTATION IN PATIENTS WITH MULTIPLE MYELOMA

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Abstract: *Background* – Multiple myeloma is a malignant plasma-cell proliferative disorder, the second most common haematologic cancer. Treatment with high-dose therapy (HDT) and single autologous stem cell transplantation (ASCT) is a category I recommendation of the National Comprehensive Cancer Network. Double transplantation can be proposed for patients failing to achieve a very good partial response (VGPR) after a first ASCT.

Aims – The aim of this study is to analyse the effect of treatment with high-dose chemotherapy and autologous stem-cell support on survival in patients with multiple myeloma, and to compare our results with the results from other transplant centres.

Material and methods – during a 7-year period we have performed 20 high-dose chemotherapy courses and autologous stem-cell transplantation on 17 patients (3 tandem transplantations) with multiple myeloma. In this trial we retrospectively analysed the epidemiology characteristics of these patients. Female: 9 Male – 8. Median age: 53 years (from 43–64 years).

Results: diagnosis was made according to Salmon and Durie criteria. High-dose regimen consisted of Melphalan doses of 200mg/m². In tandem transplantations the dose of the second high-dose regimen was 140mg/m². The volume of CD34+ cells was approximately 3.8 × 10⁸/Kg.bw. In 3 patients we used phlebotomy as a source of added stem cells. The period from diagnosis to transplantation was 12 months. Of 17 patients 70% are alive, 5 have died (3 renal failure, 1 fatal cerebral bleeding and 1 with multiorgan failure). The disease-free survival was 22 months in our group of patients. Overall survival was 48 months and survival after transplantation was 35 months. The probability of 7 years' overall survival exists in 50% of patients.

Conclusion: Patients treated with high-dose chemotherapy followed by autologous stem-cell support have a better survival and quality of life compared with patients treated with standard chemotherapy.

Key words: multiple myeloma; autologous stem cell transplantation.

Background

Multiple myeloma is a malignant plasma cell proliferative disorder [1]. Malignant clonal expansion of plasma cells can be expressed as multiple myeloma, plasma cell leukemia, solitary plasmacytoma, extramedullary plasmacytoma, macroglobulinaemia Waldenstrom, and heavy chain disease. Relatively benign plasma cell proliferation can be expressed as primary amyloidosis, or POEMS syndrome. The incidence of myeloma is 4–5 cases of 100,000 per year and 1% of all malignant diseases in humans [2]. Multiple myeloma is the second most common haematological cancer. The median age of appearance of the disease is 69 years in males and 71 in females [3]. The diagnostic criteria according to Salmon and Durie are usually used for establishing the diagnosis [4]. The prognosis of the disease is in close relation with the initial stadium, beta-2 microglobulin and albumin level at the presentation. A bad prognosis is associated with partial or complete deletion of chromosome 13. For many years, melphalan prednisone had remained the standard therapy for this disease. Response rates with this therapy are approximately 50% and median survival is approximately 3 years. Recently, autologous stem cell transplantation has been shown to be effective in treatment of multiple myeloma in randomized clinical trials [4, 5]. Patients eligible for stem-cell transplantation typically avoid alkylator-based induction therapy to enable adequate and safe stem-cell collection early in the course of the disease. Vincristine, doxorubicin and dexamethason (VAD) have been used as pretransplantation induction therapy for patients who are considered candidates for stem-cell transplantation. [6] Treatment with high-dose therapy (HDT) and single autologous transplantation is a category I recommendation of the National Comprehensive Cancer Network. In young patients, the impact of dose intensity has been demonstrated, and single HDT supported with autologous stem-cell transplantation (ASCT) using a conditioning regimen with Melphalan alone (without total body irradiation-TBI) should be considered as a standard of care. [7] Double transplantation can be proposed to patients failing to achieve a very good partial response (VGPR) after a first ASCT, ideally as part of a clinical trial. [8, 9, 10] Furthermore, the introduction of new drugs in the high-dose strategy (induction, HDT, consolidation and maintenance) appears dramatically to improve the complete remission (CR) rate (up to 70% to 80% can be expected) and response duration. [11, 12, 13] Conversely, different stu-

dies have reported that the combination of chemotherapy plus new drugs can induce 70% to 90% partial response (PR) and 30% to 40% CR. [14, 15, 16] Thus, new prospective trials are required to compare new drugs plus conventional chemotherapy versus new drugs plus HDT/ASCT. The introduction of novel agents such as thalidomide (THAL), bortezomib or lenalidomide in the high-dose therapy strategy is logical and has been actively investigated to try to improve the quality of response [17, 18, 19].

