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Role of Decitabine in Myelodysplastic Syndrome-An Experience from a Tertiary Care Centre

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Abstract

A number of emerging therapeutic options are currently being evaluated for the treatment of MDS that will, add to the treatment options for patients who are ineligible to receive HSCT or intensive chemotherapy. Decitabine has recently been approved by FDA for the treatment of MDS. The aim of our study was to evaluate efficacy of Gemcitabine verses best supportive treatment in myelodysplastic syndrome. 48 subjects with myelodysplasia who attended clinical hematology OPD or were admitted in the concerned ward were enrolled as from June, 2014 to May, 2016. The diagnosis was based on history, clinical examination, bone marrow examination and cytogenetics. 31 subjects were taken as controls among whom 12 (38.7%) were males and 19 (61.3%) were females with mean age of 62.81 ± 9.232 years. 17 subjects were taken as cases among whom 7 (41.2%) were males and 10 (58.8%) were females with mean age of 53.82 ± 13.626 years. In our study, there was no statistically significant difference in hematologic improvement and overall survival among subjects receiving best supportive care and Decitabine compared to the subjects receiving best supportive care only. However, among subjects who received Decitabine there was statistically significant rise in mean hemoglobin level from 5.7 gm% to 7.1 gm% and there was statistically significant reduction in RBC transfusion requirement from mean of 2.76 transfusions per month to 1.09 transfusions per month with P value of <0.05. Decitabine treatment was associated with only limited non-hematologic toxicity. Myelosuppression was the major adverse effect; particularly during early treatment (prolonged cytopenias in some patient's necessitated delay of subsequent treatment or even termination).

Keywords: Decitabine; Myelodysplastic syndromes; Efficacy; Treatment; Leukemia

Introduction

Myelodysplastic syndromes (MDS) are group of clonal hematopoietic stem cell disorders that are characterized by dysplastic changes in one or more cell lineages, ineffective haematopoiesis resulting in anemia, neutropenia and/or thrombocytopenia and a variable predilection to development of acute myeloid leukemia (AML) [1]. MDS can occur spontaneously (primary) or can occur as a result from exposure to chemotherapy or chemicals including benzene and others (secondary) [1-3]. MDS is seen in approximately 5 per 1,00,000 people per year. MDS is a disease of elderly. The risk of MDS increases with advancing age; approximately 86% of patients with newly diagnosed MDS are 60 years old (median age, 76 years with slight male preponderance [4]. Rare in children. Secondary or therapy related MDS is not age related. The standard care for patients with Myelodysplastic Syndrome (MDS) and decreased blood counts is constantly changing. The approach to therapy is based on the revised International Prognostic Scoring System (IPSS-R) score, the patient's age and co-morbidities. The more toxic and aggressive forms of therapy, such as stem cell transplantation and aggressive chemotherapy, are reserved for younger and fit patients with high-risk disease. Prognostic scoring systems are also commonly used in clinical decision making. Common regimens for MDS treatment are hematopoietic stem cell transplantation (HSCT), immunotherapeutic strategies, chemotherapy, supportive care, iron-chelating therapy, targeted therapies. Historically, the therapy of MDS has been unsatisfactory. Stem cell transplant (SCT) [5] is the only treatment that can potentially cure myelodysplastic syndrome (MDS). Success of bone marrow

