Autologous Hematopoietic Stem Cell Transplantation in patients with high risk Neuroblastoma treated with/without Metaiodobenzylguanidine

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History of Stem Cell Transplantation in HORCSCT

The Hematology-Oncology Research Center and Stem Cell Transplantation (HORCSCT) is affiliated to Tehran University of Medical Sciences (TUMS), Tehran, Iran.

The Center was founded in 1991 by Professor Ghavamzadeh, who is currently the Center director.
Since 2007 one of SCT wards specialized to children which named Pediatric SCT ward. It had 7 active beds at first, now has 11 active beds.
Pediatric SCT Unit

- HORCSCT is among the most prominent stem cell transplantation centers in the world, with more than 400 transplantations performed per year.

- EACH YEAR MORE THAN 110 HSCT IN PEDIATRIC
From the first days of its activity, it was possible to perform transplantation of all the

- Malignant hematologic diseases
- Non-malignant hematologic diseases
- Solid tumors
- Primary Immunodeficiencies
- Metabolic diseases
Pediatric SCT Unit

- Now in addition, even transplantation of infants less than 4 months is being performed in this section.
Pediatric SCT Unit

Between 1991 and July 2013
Total: 1160 patients
   691 boys, 469 girls
<15 year old
Median age = 8 years (4 months -15 years)
Mean age = 8 ± 4.4
Pediatric HSCT in IRAN from 1991 till December 2012
Pediatric HSCT in IRAN from 1991 till December
By Graft

- Allogeneic 1028 (88.6%)
- Autologous 129 (11.1%)
- Syngenic
By Disease

- Leukemias: 28%
- PID: 5%
- Lymphomas: 2%
- Inborn errors of Metabolism: 3%
- BMF’s: 12%
- Solid Tumors: 4%
- Histiocytic disorders: 0%
- Inherited abnormalities of RBC: 46%
By Disease

- Inherited abnormalities of RBC  531
- Leukemias and lymphomas  343
- Bone Marrow Failure syndrom  144
- Primary Immunodeficiencies  60
- Solid Tumors  44
- Inborn Errors of Metabolism  38
Solid Tumors

- 44 (3.7%)
Introduction

- Neuroblastoma is the most common extracranial, solid tumor in children

- Accounting for 8% to 10% of all childhood cancers.

- Approximately 70% of patients have metastatic disease at diagnosis.
Risk-based Neuroblastoma Treatment Plan

1. Age at diagnosis
2. Clinical stage of disease
3. Tumor histology
4. Presence of the N-myc

- Risk-based treatment plan assigns each patient to a low-risk, intermediate-risk or high-risk group.
<table>
<thead>
<tr>
<th>Risk category</th>
<th>Description</th>
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| **Low risk**  | • stage 1 disease  
|               | • stages 2A and 2B, except for a child age one or older with MYCN amplification and unfavorable histology  
|               | • stage 4S with no MYCN amplification, favorable histology, and hyperdiploid |
| **Intermediate risk** | • stage 3, age less than one year and no MYCN amplification  
|               | • stage 3, age one or older with no MYCN amplification and favorable histology  
|               | • stage 4, age less than one year with no MYCN amplification  
|               | • stage 4S with no MYCN amplification, unfavorable histology, and/or diploid |
| **High risk** | • stages 2A and 2B, age one or older, MYCN amplification and unfavorable histology  
|               | • stage 3 with MYCN amplification  
|               | • stage 3, age one or older, no MYCN amplification and unfavorable histology  
|               | • stage 4, age one or older  
|               | • stage 4, age less than one year with MYCN amplification  
|               | • stage 4S with MYCN amplification |
Autologous Hematopoietic Stem Cell Transplantation (HSCT)

- According to the NCI (2008), autologous HSCT is listed as a standard treatment option for individuals classified as having high-risk disease.

- Berthold, 2005; Matthay, 1999; Ladenstein, 2008; Zage, 2008; Trahair, 2007; Vedeguer, 2004
The aim of this study is to compare two main strategies of auto-HSCT for patients with high risk Neuroblastoma:

1. Auto-HSCT alone in patients with negative diagnostic MIBG
2. Auto-HSCT with therapeutic MIBG before HSCT in patients with positive diagnostic MIBG.
Methods

- We prospectively analyzed the outcome of 20 patients (9 girls, 7 boys) with high risk Neuroblastoma who had undergone auto-HSCT between May 2007 and December 2012.

- Median age at transplantation was 5.1 years.
Methods

- According to the results of diagnostic MIBG, patients were divided into two groups:
  MIBG-avid (n=10)
  non MIBG-avid (n=10)

- MIBG-avid patients received 131I-MIBG (12mci/kg) on day 21 before transplantation.
Methods

- The conditioning regimen used in all patients consisted of

1. Etoposide
2. Carboplatin
3. Melphalan
Methods

- Patients received 13-cis-retinoic-Acid 120-160 mg/m²/2 weeks per month, as maintenance from day sixty after HSCT until one year later.
MIBG-avid patients received 131I-MIBG (12mci/kg) on day 21 before transplantation.
Non-MIBG-avid versus MIBG-avid?

MIBG-avid

BMT

non MIBG-avid
Results

• Engraftment occurred in all patients.

• No severe side effects were observed in any patients in MIBG-avid group.
Results

- Patient age at diagnosis and transplant, diagnosis to transplant interval did not significantly associate with the outcome.

- Moreover patient sex, Shimada classification, N- MYC amplification and Pre-MIBG scan scores did not predict survival of patients.
Results

• The median time to neutrophil engraftment after ASCT was 10 days (range, 9-13 days) in MIBG avid and 11 days (range, 9-13 days) in MIBG non-avid subgroups.

• The median time to platelet engraftment was 13 days (range, 10-20 days) in MIBG avid cases and 12 days (range, 9-13 days) in MIBG-non-avid patients.
Results

- In MIBG avid patients, 3-y-OS was 66% ± 21% while in MIBG non-avid subgroup, 3-y-OS was 53% ± 20%.

- In MIBG avid and MIBG non-avid subgroups 3-y-EFS were 66% ± 21% and 47% ± 19% respectively.
Conclusion

- MIBG-avid patients showed better survival and lower relapse rate.

- It is, however, necessary to study large numbers of patients to determine the role of MIBG therapy in pre-transplant conditioning regimen for these patients.
Conclusion

- These findings may suggest a more effective role for pre-transplant MIBG scintigraphy in high-risk neuroblastoma. Patients with MIBG avid lesions in pre-transplant scintigraphy may benefit from combination of therapeutic MIBG and higher dose of chemotherapy.
Conclusions

At this time a number of world’s most advanced and complicated procedures of transplantation are being held in this section, including

- Unrelated transplantation
- Target therapy in pre-transplant conditioning regimen
- Transplant of one or two units of unrelated cord blood,
- Transplantation from Mesenchymal stem cells,
- Other relative transplantation
- Haploidentical transplantation
- Transplantation from mismatch related donors
Pediatric SCT Unit

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