Aims

The aim of this study is to analyse the effect of the treatment with high-dose chemotherapy and autologous stem-cell support on survival in patients with multiple myeloma, and to compare our results with the results from other transplant centres.

Material and Method

Over a 7-year period, from September 2000 to March 2008, at the Department of Haematology, Medical Faculty, Skopje 130 stem-cell transplantations were performed on various hematological malignancies. (AML: 70 ALL: 5 CML: 7 CLL: 1 NHL: 13 HD: 12 MM: 20 Myelofibrosis: 1 Ewing sarcoma: 1.) Allogeneic transplantation from HLA identical sibling: 40; Autologous transplantation: 90 patients. As a source of stem cells, peripheral blood was used in 100 transplantations, and bone marrow in 30. In 17 patients with multiple myeloma 20 high dose chemotherapy and autologous stem-cell support (3 tandem transplantations) were performed. In this trial we retrospectively analysed the epidemiological characteristics of patients with multiple myeloma treated with these therapeutic options. All patients were treated in a sterile room conditioned with HEPA filters. The high-dose regimen consisted 200mg./m² Melphalan. In the second transplantation (tandem transplantations) the dose of Melphalan was 140mg./m².

Table 1 – Табела 1

Epidemiological and clinical data on patients Епидемиолошки и клинички податоци за пациентите

| Patient | Age | Gender | Ig | B.J. | Chr. renal failure | Fracture | Ro.Th | Months Dg./ Tx | A/D months |
|---------|-----|--------|-----|----------|--------------------|----------|-------|----------------|------------|
| A.V. | 64 | M | IgG | Negative | no | Th12/L1 | yes | 6 | A = 62 |
| T.S. | 45 | F | IgG | Negative | no | no | no | 4 | A = 66 |
| N.V.1 | 43 | M | IgG | Negative | no | Th12/L1 | yes | 5 | A = 31 |

| Patient | Age | Gender | Ig | B.J. | Chr. renal failure | Fracture | Ro.Th | Months Dg./ Tx | A/D months |
|---------|-----|--------|------|----------|--------------------|----------|-------|----------------|------------|
| M.M. | 47 | M | Kapa | Positive | yes | no | no | 4 | A = 45 |
| V.Z.1 | 53 | F | IgG | Negative | no | hip | yes | 11 | A = 28 |
| V.Z.2 | 53 | F | IgG | Negative | no | hip | yes | 17 | A = 34 |
| G.Z.1 | 51 | F | IgG | Positive | no | no | no | 7 | A = 33 |
| G.Z.2 | 51 | F | IgG | Positive | no | no | no | 10 | A = 36 |
| S.J. | 46 | F | IgG | Negative | no | no | no | 5 | A = 72 |
| P.N. | 60 | F | IgA | Negative | no | no | no | 12 | A = 42 |
| A.C. | 57 | F | IgG | Negative | no | no | no | 44 | A = 117 |
| B.J. | 60 | M | IgA | Negative | no | L1 | yes | 6 | A = 30 |
| Z.S. | 59 | M | IgG | Negative | no | no | no | 12 | A = 30 |
| A.Dz. | 50 | M | IgG | Negative | no | L2 | yes | 22 | A = 45 |
| N.V.2 | 43 | M | IgG | Negative | no | Th12/L1 | yes | 8 | A = 39 |
| D.K. | 63 | M | IgG | Negative | no | no | no | 20 | D = 45 |
| Di.Ko. | 46 | M | IgG | Negative | no | no | no | 8 | D = 36 |
| T.K. | 42 | F | IgG | Negative | no | Th-12 | yes | 15 | D = 44 |
| D.L. | 52 | F | IgG | Positive | yes | L2 | yes | 22 | D = 36 |
| A.L. | 56 | F | IgG | Positive | yes | no | no | 8 | D = 54 |

