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Research Article

HEMATOLOGICAL RESPONSE AND GENDER OF THE PATIENT: IN THE FOLLOW-UP OF CHEMORADIOTHERAPY

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ABSTRACT

Cancer is a foremost cause of death all over the world and invasive surgeries chemo-radiotherapy are the treatment of choice. There are cases where there is need to rely on chemo-radiotherapy either independently or in combination with surgery. However, these therapies highly compromise the patient's quality of life due to their side effects. The current study was aimed to analyse the side effects of chemo-radiotherapy after three weeks of exposure to therapy, to see the pattern of haematological parameters on subsequent cycle and to assess the gender wise response of treatment with simple cost effective investigation. It was a retrospective analysis of cancer patients who were planned for chemo-radiotherapy for solid malignancies in a cancer institute. A retrospective study was carried out to evaluate effects of the chemo-radiotherapy on the various blood cells in 444 cancer patients with male to female ratio of 1:1. Patients were divided into different groups. All the haematological parameters were reassessed and mean values was collected. Data were analyzed statistically where ever needed. A good leucocytic and neutrophilic response after first cycle was seen in males rather than females. A statisitically significant increased number of lymphocytes (p value 0.02), monocytes (p value 0.05) and platelets (p value 0.05) was seen in male patients after later on cycles of treatment. All the hematological parameters were stable in females except low leucocytic counts and neutropenia after first cycle of treatment with very low leucocytic counts in the later cycles. Investigation of complete blood count is still a cost effective tool to assess the hematological effects of therapy in cancer patients. Increased number of lymphocytes and monocytes can also be correlated with good hematological response for treatment.

Keywords: *Haematological Parameters, Cancer, Chemo-Radiotherapy, Neutropenia*

INTRODUCTION

Cancer has emerged as a major leading cause of death in India as well as world. The carcinoma is treated depending on the stage of the spread and type and its origin such as epithelial or mesenchymal. Majority of the malignancies, diagnosed in the early phase are to be treated either by radiotherapy, surgery or chemotherapy (Ferrara *et al.,* 2004; Motzer *et al.,* 2006; Gurgan *et al.,* 2008). Many chemotherapeutic agents, in addition to destroying the malignant cells can have some adverse effects during and after the treatment (Gibson and Keefe, 2006). But chemotherapy also induces some changes in the bone marrow hence results in various haematological manifestations like anaemia, leucopenia and thrombocytopenia. In addition radiation also causes haemolysis of the red blood cells hence resulting in anaemia (Zeuner *et al.,* 2007).

Thrombocytopenia is a general problem experienced by cancer patients, which usually is a result of the use of conventional chemotherapy (Trinova *et al.,* 2007; Kuter, 2006; Elting *et al.,* 2001 and Cantor *et al.,* 2003). Many studies have been done on the haematological manifestation of cancer therapy. The current study was aimed to analyse the side effects of treatment after three weeks, to see the pattern of haematological parameters on subsequent cycle of therapy and to assess the gender wise response of treatment.

MATERIALS AND METHODS

Methods

Total 444 samples collected from patients of various solid malignancies, intended for chemo-radiotherapy were analysed retrospectively. The age group for all samples ranged between 6-94 years with male (M) to female (F) ratio of 1:1. Reports of all the blood samples collected in EDTA vacutainers and processed with automated hematology analyzer were re-collected. All the patients were divided into different groups depending upon the number of cycle of therapy (Table 1). Detailed statistical analyses of haematological parameters such as hemoglobulin concentration (Hb gm%), total leucocytic count (TLC), absolute values of granulocytes/agranulocytes and platelets was carried out (Lewis, 2006). Prechemo-radiotherapy values of all parameters both in males as well as females were compared with three weeks post treatment values of subsequent cycles.

Statistical Analysis Used

The descriptive data were given as means ± SD. The groups were compared through ANOVA single factor assessment and the differences were considered to be statistically significant and very significant when the *p* value obtained was <0.05, <0.002, respectively.

