Cost of the treatment of myelodisplastic syndrome in Brazil

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Introduction: *Myelodysplastic syndrome is an incurable and rare hematological disease that affects the production of blood cells. One aim of treatment is to maintain the blood-cell count to near-normal levels. This is mainly achieved with hematopoietic- growth factors and transfusions. Our objective was to determine the cost of supportive treatment/care for patients with low and intermediate I risk myelodysplastic syndrome in respect to private healthcare plans in Brazil.*

Method: *We adapted the National Comprehensive Cancer Network treatment guidelines for intermediate risk myelodysplastic syndrome patients to the Brazilian reality, adopting a decision tree to explore treatment combinations. Then, we calculated the costs for each branch of the tree, according to national prices. We also estimated total costs for a cohort of 100 patients, distributed across treatment combinations according to the expected epidemiology. We assumed a horizon of one year of treatment.*

Results: *The mean cost of treatment for low and intermediate I risk myelodysplastic syndrome is US$ 42,758/patient/year. This cost can vary from US$ 24,282 to US$ 121,952, according to patient characteristics and the treatment used. Overall, patients that require immunotherapy with antithymocyte globulins are associated with the highest cost. Those that achieve disease stability solely with the use of erythropoietin were associated with the lowest cost.*

Conclusion: *In Brazil, treatment of low and intermediate I risk myelodysplastic syndrome is associated with a mean cost of the order of US$ 42,700/patient/year. New types of therapy have the potential to change this scenario if they can diminish the requirements for supportive care.*

Keywords: *Neoplasms; Cost of illness; Hematologic neoplasms*

Introduction

Myelodysplastic syndrome (MDS) is a designation for clonal hematopoietic diseases that present as a common characteristic blood cytopenias, cellular dysplasia and a predisposition to develop leukemia (usually acute myelogenous leukemia) in the course of the disease. The clinical presentation and the prognosis are very variable.[1,2] The morbidity of the MDS is related to two of the clinical characteristics: cytopenia and the development of acute myelogenous leukemia.[3]

MDS has many different prognostic indexes but one of the most used is the "International Prognostic Scoring System (IPSS)" which classifies the patient according to three factors: percentage of blast cells in bone marrow, cytogenetic findings and peripheral red blood cell count.[4]

According to these results, patients are classified as low risk, intermediate I (Int I), intermediate II (Int II) or high risk. Patients classified as Int II or high risk have a bad prognosis, with a median survival of between four and twelve months.[5,6]

The real prevalence of MDS in Brazil in unknown, but in the USA it is approximately 35 cases for every one million of people, that is, approximately one in every 12,000 individuals has MDS.[1]

Until recently, no specific treatment existed for MDS, and the therapeutic effort was focused to hematologic complications, such as anemia, neutropenia and thrombocytopenia. These treatments are of high cost and require intensive use of medical resources.[3,7,8] The aim of treatment is to improve the red blood cell indices of these patients in order to improve the length or the quality of life of patients and to delay transformation to leukemia.[5,6]

In studies made in Europe and in USA, one year of supportive treatment for MDS costs between US$ 63,000 and US$ 87,000.[3,7,9] Only with transfusions, the cost is between US$ 4,000 and US$ 13,000 for each patient.[8,10]

Our aim was to estimate the costs of supportive treatment of MDS in patients classified as low or Int I risk for the Brazilian private healthcare system.

Conflicts of interest: Both authors, Otávio Clark and Enéas Faleiros, work for Evidências Consultoria , Campinas (SP), Brazil

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Methods

We adapted the National Comprehensive Cancer Network (NCCN) guidelines for the treatment of low and int I risk MDS,[3] for the Brazilian reality. Then we calculated the direct costs of treatment with a horizon of one year. The choice to use an American guideline was due to the lack of publications and studies performed in Brazil.

We developed a decision tree for a hypothetic cohort of 100 patients (Figure 1). The probability of success of failure for each treatment strategy has been described previously by Greenberg et al.[3]

The treatment regimens recommended by the NCCN guidelines include the use of hematopoietic stimulating factors [erythropoietin (EPO) and neutrophil colony stimulating factors (CSF)], chemotherapy (chemo) with cytarabin and idarubicin, use of anti-thymocyte globulin (ATGAM), cyclosporin and blood cell transfusions (Tx) (red blood cells and platelets) and the use of iron chelators (Chel), due to transfusion iron overload.[5]

According to the NCCN and the Greenberg study,[3,5] patients are initially classified according to the presence of anemia (83%) or thrombocytopenia/neutropenia (7%). A third group of patients (10%) has a mutation in the 5q gene (Del-5q). This last group was excluded in this analysis due to the fact that their first therapeutic option is lenalidomide, which has not been licensed in Brazil yet.