Table 2 – Табела 2

Epidemiological and clinical data on patients
Епидемиолошки и клинички податоци за пациентите

| | |
|------------------------------------|--|
| Number of patients | 17 |
| Number of transplantations | 20 (3 tandem transplantation) |
| Age | 53 years (43-64 years) |
| Gender | Male = 8 (47%) Female = 9 (53%) |
| Myeloma types | IgG = 14 (82%) IgA = 2 (12%) Light chain disease = 1 (6%) |
| Bence-Jones proteinuria | 5 (25%) |
| Creatinin > 110mmol/L. | 4 (23.5%) |
| Lytyc bone lesion | 13 (76.5%) |
| Pathological fracture | 7 patients: Spine = 5 Hip = 2 |
| Induction of remission | VAD = 10 (58%) VAD + Thalidomide/Dexameth.= 5(30%) VAD + Thal/Dex + Bortezomib = 2 (12%) |
| Previous radiotherapy | 7 (41%) |
| Period from Dg. to Transplantation | 12.4 months (4-44 months) |

We analyzed 17 patients with multiple myeloma. Females: 9 Males: 8. Median age: 53 years (from 43–64 years). The diagnosis was made according to Salmon and Durie diagnostic criteria. According to monoclonal proliferation, the patients had these types of myelomas: IgG: 14 patients, IgA: 2, Kappa light chain disease: 1. Osteolytic bone lesions were diagnosed at the presentation in 13 patients. Fracture of the spine: 5; hip fracture: 2 patients. Radiotherapy prior to transplantation was conducted in 7 (41%) of patients. Bence-Jones positive myelomas were diagnosed in 4 patients. Renal failure with creatinin level > 110mmol/L was presented in 4 patients. The standard chemotherapy regimen for the induction of remission in our Clinic is VAD protocol (Vincristin, Adriamycin, Dexamethason) – 4 cycles. Patients who achieved complete remission received Endoxan 2gr./m² and G-CSF for peripheral stem cell mobilization and harvesting. Non-responders received Thalidomide+Dexamethason as a second-line chemotherapy for a 5-month period. As a third-line therapy we used Bortezomib (Velcade). The median period from diagnosis to transplantation in our group of patients was 12.4 months (from 4–44 months). For harvesting an adequate number of CD34+ cells we usually performed 2 (1–3) apheresis procedures. A Baxter CS 3000 cell separator was used in 32 procedures and a Cobe-Spectra in 8 procedures. DMSO (dymethylsulphoxid) and autologous plasma were used as a cryoprotectant. The cryopreservation of stem cells was performed using a controlled Air Space Freezing system. Cryopreserved stem cells were stored at a temperature of -172 C⁰. The high-dose chemotherapy with 200mg/m² Melpalan was administered on day -2 and -1 in 30-minute infusions. 24 hours after chemotherapy was completed the autologous stem cells were towed in a sterile bath and reinfused into the patient. As an anti-infective prophylaxis patients received 500mg Cyprofloxacin, 200mg Fluconazole, 600mg Acyclovir. As VOD (veno-occlusive disease) prophylaxis low weight Heparin and Vitamin K were administered. During a period of deep neutropenia (from day +5 until neutrophil count recovery) we introduce G-CSF (granulocyte colony stimulating factor). Every patient received intravenous biphosphonates after transplantation every 28 days over a 2-year period.