transplantation has been found to correlate with severity of MDS as determined by the IPSS score, with patients having a more favorable IPSS score tending to have a more favorable outcome with transplantation. Supportive therapy [6], including transfusions of the cells that are deficient (i.e., red blood cells [RBCs], platelets), and treatment of infections are the main components of care. Supportive care, including anti-infection and improvement of anemia/thrombocytopenia/neutropenia, would give rise to blood transfusion dependency, iron overload and impaired quality of life. The identification of multistage epigenetic modification brings a revolution in understanding of the pathogenesis of MDS. Decitabine, the Food and Drug Administration (FDA) approved hypomethylating agent, has doubtless improved the outcome and prolonged overall survival of patients with MDS. Noticeably, the elderly patients, who cannot tolerate certain types of intensive chemotherapy or HSCT, would probably better fit the Decitabine strategy, because of the mild toxicity profile of decitabine [7,8]. The efficacy of hypomethylating agents is based on epigenetics [9,10]. Decitabine (5-aza-2'-deoxycytidine) is a cytosine analogue modified in position 5 of the pyrimidine ring. Higher doses, Decitabine inhibits cell proliferation through nonreversible covalent linking with DNA methyltransferase and blocking of DNA synthesis [11]. At lower doses, Decitabine induces hypomethylating, thereby promoting cell differentiation, re-expression of tumor suppressor genes, stimulation of immune mechanisms, and suppression of tumor growth [12,13]. Decitabine is approved for the treatment of patients with MDS, including previously treated or untreated, de novo or secondary MDS of all FAB subtypes (RA, RARS, RAEB,RAEB-T, and CMML) and intermediate-1, intermediate-2, and high-risk IPSS groups. Decitabine dosing for MDS is 15 mg/m^2 *via* a 3-hour continuous infusion three times a day for 3 days for the first treatment cycle, repeated every 6 weeks. It is recommended that patients be treated for a minimum of four cycles; however, it is noted that a complete or partial response may take longer than four cycles. Treatment may be continued as long as the patient continues to benefit.

Materials and Methods

The present work is a hospital based study that was carried out in the Department of Clinical Hematology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar. 48 subjects with myelodysplasia who attended clinical hematology OPD or were admitted in the concerned ward were enrolled as from June, 2014 to May, 2016. Age of subjects ranged from 18 to 75 years with mean age of 53.82 ± 13.626 years in cases and 62.81 ± 9.232 years in controls. The diagnosis was based on history, clinical examination, bone marrow examination and cytogenetics. 31 subjects were taken as controls among whom 12 (38.7%) were females and 19 (61.3%) were males with mean age of 62.81 ± 9.232 years. 17 subjects were taken as cases among whom 7 (41.2%) were females and 10 (58.8%) were males with mean age of 53.82 ± 13.626 years. Our population of interest was all those patients diagnosed to have myelodysplastic syndrome.

Inclusion criteria

- Patients with myelodysplastic syndrome
- Patients of both sexes were selected
- Random sample of patients were taken

Exclusion criteria

- Marrow blast count of >20%
- Unstable cardiovascular status (e.g.; recent MI, unstable Angina or PTE)
- Pregnancy
- Hepatic impairment
- Renal impairment

Study Design and Conduct

An informed consent was taken from all the subjects found fit for the study. After proper consent, subjects with myelodysplastic syndrome were enquired about the history of related risk factors (smoking, alcohol use, previous history of chemotherapy or radiotherapy) and their medical records were checked. Patients were considered active smokers if they had smoked at all during the last month; ex-smokers if they had ever smoked; and non-smokers if they had never smoked. They were thoroughly examined, height and weight were measured and BMI and body surface area calculated. They were subjected to baseline investigations including complete blood count, bone marrow examination, kidney function test, serum calcium levels, serum phosphorus levels, liver function test, LDH, lipid profile, ECG and chest X-ray, vitamin B12 levels. All the patients had varying number of cytopenias in CBC with dysplasia in one or more cell lineages on bone marrow examination. Cytogenetics of all the subjects was done.

The cases received injection decitabine 20 mg/m^2 intravenously in 100 ml of normal saline over a period of 1 hour for 5 days. This was repeated every 28 days for total of 4 cycles. Cases were followed with CBC, KFT, LFT weekly and bone marrow examination at the end of 4 cycles. The cases also received the supportive care in the form of RBC transfusion, platelet transfusion. Due to prolonged myelosupression with decitabine 20 mg/m^2 in initial two cases, dose of decitabine was decreased from 20 mg/m^2 to 5 mg/m^2 intravenously daily for 5 days. 4 such cycles were given every 4 weeks to cases. 31 subjects with myelodysplastic syndrome who attended Clinical Hematology OPD or were admitted in the concerned ward were enrolled as controls in the study. Age of controls ranged from 47 to 75 years with mean age of 62.81 ± 9.232 years. Among controls 12 (38.7%) were males and 19 (61.3%) were females. The controls received best supportive care only. They were followed with CBC monthly and bone marrow examination.