RESULTS AND DISCUSSION

Results

The values of all haematological parameters after each subsequent cycle were compared and results were obtained. The mean values of haemoglobin (Hb gm%) were low in both the males and female patients before the start of treatment and no statistic significance was detected during the cycles (Table 2).

There was statistically insignificant 17.3% increase in TLC values in male and 2.6% fall in female patients. A significant fall in TLC was detected in fourth and fifth cycles in males and later on cycles in females (Table 3).

A significant fall in ANC was detected in female patients on first cycle followed by continuous reduction in ANC in males up to fifth subsequent cycle (Table 4). In addition, significant reduction in absolute lymphocytic count (ALC) was noticed in males on first cycle with significant increase in subsequent cycles. A very significant rise in ALC was seen after fifth cycle in males (Table 5).

Increased AMC, AEC and reduced platelets count were seen in male patients whereas female patients have shown increased AMC only (Table 6).

The results showed that the platelet counts in males and females were decreased by 62.5% and 54.3 % respectively after first dose and showed continuous decrease at subsequent visits with maximum low counts by 52.5% and 23.9% respectively during treatment. A significant fall in platelet counts was seen in male patients after fifth cycle of treatment. With later on cycles female patients showed increased platelets counts.

Discussion

The haematopoietic cells are placed among the most rapidly dividing cells in the body, so are most sensitive to chemo-radiotherapy (Younis *et al.,* 2014). The various hematopoietic growth factors, commonly used to promote hematopoietic improvement following chemotherapy cannot prevent the occurrence of drug induced suppression of hematopoietic elements (Broudy, 1997). Although, occurrence of low platelets count is more common amongst the acute leukaemia patients but it also acts like a dose limiting factor for chemo-radiotherapy administration in solid malignancies too (Trinova *et al.,* 2007; Kuter, 2006; Elting *et al.,* 2001 and Cantor *et al.,* 2003). Approximately, 10-25% of malignant neoplasm patients that have been treated with intensive chemotherapy, suffer from incidence of thrombocytopenia (Dolan, 2000).

Anaemia is a common complication in cancer patients on treatment with chemo-radiotherapy. It is well associated with poor clinical outcomes (Younis *et al.,* 2015). Various supportive measures can be used to treat the anaemia such as erythropoiesis-stimulating agents, red blood cell transfusions, or both. In the current study no significant fall in heamoglobin levels was detected after 21 days of exposure to the therapy. The reason may be the appropriate use of additional supportive measures, along with the therapy.

As treatment with erythropoiesis-stimulating agents should not be considered until hemoglobin levels are less than 10 g/dl, oral preparation were given to the patients prophylectically (Beghe *et al.*, 2004).

Table 1: Showing Division of Patients into Groups

Groups	Number of Cycle
Group1	Before therapy
Group 2	First
Group 3	Second
Group 4	Third
Group 5	Fourth
Group 6	Fifth
Group 7	Sixth
Group 8	Random next subsequent cycle
Group 9	Random later on cycle

The TLC in both male and female patients, before and after treatment were analysed. The values of parameter were decreased in females by 3.1% with significant reduction in values in later on cycles. In addition TLC was increased in males by 16% after 21 days of first cycle of treatment with significant fall in counts on subsequent levels but improved counts were seen late in the treatment. These findings indicate the significant effects of therapy in cancer patient's hematology. Upon exposure to the radio and certain chemotherapeutic agents, significant fall in the TLC in the patient can be seen. And decreased TLC can further compromise the immune response in the patients (Spitz *et al.*, 2005). The first cycles of treatment has predictive value of leucocytic counts and can help in determining the patients who are at risk. And also helps in predicting neutropenic complications in later cycles as seen in female patients in the current study (Blay *et al.*, 1996; Silber *et al.*, 1998).