Results

High-dose therapy with stem cell support was performed on 17 patients. A second transplantation was performed on 3 patients (at a period of 6 months after the first one). The dose of Melpalan was 200mg/m² in the first, and 140mg/m² in the second transplantation. The median number of reinfused stem cells was 3.8×10^8 /Kg. b.w. (from 2.1 – 12.5). Because of lack of mobilization of a sufficient number of stem cells, we added peripheral stem cells with phlebotomy for 3 patients. The median number of reinfused cells in these cases was 2.4×10^8 /Kg.b.w. CD34+ cells. Engraftment was established on day +11 (from day +7 to day +14). The median days with G-CSF was 10 days (from 7–14

days). During a period of deep aplasia there was a need for blood product support in 12 transplantations. The median need for blood transfusion was 2 doses (from 0–6), and platelet transfusion 10 doses (from 0–50). During the first 30 days we had only a few infective complications. The most common complication after transplantation was mucositis, gr. IV in 4 patients, central venous catheter infections with coagulaza negative staphylococcus in 4 patients, and cystitis in 2 patients. There were no serious complications or fatal outcome during the first 30 days after transplantation.

Table 3 – Табела 3

Data on transplants
Податоци за трансплантациите

| | |
|---|---|
| High-dose chemotherapy | Melphalan 200mg/m ² = 17 patients Mel 200 + Mel 140mg/m ² = 3 patients |
| CD34 + cells from peripheral blood | 3.8 × 10 ⁸ /Kg.bw (2.1 – 12.5) |
| CD34 + cells from peripheral blood + phlebotomy | 2.4 × 10 ⁸ /Kg.bw (in 3 patients) |
| Engraftment | Day +11 (day + 7 – day + 14) |
| G-CSF | 10 days |
| Blood transfusion | 2 (0–6) |
| Platelets transfusion | 10 (0–50) |
| Infective complications | 10 patients-Central venous catheter = 4 Cystitis = 2 Mucositis gr IV = 4 |

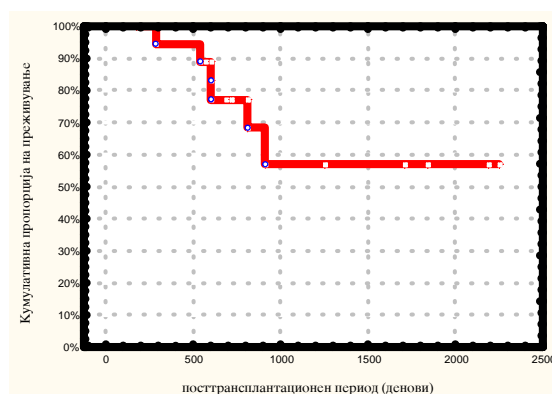


Figure 4 – Cumulative proportion of survival in patients with multiple myeloma treated with autologous transplantation of peripheral blood-cells at the Haematology Clinic in the period 2000–2008

Слика 4 – Кумулативна пропорција на преживување (OS – overall survival) кај болните со мултиплен миелом лекувани на Клиниката за хематологија во периодот 2000–2008 год. со автолошка трансплантација на периферни матични клетки

In an observation period of 3–96 months (median 48 months) survival was 68.42%, and there were 31.58% deaths. 90% of the patients were alive for 2 years, 70% for 3 years and 50% alive for 7 years.

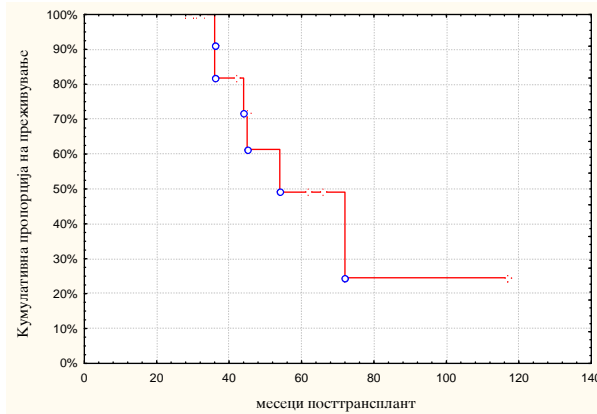


Figure 2 – Cumulative proportion of survival in patients with multiple myeloma treated with autologous transplantation of peripheral stem-cells at the Haematology Clinic in the period 2000–2008 from diagnosis to death