Statistical Analysis

The pearson Chi-square test and Fisher exact test was applied for statistical analysis of the data obtained. Significant values were taken if the p-value was less than 0.05. Statistical package for social sciences (SPSS) was used as a software tool for the

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analysis of the data. Data obtained from case study were compared with controls.

Results

The study was carried out at SKIMS Soura, in the Department of Clinical Hematology with the purpose to find the effect of decitabine in myelodysplasia in our population. All the patients were known cases of Myelodysplastic syndrome (diagnosed or first time evaluated) following clinical hematology OPD at SKIMS. Of 48 cases 6 (12.5%) were RCUD, 39 (81.2%) were RCMD, 1 (2.1%) was RAEB-1 and 2 (4.2%) were RAEB-2 WHO subtype. Our study population included 48 subjects out of which 19 (39.6%) were females and 29 (60.4%) were males. The age ranged from 18 years to 70 years in the case group with mean age of 53.82 ± 13.626 years and in the control group the age ranged from 47 years to 75 years with mean age of 62.81 ± 9.232 years with male: female ratio of 1.52. Of the studied population, 52.08% was above the age of 60 years and 47.91% were below age of 60 years. Among cases 10 (58.8%) belonged to rural area and 7 (41.2%) belonged to urban area. Among controls 20 (64.5%) belonged to rural area and 11 (35.3%) belonged to urban area. Among cases 9 (52.9%) subjects were smokers and 8 (47.05%) were non-smokers. Among controls 10 (32.2%) were smokers and 21 (67.7%) were non-smokers. The prevalence of anemia was present in 17 (100%) of subjects among cases out of which 7 (41.2%) were female and 10 (58.8%) were male.

Among controls, anemia was present in 28 (90.3%) of subjects individuals out of whom 17 (60%) were male and 11 (40%) were female. The bleeding manifestations were present in 8 (47.1%) of cases and 12 (38.7%) of controls. The evidence of infections was present in 9.7% (3) of control subjects and none of the cases had any evidence of infections. Out of 48 subjects enrolled in the study, 1 (2.1%) was very high risk, 3 (6.2%) were high risk, 35 (72.9%) were intermediate risk and 9 (18.8%) were low risk as per IPSS-R. Of 17 subject enrolled as cases 1 (5.9%) belonged to very high risk group for developing AML, 3 (17.6%) belonged to high risk, 7 (41.2%) belonged to intermediate risk, 6 (35.3%) belonged to low risk group. Among 31 subjects enrolled as controls 28 (90.3%) belonged to intermediate risk group and 3 (9.7%) belonged to low risk group.

Of 17 subject enrolled as cases 1 (5.9%) belonged to very high risk group for developing AML, 3 (17.6%) belonged to high risk, 10 (58.8%) belonged to intermediate risk, 3 (17.6%) belonged to low risk group. Among 31 subjects enrolled as controls 27 (87.1%) belonged to intermediate risk group and 4 (12.9%) belonged to low risk group. Among 48 subjects 2 (4.2%) had poor cytogenetics (del 8 and 7) while 46 (95.8%) were having good cytogenetics. Among subjects enrolled as cases after 4 cycles of Decitabine, mean haemoglobin level increased from 5.7 gm% to 7.1 gm% with a P-value of <0.05 which was statistically significant. Among 31 subjects enrolled as controls, mean haemoglobin level increased from 6.48 gm% to 7 gm% with a P-value of <0.05 (**Table 1**).

Table 1: Distribution of Haemoglobin, gm% [S=significant, NS=Non-Significant].