The modeling of the decision tree was performed according to the following distribution (Figure 1):

Anemia patients (92%)

– EPO arm (72%) those with blood erythropoietin < 500 mU/ML

– 30% responsive to EPO

– in 20% CSF is added to EPO

- 25% are not responsive and also receive chemotherapy

– The remaining are treated with transfusions and require iron chelators (Tx + Chel)

– EPO + SCF (13%) those with blood erythropoietin < 500 mU/ML and presence of sideroblasts

– Initial treatment with EPO + CSF

- 35% achieve a response
- 25% do not respond, chemotherapy is added
- The others receive Tx + Chel

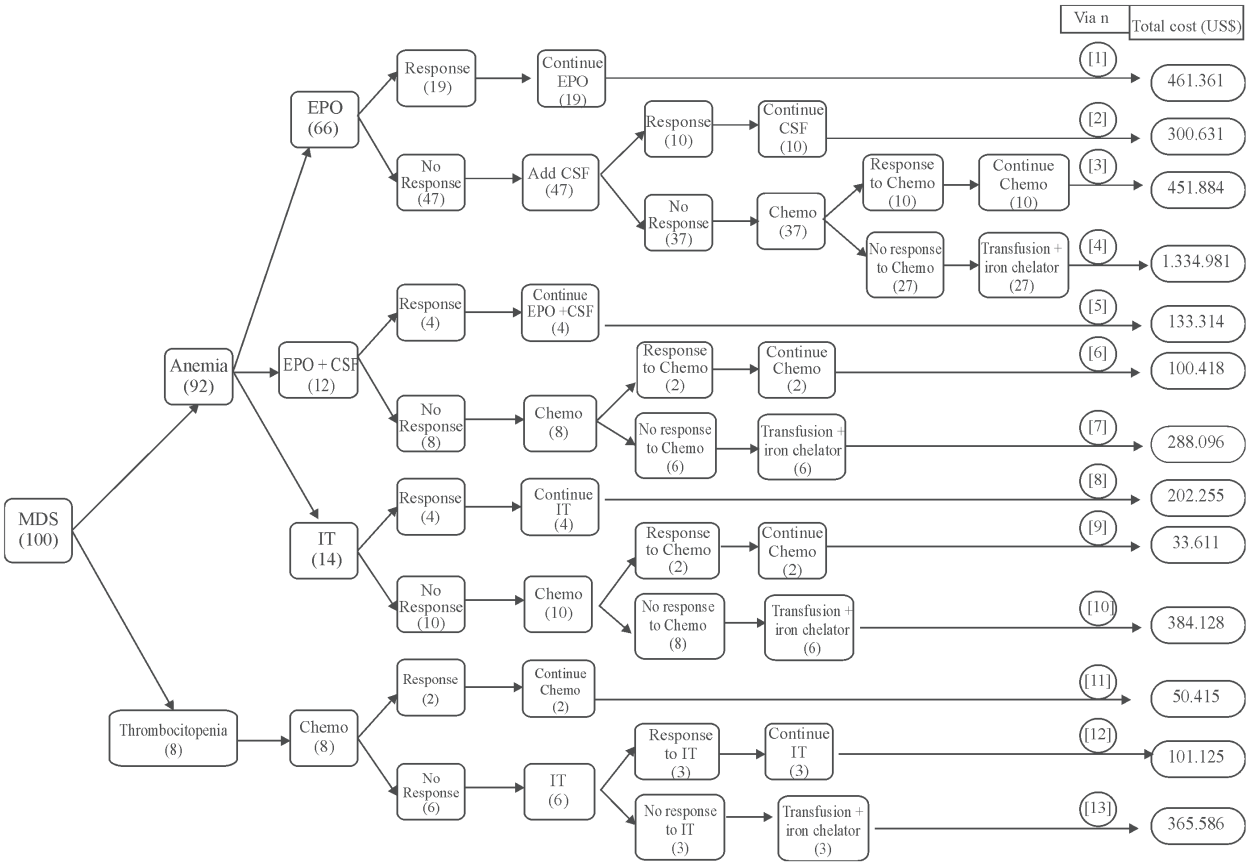

Figure 1 – Treatment of MDS, with the probabilities, percentage of response, treatment used and total cost for all patients for each pathway over one year according to this model. MDS: Myelodisplastic syndrome; Chemo: chemotherapy; EPO: erythropoietin; CSF: colony stimulating factors; IT: immunotherapy. The number between square brackets [ ] means the number of the pathway and the number in brackets ( ) means the number of patients in each treatment arm

– *Immunotherapy arm (IT) (15%): those with blood erythropoietin > 500 mU/ML*

– 25% achieve a response with ATGAM + Cyclosporin

– If resistant, 25% respond to chemotherapy and 75% receive Tx + Chel

Patients with thrombocytopenia/ neutropenia (8%)

– *Chemotherapy*

– 25% achieve a response and continue with chemotherapy

– 75% are not responsive to chemotherapy and receive ATGAM

-50% continue with the treatment

- 50% Tx + Chel

According to the model, patients who are resistant to all treatments all end up receiving chronic transfusions of red blood cells, platelets and iron chelation.

Following this sequence of treatment, there are 13 possible pathways that a patient can follow on the decision tree (numbered 1 to 13 on Figure 1).