Слика 2 – Кумулативна пропорција на преживување кај болниите со мултиплиен миелом лекувани на Клиниката за хематологија во периодот 2000–2008 год. со аутолошка трансплантација на периферни матични клетки од дијагноза до настапување на смртен исход

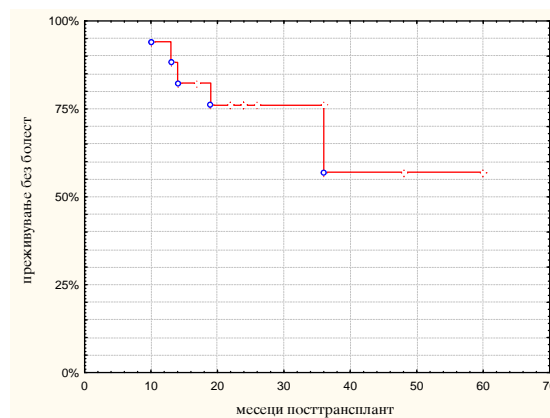


Figure 3 – Disease-free survival of patients with multiple myeloma treated with autologous transplantation of peripheral stem-cells (ATPSC) at the Haematology clinic in the period 2000–2008

Слика 3 – Преживување без болест кај болниите со мултиплиен миелом лекувани на Клиниката за хематологија во периодот 2000–2008 год. со аутолошка трансплантација на периферни матични клетки (АТПМК)

In 75% of the patients a relapse of the basic disease occurred 24 months after the transplantation.

Discussion

Multiple myeloma (MM) is one of the key haematologic malignancies in which the impact of dose intensity has been demonstrated. Consequently, in 2005, MM was the most common disease for which autologous stem cell transplantation (ASCT) was indicated both in Europe and in the U.S. However, ASCT is not curative, and most patients relapse within a median of 3 years. The Intergroupe Francophone du Myelome (IFM) was the first to demonstrate in a randomized trial the superiority of high-dose therapy (HDT) supported by autologous bone marrow transplantation (BMT) compared with conventional chemotherapy (CC) for multiple myeloma (MM). In this IFM 90 trial, HDT significantly increased the complete remission (CR) rate, the event-free survival (EFS) and the overall survival (OS) in patients with newly diagnosed MM up to the age of 65 years. [21] Following this publication, similar randomized trials have been reported. Three trials (including the IFM 90 trial) used a conditioning regimen without or with low-dose total body irradiation (TBI) [22, 23, 24]. HDT was found to improve OS in these three studies. High-dose TBI or high-dose busulfan was used in three other studies, and none of these studies reported a survival benefit of HDT.

In the IFM 90 trial, achievement of at least a very good partial remission (> 90% reduction of the M-component) correlated significantly with longer survival. This suggests that in MM, as in other haematologic malignancies, the primary objective of induction and consolidation therapy should be to achieve CR. Barlogie and colleagues in Arkansas reported that one approach to increasing the CR rate was to repeat intensive treatments. [25] The IFM conducted a randomized trial (IFM 94) comparing single and double ASCT. [26] In this study, 399 previously untreated patients younger than 60 years old were randomly assigned to undergo either a single ASCT prepared by melphalan 140 mg/m² (Mel 140) plus TBI or a double ASCT, the first being prepared by Mel 140 and the second by Mel 140 plus TBI. On an intention-to-treat basis, CR or very good partial remission was achieved by 42% of patients in the single-ASCT group versus 50% in the double-ASCT group ($P = 0.10$). The probability of 7-year EFS was 10% versus 20% ($P = 0.03$), and the probability of 7-year OS was 42% versus 21%, respectively. However, the survival benefit of double transplantation was only observed among patients failing to achieve a very good partial response after the first transplantation. On the other hand, patients already in very good partial response after the first transplantation did not significantly benefit from the second one. Similar randomized trials comparing single versus

double ASCT have been reported. [27, 28]. Three out of these 5 studies (including the IFM 94 trial) have reported a survival benefit in favour of tandem transplantation, although 2 did not. [29, 30] Thus, double transplantation can be proposed to young patients failing to achieve a very good response after a single transplantation as a potential treatment option, with participation in a clinical trial.