Group	N	Pre-Hb		Post-Hb		P-value	Significance
		Mean	Std. deviation	Mean	Std. deviation		
		Gm%		Gm%			
Case	17	5.753	1.92163	7.135	2.10385	0.009	S
control	31	6.487	2.05584	7.084	1.70979	0.004	C

After 4 cycles of Decitabine mean total leukocyte count in cases changed from 2.35 × 10^3/µl to 2.1 × 10^3/µl with a P-value of 0.521. Among controls, mean total leukocyte count remained 2.30 × 10^3/µl. Among cases mean absolute neutrophil count (ANC) changed from 929.35 × 10^3/µl to 877.35 × 10^3/µl with P-value of 0.723 and among controls ANC changed from 1055.67 × 10^3/µl to 1034.67 × 10^3/µl with P-value of 0.739 (**Table 2**).

Table 2: Distribution of total leukocyte count.

Group	N	Pre-TLC × 10^3/µl		Post-TLC × 10^3/µl		P-value	Significance
		Mean	Std. deviation	Mean	Std. deviation		
Case	17	2.3518	1.71626	2.1676	1.20121	0.521	NS
Control	31	2.3042	1.36247	2.3035	1.2037	0.995	NS

Among cases, mean platelet after 4 cycles of decitabine based chemotherapy increased from 47000/µl to 75000/µl with a P-value of 0.209 while in control group mean platelet count remained same 40000/µl (**Table 3**).

Table 3: Distribution of platelet count.

Group	N	Pre-platelet × 10^3/µl		Post-platelet × 10^3/µl		P-value	Significance
		Mean	Std. deviation	Mean	Std. deviation		
Case	17	47	50.58532	75.529	91.30862	0.209	NS
Control	31	40.87	39.84699	40.807	42.62583	0.983	NS

Blast count in bone marrow remained <5% in both groups (case/control). Myelosuppression was noted in 13 (76.47%) of cases while 4 (25.52%) did not have Myelosuppression. Transaminitis was found in 2 (11.76%) of cases. AKI was noted in 1 (5.8%) of cases. Among subjects in the study, cases have mean follow-up of 16.35 months and controls have mean follow-up of 14.09 months. In our study, there was no statistically significant difference in hematologic improvement and overall survival among subjects receiving best supportive care and Decitabine compared to the subjects receiving best supportive care only. However, among subjects who received Decitabine there was statistically significant rise in mean hemoglobin level from 5.7 gm% to 7.1 gm% and there was statistically significant reduction in RBC transfusion requirement from mean of 2.76 transfusions per month to 1.09 transfusions per month with P-value of <0.05 (**Table 4**).

Table 4: RBC Transfusion requirement per month.

Group	N	Pre-Transfusion		Post-Transfusion		P-value	Significance
		Mean	Std. deviation	Mean	Std. deviation		
Case	17	2.76	1.09	1.41	1.18	0.002	S
Control	31	2.52	1.06	2.58	1.36	0.836	NS

Decitabine treatment was associated with only limited non-hematologic toxicity. Myelosuppression was the major adverse effect; particularly during early treatment (prolonged cytopenias in some patient's necessitated delay of subsequent treatment or even termination). Due to prolonged Myelosuppression with Decitabine 20 mg/m^2, dose of Decitabine was decreased from 20 mg/m^2 to 5 mg/m^2 intravenously daily for 5 days. 4 such cycles were given 4 weekly to cases.

Discussion

The present study is the first population based epidemiological study carried out in Kashmir in which DECITABINE along with best supportive care was used as a standard for treatment of patients having myelodysplasia. The study was carried out at SKIMS Soura, in the Department of Clinical Hematology with the purpose to find the effect of decitabine in myelodysplasia in our population. All the patients were known cases of Myelodysplastic syndrome (diagnosed or first time evaluated) following clinical hematology OPD at SKIMS. Of 48 cases 6 (12.5%) were RCUD, 39 (81.2%) were RCMD, 1 (2.1%) was RAEB-1 and 2 (4.2%) were RAEB-2 WHO subtype. Our study population included 48 subjects out of which 19 (39.6%) were females and 29 (60.4%) were males. The age ranged from 18 years to 70 years in the case group with mean age of 53.82 ± 13.626 years and in the control group the age ranged from 47 years to 75 years with mean age of 62.81 ± 9.232 years with male: female ratio of 1.52. Of the studied population, 52.08% was above the age of 60 years and 47.91% were below age of 60 years. Among cases 10 (58.8%) belonged to rural area and 7 (41.2%) belonged to urban area. Among controls 20 (64.5%) belonged to rural area and 11 (35.3%) belonged to urban area. Among cases 9 (52.9%) subjects were smokers and 8 (47.05%) were non-smokers. Among controls 10 (32.2%) were smokers and 21 (67.7%) were non-smokers. The prevalence of anemia was present in 17 (100%) of subjects among cases out of which 7 (41.2%) were female and 10 (58.8%) were male. Among controls, anemia was present in 28 (90.3%) of subjects individuals out of whom 17 (60%) were male and 11 (40%) were female. The bleeding manifestations were present in 8 (47.1%) of cases and 12 (38.7%) of controls. The evidence of infections was present in 9.7% (3) of control subjects and none of the cases had any evidence of infections.