We adopted an assumption that all patients stay on treatment for one year and thus did not take into account early deaths or abandonment of treatment. We only considered changes in treatment due to therapeutic failure. No costs with hospitalizations or side effects were included.

For the costs, we considered purchase costs of medicines for outpatients care. The source of costs was the Brazilian official price list[11] and for medical procedures we used the official price list of the Associação Médica Brasileira.[12] ATGAM is only available from other countries and so, we considered the imported price (Table 1).

Table 1 - Price of the medications used to the supportive treatment of MDS

Item	Dose	Frequency	Cost of dose (US$)	Yearly cost (US$)
EPO	40 MU	Weekly	467	24,284
Filgrastim	300 mcg	Weekly	175	9,120
ATGAM	40 mg/kg/day	4 days	8,250	99,000
Cyclosporin	5 mg/kg/day	Daily	6	2,128
Desferasirox	20 mg/kg/day	Daily	39	43,096
Red cell transfusion	Unit	11 per year	164	4,920
Platelets transfusion	Unit	7 per year	134	8,040
Chemotherapy (idarubicin + cytarabin) (6 cycles)		6 cycles	2,801	16,806

Results

The costs of treatment for the whole cohort were US$ 4,275,800 /year or US$ 42,758 /patient/year. This cost varies greatly between the 13 different treatment pathways that are possible in our model (Figure 1 and Table 2).

Table 2 - Yearly total cost and mean cost per patient according to the treatment pathway

Pathway number	Number of patients	Total cost (US$)	Cost/patient (US$)
1	19	461,361	24,282
2	10	300,632	30,063
3	10	451,884	45,188
4	27	1,334,982	49,444
5	4	133,614	33,404
6	2	100,419	50,209
7	6	288,096	48,016
8	4	202,256	50,564
9	2	33,612	16,806
10	8	384,129	48,016
11	2	50,418	25,209
12	3	101,113	33,704
13	3	365,857	121,952

Pathway 1 (patients that started treatment with EPO and are responsive) has the lowest cost/patient/year (US$ 24,282), and pathway 13 (patients with thrombocytopenia, that do not respond to chemotherapy or to IT) is the most expensive (US$ 121,952).

Patients that started treatment with EPO (US$ 37,244) or IT (US$ 38,461) have a lower final mean cost when compared to those that initially received chemotherapy (US$ 60,288) or EPO + CSF (US$ 43,876).

The response to initial treatment is usually a factor associated to a lower cost: Pathways 1, 5 and 11 (the first pathway of each treatment arm) are the cheapest. The exception is the pathway of immunotherapy (pathway 8) due to the high cost of ATGAM.

Among the therapeutic needs, transfusions and the use of iron chelators were alone responsible for more than half of the total costs: US$ 2,450,000 or 57.5% of the total costs.

If we accept that the incidence of MDS in Brazil is similar to that of the USA,[1] we can expect around 1500 MDS cases in the private healthcare system. From these, 70% (1050) will be from the low and Int I risk categories. And thus, according to the estimate of this model, we can expect around US$ 45,000,000 to be spent in MDS supportive care each year.

Discussion

These results show that the costs linked to the supportive care of MDS in the private healthcare system in Brazil are high, but lower than in other countries. If we compare the mean cost (US$ 42,758) of a patient from our model to the lowest cost described for USA (US$ 63,000), in Brazil a patient costs around 35% less.[8,10]

In this analysis, patients were categorized according to the initial symptoms and followed for one year. As we did not take into account losses to treatment including deaths, our results may be an overestimate, as some patients die or stop treatment in the course of this period. Also, the costs may have been overestimated due to the intensive use of transfusions and chelators in the model, as recommended by the NCCN guidelines; this intensive use may not reflect the reality in Brazil.[13] On the other hand, we did not take into account hospitalizations, progression to leukemia and indirect costs that increase the price, and hence, in these cases, our numbers are an underestimation.[3]

The two major sources of costs are EPO support and the need of iron chelators. These two medications are used due to the profound anemia that MDS patients develop during the course of the disease.[14]

Recently, new drugs have been developed specifically for MDS and have reached the market. The most important effect of decitabine and azacitidine is an improvement in red blood cell indexes with a consequent reduction in the needs for transfusions and chelators.[13,15] Therefore, there is a possibility that these new medications may have a strong influence on the cost of treatment. In the future another pharmacoeconomic analysis should be performed to take the effectiveness and the costs of decitabine and azacitidine into account.

The estimate of the total costs associated to the supportive treatment of MDS in the private healthcare system in Brazil is very high – US$ 45 million for patients with low and Int I risk. This calls attention to this disease that, although rare, has an important clinical and financial impact on the system as well as on the patients.

In face of these data, it is important that some measures are taken to guarantee early access of patients to treatment, as patients that are responsive to therapy have a better prognosis and a lower cost than those that do not respond. For instance, patients that are responsive to EPO (Pathway 1) have a lower cost than those that did not respond (Pathways 2, 3 and 4).

Conclusion

The mean cost for the treatment of MDS in the Brazilian private healthcare system is US$ 42,758 /patient/ year. This value varies greatly depending on the interventions used.

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