The introduction of novel agents such as thalidomide (THAL), bortezomib or lenalidomide in the HDT is logical and has been actively investigated to try to improve the quality of response: [1] the induction therapy, [2] HDT, and [3] maintenance therapy after ASCT. Thalidomide has shown significant single agent activity in relapsed and refractory multiple myeloma. In combination with dexamethasone, response rates increase to approximately 50% in relapsed refractory disease. The combination of thalidomide plus dexamethasone (Thal/Dex) has also shown high activity in newly diagnosed myeloma. (Three phase II clinical trials) responses rates range from 65% to 70% which are comparable to those obtained with VAD. Thal/Dex has the advantage of being an oral regimen without the neurotoxicity, cardiotoxicity, alopecia and other complications related to infusional VAD. However, in the last several years, different studies have reported that the association of DEX plus new drugs significantly improves the response rate before ASCT. The association of THAL and DEX has been extensively investigated. In a matched case-control analysis, Cavo *et al.* reported 52% of partial response (PR) including 8% CR after VAD, versus 76% PR, including 10% CR after DEX-THAL ($P < .001$).

The association of bortezomib and dexamethasone has been evaluated in a pilot study of the Intergroupe Francophone du Myélome, and they found that this combination could induce a remarkable 67% PR, including 21% CR with DEX-bortezomib. This association has been compared to VAD in a large phase 3 trial (IFM 2005 01 trial). The first analysis of this protocol reported 82% PR, including 43% CR with DEX-bortezomib, versus 67% PR, including 26% CR with VAD. The association of lenalidomide and DEX has been evaluated in a small pilot study (31 patients), and Rajkumar *et al.* (30) reported an unprecedented 91% PR, including 32% CR or near-CR. Thus, although randomized trials are still ongoing, it is reasonable to expect these new drugs with DEX will increase the PR and CR rate before HDT as compared with VAD.

In MM, the standard HDT is single-agent Mel at a dosage of 200 mg/m². Attempts to improve this regimen with conventional drugs or TBI have failed to improve the response rate but have increased both haematologic and nonhaematologic toxicities. A synergistic effect between bortezomib and melphalan has been demonstrated. Furthermore, the toxicity of these two drugs is different. Thus, the combination of bortezomib and HDM is a logical approach to study. Thirty-five patients with poor-risk features (defined as failing to achi-

eve PR after induction therapy [n = 26] or failing to achieve a very good partial response [VGPR] after a first transplant [n = 9]) were enrolled. Three months after ASCT, a dramatic ORR of 63% VGPR, including 31% of true CR, was observed. Furthermore, 6 of 9 patients failing to achieve VGPR after the first ASCT prepared with Mel alone achieved CR (n = 4) or VGPR (n = 2) with this combination. Thus, this study suggests that the combination of bortezomib and melphalan could substantially improve the VGPR rate compared with melphalan alone without additive toxicity.

The role of maintenance therapy in MM remains an area for active investigation. Maintenance chemotherapy has failed to demonstrate any benefit. Most randomized studies and meta-analyses evaluating maintenance interferon showed a modest increase in progression-free survival (PFS) with minimal or no survival benefit after conventional therapy or HDT, and added toxicity. Corticosteroid maintenance was found to prolong the duration of response; however, the impact on survival has been modest. [31] THAL is an oral agent with immunomodulatory properties, which is active in one-third of patients with refractory disease at doses as low as 50 mg and without myelosuppressive toxicity. Thus, THAL was an attractive candidate for use in maintenance situations, particularly after HDT.

Allogeneic stem cell transplantation (SCT) was introduced in the treatment of MM 25 years ago. However, toxicity was excessively high, with a transplant-related mortality (TRM) in excess of 50% in studies including heavily pretreated patients. [32, 33, 34, 35]. As a consequence of this prohibitive toxicity, allogeneic SCT could not be proposed to patients older than 50 to 55 years while the median age at diagnosis for patients with MM is 65, and only a small minority of younger patients had an HLA-identical sibling and could be considered eligible for this approach.