Out of 48 subjects enrolled in the study, 1 (2.1%) was very high risk, 3 (6.2%) were high risk, 35 (72.9%) were intermediate risk and 9 (18.8%) were low risk as per IPSS-R. Of 17 subject enrolled as cases 1 (5.9%) belonged to very high risk group for developing AML, 3 (17.6%) belonged to high risk, 7 (41.2%) belonged to intermediate risk, 6 (35.3%) belonged to low risk group. Among 31 subjects enrolled as controls 28 (90.3%) belonged to intermediate risk group and 3 (9.7%) belonged to low risk group. Of 17 subject enrolled as cases 1 (5.9%) belonged to very high risk group for developing AML, 3 (17.6%) belonged to high risk, 10 (58.8%) belonged to intermediate risk, 3 (17.6%) belonged to low risk group. Among 31 subjects enrolled as controls 27 (87.1%) belonged to intermediate risk group and 4 (12.9%) belonged to low risk group. Among 48 subjects 2 (4.2%) had poor cytogenetics (del 8 and 7) while 46 (95.8%) were having good cytogenetics. Among subjects enrolled as cases after 4 cycles of decitabine, mean haemoglobin level increased from 5.7 gm% to 7.1 gm% with a P-value of <0.05 which was statistically significant. Among 31 subjects enrolled as controls, mean haemoglobin level increased from 6.48 gm% to 7 gm% with a P-value of <0.05. After 4 cycles of decitabine mean total leukocyte count in cases changed from 2.35 × 10^3/µl to 2.1 × 10^3/µl with a P-value of 0.521. Among controls, mean total

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leukocyte count remained 2.30 × 10^3/µl. Among cases mean absolute neutrophil count (ANC) changed from 929.35 × 10^3/µl to 877.35 × 10^3/µl with P-value of 0.723 and among controls ANC changed from 1055.67 × 10^3/µl to 1034.67 × 10^3/µl with P-value of 0.739.

Among cases, mean platelet after 4 cycles of decitabine based chemotherapy increased from 47000/µl to 75000/µl with a P-value of 0.209 while in control group mean platelet count remained same 40000/µl. Blast count in bone marrow remained <5% in both groups (case/control). Myelosupression was noted in 13 (76.47%) of cases while 4 (25.52%) did not have myelosupression. Transaminitis was found in 2 (11.76%) of cases. AKI was noted in 1 (5.8%) of cases. Among subjects in the study, cases have mean follow-up of 16.35 months and controls have mean follow-up of 14.09 months. In our study, there was no statistically significant difference in hematologic improvement and overall survival among subjects receiving best supportive care and decitabine compared to the subjects receiving best supportive care only (**Table 5**).

However, among subjects who received decitabine there was statistically significant rise in mean haemoglobin level from 5.7 gm% to 7.1 gm% and there was statistically significant reduction in RBC transfusion requirement from mean of 2.76 transfusions per month to 1.09 transfusions per month with P value of <0.05. Decitabine treatment was associated with only limited non-hematologic toxicity. Myelosuppression was the major adverse effect; particularly during early treatment (prolonged cytopenias in some patient's necessitated delay of subsequent treatment or even termination). Due to prolonged myelosupression with decitabine 20 mg/m^2, dose of decitabine was decreased from 20 mg/m^2 to 5mg/m^2 intravenously daily for 5 days. 4 such cycles were given 4 weekly to cases.