Table 2: Values of Haemoglobin (Hb gm%) Levels

Groups	Hb gm%		Significance (P Value)	
	M	F	M	F
Group1	11.7±2.1	9.6±1.6	No	No
Group 2	11.5±2.1	10.5±1.1		
Group 3	11.4±2.1	10.7±1.7		
Group 4	11.5±1.4	10.6±1.5		
Group 5	11.8±1.4	11.0±1.4		
Group 6	10.7±2.7	11.1±1.6		
Group 7	11.1±2.7	11.1±2.7		
Group 8	11.3±3.5	14.8±2.2		
Group 9	12.3±3.5	13.5±385		

Cytotoxic chemotherapy can further suppress the hematopoietic system hence can impair the protective mechanisms of host as well as limits the doses of chemotherapy. Neutropenia, the most serious hematologic toxicity, is associated with the risk of life-threatening infections as well as chemotherapy dose reductions and delay in the treatment.

After first cycle with chemo-radiotherapy a significant absolute neutropenia in female patients was observed with significant neutrophila was seen in males. On further cycles of treatment continuous significant reduction was seen with maximum reduction of ANC in later cycles. It shows that the anticancer therapy affects the neutrophils hence resulting in neutropenia. It is also in correlation with the literature that the patient's initial good hematologic response to chemotherapy is the risk factor for later neutropenic complications (Meza *et al.*, 2002). Our results were more or less similar with the findings of Blayney *et al.*, (1987) and Silber *et al.*, (1998).

Table 3: Values of TLC Levels in all Groups

Groups	TLC (× 10^9/L)		Statistical Analysis (P Value)	
	M	F	M	F
Group1	8.6±4.1	7.7±3.9		
Group 2	10.4±1.6	7.4±5.9	No	No
Group 3	8.2±3.2	6.9±3.3		
Group 4	7.2±2.5	6.7±3.3		
Group 5	7.7±5.6	6.2±2.7	Yes, 0.05	
Group 6	5.4±3.5	8.9±1.4	Yes, 0.01	
Group 7	11.7±2.5	13.7±2.0	No	
Group 8	10.3±4.5	10.4±1.3		
Group 9	16.4±8.3	4±1.3		0.009

In the current study, after first exposure to chemotherapy a statistically significant reduction in ALC was noticed in males with constant significant increase in ALC and AMC in next subsequent cycles. And it turned out to be very significant after further cycles. On the other hand, statistically insignificant fall in ALC was noticed in females. Studies done in the past have also shown decline in ALC during treatment (Iqbal *et al.,* 2015; Lissoni *et al.,* 2008). Increased ALC are positively correlated with good tumour immunity (Rana *et al.,* 2015). But recent research in the analysis of tumor immunobiology is emphasising that chemotherapy may play some important role by acting on anticancer immunity. A study conducted by Lissoni *et al.,* (2008) have shown that, the cancer patients who achieved tumor regression in response to chemotherapy had higher lymphocytic mean count at the end of the chemotherapeutic treatment with respect to the values seen before the onset of treatment. On the opposite, low counts of lymphocyte mean was observed in patients with slow or poor response (Lissoni *et al.,* 2008). As seen in current study male patients showed good neutrophilic response along with reduced ALC in early phase of treatment. And increased ALC, AMC was observed with subsequent cycles along with neutropenia in the later stages. It may be considered that male patients in the current study have shown good immune response on chemotherapy.

Table 4: Values of ANC in Various Groups

Groups	ANC (× 10^9/L)		Statistical analysis (p value)	
	M	F	M	F
Group1	6.0±0.9	5.1±0.4		
Group 2	8.3±0.3	4.7±1.9	Yes, 0.01	Yes, 0.02
Group 3	4.5±0.2	4.7±0.9	Yes, 0.05	No
Group 4	4.4±0.2	5.1±0.2	No	
Group 5	3.9±0.2	4.3±0.3	Yes, 0.01	
Group 6	1.5±0.2	5.1±0.5	Yes, 0.006	
Group 7	7.3±0.4	10.4±0.3	No	
Group 8	6.0±0.3	7.6±0.8		
Group 9	6.7±9.0	1.4±0.5		