Long-term follow-up of patients treated with myeloablative allogeneic SCT has shown a plateau of EFS and OS curves after 4 to 5 years in the minority of patients who survive the early post-transplantation period. [36]. This plateau has been attributed to the immunological effect of donor lymphoid cells, the so-called graft-versus-myeloma (GVM) effect. Proof of this GVM effect was supported by remissions obtained by following donor lymphocyte infusions (DLI) in patients relapsing after allogeneic BMT. This antitumour effect of donor immunocompetent cells is the basis of the introduction of reduced-intensity conditioning (RIC) allogeneic SCT in MM, in which the underlying principle is to reduce transplantation-related toxicity while harnessing the GVM effect. However, up-front single autologous transplantation followed by 6 months of maintenance therapy with thalidomide (with a second transplant in reserve for relapse or progression) is an effective therapeutic strategy to treat multiple myeloma patients and appears superior to tandem transplant in this setting [37].

Conclusion

High-dose chemotherapy supported by haemopoietic stem cell rescue is an effective therapeutic strategy to treat multiple myeloma patients and appears superior to standard chemotherapy. Our statistical analysis clearly showed the positive influence of this method on better survival in patients with multiple myeloma. Compared with other transplant centres survival in our group of patients was better.

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Резиме

АВТОЛОГНА ТРАНСПЛАНТАЦИЈА НА МАТИЧНИ ХЕМАТОПОЕТСКИ КЛЕТКИ КАЈ ПАЦИЕНТИ СО МУЛТИПЕН МИЕЛОМ

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Апстракт: *Вовед* – мултипниот миелом е малигна плазма-клеточна пролиферација. Тоа е второ по честота хематолошко малигно заболување. Високо-дозната хемиотерапија (ВДХ) и единечна автологна стем клеточна трансплантација (АСКТ) денес е категорија бр. 1 за третман на мултипниот миелом, според препораките на националната мрежа за карциноми. Тандем трансплантација може да биде препорачана за пациентите кои не успеале да постигнат ниту парцијален одговор по првата АСКТ.

Цел на трудот – да се прикажат резултатите од третманот на пациенти со мултипен миелом со високо-дозна хемиотерапија и АСКТ и влијанието на овој тип на лекување врз преживувањето.

Материјал и методи – Во текот на 7-годишен период на Клиниката за хематологија при Медицинскиот факултет во Скопје кај 17 пациенти со мултипен миелом, спроведени се 20 процедури на високо-дозна хемиотерапија поддржани со АСКТ (3 тандем трансплантации). Во оваа студија ретроспективно ги анализираме карактеристиките на овие пациенти, жени = 9, мажи = 8, средна возраст 53 години (43–64). Дијагнозата мултипен миелом е поставена согласно критериумите на Салмон и Дјури.

Резултати – Високо-дозниот протокол содржеше Мелфалан $200\text{mg}/\text{m}^2$. Во тандем трансплантациите дозата на вториот високо дозен режим содржеше Мелфалан $140\text{mg}/\text{m}^2$. Количината на $\text{CD}34^+$ клетки е $3,8 \times 10^6/\text{kgTT}$. Кај 3 пациенти употребивме флеботомија како дополнителен извор на стем клетки. Периодот од дијагноза до трансплантација изнесува 12 месеци. Од 17 пациенти, 12 (70%) се живи, 5 (30%) се починати (3 од бубрежна инсуфициенција, 1 церебрална хеморагија, 1 мултиорганска слабост заради сепса). Периодот од трансплантација до релапс изнесува средно 22 месеци. Вкупното преживување од поставување на дијагнозата изнесува 48 месеци, а преживување по трансплантација е 35 месеци. Кај 50% од пациентите се предвидува 7-годишно преживување.

Заклучок – употребата на автологната трансплантација на матични хематопоеетски клетки значително го подобрува преживувањето и квалитетот на живот кај пациентите со мултипен миелом споредено со стандардната хемиотерапија.

Клучни зборови: мултипен миелом, автологна трансплантација на матични клетки.

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