Table 5: Comparison of pretreatment and post treatment hematological parameters for cases and controls.

Haematological Parameters		N	Mean	Std. deviation	Str. error mean	P-value
Pre-treatment Hb	Case	17	5.7529	1.92163	0.46606	0.232
	Control	31	6.4871	2.05584	0.36924	
Post-treatment Hb	Case	17	7.1353	2.10385	0.51026	0.927
	Control	31	7.0839	1.70979	0.30709	
Pre-treatment TLC	Cases	17	2.3518	1.71626	0.41625	0.916
	Controls	31	2.3042	1.36247	0.24471	
Post-treatment TLC	Case	17	2.1676	1.20121	0.29134	0.71
	Control	31	2.3035	1.2037	0.21619	
Pre-treatment ANC	Case	17	929.3529	1049.92755	254.64484	0.642
	Control	31	1055.677	797.26032	143.19218	
Post-treatment ANC	Case	17	877.3529	633.99753	153.76699	0.476
	Control	31	1034.677	769.05741	138.12679	
Pre-platelet	Case	17	47	50.58532	12.26874	0.646
	Control	31	40.871	39.84699	7.15673	
Post-platelet	Case	17	75.5294	91.30862	22.14559	0.078
	Control	31	40.8065	42.62583	7.65582	
Pre-treatment blasts	Case	17	2.6588	3.59567	0.87208	0.18
	Control	31	1	0.85635	0.1538	
Post-treatment blasts	Case	17	1.5294	2.03463	0.49347	0.138
	Control	31	0.9355	0.62905	0.11298	
Pre RBC transfusion	Case	17	2.7059	1.21268	0.29412	0.576
	Control	31	2.5161	1.06053	0.19048	
Post-transfusion	Case	17	1.8235	1.62924	0.39515	0.092
	Control	31	2.5806	1.36074	0.2444	

Conclusion

Decitabine, a hypomethylating agent that allows for the re-expression of tumor suppressor genes, represents an exciting new treatment option for MDS patients. Decitabine is effective in the treatment of MDS, resulting in durable clinical responses and delayed time to AML transformation or death.

References

1. Saba HI (2005) Myelodysplastic Syndromes. In: Hematology Today. Ed. M.B. Agarwal pp: 175-193.
2. Kurzrock R (2002) Myelodysplastic syndrome overview. Semin Hematol 39: 18-25.
3. Saba HI, List AF (2005) Melodysplastic syndromes: New frontiers in management. Thehaematologist: ASH News and Reports.
4. Foran JM, Shammo JM (2012) Clinical presentation, diagnosis, and prognosis of myelodysplastic syndromes. Am J Med 125: S6-S13.
5. Greenberg P (1997) International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood 89: 2079-2088.
6. Greenberg PL (2012) Revised international prognostic scoring system for myelodysplastic syndromes. Blood 120: 2454-2465.
7. Malcovati L (2007) Time-dependent prognostic scoring system for predicting survival and leukemic evolution in myelodysplastic syndromes. J Clin Oncology 25: 3503-3510.
8. Stephen DN (2008) Myelodysplastic syndromes. Blood 111: 4841-4851.
9. Kuendgen A, Lubbert M (2008) Current status of epigenetic treatment in myelodysplastic syndromes. Ann Hematol 87: 601-611.
10. Navada SC, Steinmann J, Lubbert M, Silverman LR (2014) Clinical development of demethylating agents in hematology. J Clin Invest 124: 40-46.
11. Kelly TK, De Carvalho DD, Jones PA (2010) Epigenetic modifications as therapeutic targets. Nat Biotechnol 28: 1069-1078.
12. Cashen AF, Schiller GJ, O'Donnell MR, DiPersio JF (2010) Multicenter, phase II study of decitabine for the first-line treatment of older patients with acute myeloid leukemia. J Clin Oncol 28: 556-561.
13. Dacogen: Package insert (2006) MGI Pharmaceuticals Inc.

This article is available from: 10.21767/2471-9897.1000303