In the current study the thrombocytopenia was noticed in males and females by 62.5% and 54.3 % decrease in platelets count in comparison to pre treatment counts with maximum low counts by 52.5% and 23.9% respectively. These finding are comparable with the results shown in the study done by Younis *et al.,* (2014). These results evidently reveal thrombocytopenia in the cancer patients when exposed to the radio and chemo therapy (Hassan, 2013). Therefore, a reduction in platelet count may primarily lead to incidence of bleeding that may range from mild to severe. Severe bleeding in the presence of thrombocytopenia or when coupled with other clotting disorders can lead to serious morbidity or death (Trinova *et al.,* 2007; Kuter, 2006; Elting *et al.,* 2001 and Cantor *et al.,* 2003).

Table 5: Values of ALC in Various Groups

Groups	ALC (× 10^9/L)		Statistical Analysis (P Value)	
	M	F	M	F
Group1	2.2±0.2	2.2±0.9		
Group 2	1.7±0.2	2.4±0.2	Yes, 0.006	No
Group 3	2.7±0.1	2.6±0.3	Yes, 0.02	
Group 4	2.3±0.1	1.6±0.2	No	
Group 5	3.0±0.1	1.6±0.3	Yes, 0.01	
Group 6	2.9±0.2	2.7±0.3	Yes, 0.01	
Group 7	3.7±0.2	2.8±0.2	No	
Group 8	2.5±0.1	2.1±0.4	No	
Group 9	9.0±1.0	1.4±0.7	No	

In short, at our institution complete blood counts has been used to assess the hematological parameter status of cancer patients after three weeks of exposure to therapy. It was observed that both the genders respond differently to the chemo-radiotherapy on subsequent cycles. It is also mentioned in the literature that different individuals respond differently to the same chemotherapeutic agent. Furthermore, other factors like genetic, physiologic, and environmental are also likely to contribute to variation in individuals. A range of clinical studies done in the past years have also suggested that population is a significant predictor of response to chemotherapy and side effects (Lavey *et al.*, 1994; Millward *et al.*, 2003).

Table 6: Values of AMC and AEC in Various Groups

Groups	AMC (× 10^9/L)		AEC (× 10^9/L) F		Significance (p value) (AMC)		(AEC)	
	M	F	M	F	M	F	M	F
Group 1	0.3±0.02	0.3±0.04	0.1±0.01	0.1±0.01	No	No	No	No
Group 2	0.2±0.03	0.2±0.06	0.2±0.02	0.1±0.04				
Group 3	0.2±0.06	0.1±0.03	0.1±0.01	0.1±0.04				
Group 4	0.3±0.04	0.3±0.04	0.1±0.01	0.2±0.04				
Group 5	0.5±0.06	0.2±0.06	0.3±0.01	0.1±0.04	Yes, 0.01	No	Yes, 0.01	No
Group 6	0.9±0.04	0.9±0.5	0.1±0.02	0.2±0.03	Yes, 0.01	No	No	No
Group 7	0.5±0.01	0.3±0.5	0.2±0.01	0.2±0.03	No	No	No	No
Group 8	0.6±0.08	0.4±0.8	0.2±0.01	0.3±0.02				
Group 9	0.5±0.10	0.1±0.4	0.2±0.26	0.03±0.002				

Conclusion

A lot of research work has already been done on the haematological side effects of chemo-radiotherapy and new techniques have been developed to make out these. The routine investigation of complete blood count is still an efficient as well as an economical tool to assess the hematological effects of therapy in cancer patients. The dissimilar host reaction was seen in males and females. Increased number of lymphocyte and monocytes are correlated with good hematological response for treatment. On the other hand leucopenia and neutropenia at first cycle of therapy is associated with poor hematological outcome late in the treatment.

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