

EFFECT OF CURCUMIN ON SIDE EFFECTS OF CHEMOTHERAPY AS ASSESSED BY COMPLETE BLOOD COUNTS, R.F.T., L.F.T. IN PATIENT OF HAEMATOLOGICAL MALIGNANCIES AND SOLID TUMOURS

Dr. Surendra Yadav¹, Dr Makkhan Lal Saini², Dr Sangeeta Gahlot³

¹Senior Resident, General Medicine, Shri Kalyan Govt Medical College, Sikar

²Associate Professor General Medicine, Shri Kalyan Government Medical College, Sikar Rajasthan

³Assistant Professor Microbiology, Shri Kalyan Government Medical College, Sikar, Rajasthan.

Article Info: Received 28 May 2021; Accepted 24 July 2021

DOI: <https://doi.org/10.32553/ijmbs.v5i8.2059>

Corresponding author: Dr. Surendra Yadav

Conflict of interest: No conflict of interest.

Abstract

Background: Effect of curcumin on side effects of chemotherapy as assessed by complete blood counts, R.F.T., L.F.T. in patient of haematological malignancies and solid tumours.

Methods: The study population consisted of male and female patients of Haematological Malignancies & patient of solid tumours (stage 3 & 4 lung, breast, head & neck, ovary Cancer) selected from patients attending medical, radiotherapy and Birla Cancer OPD and medical in-patient wards.

Results: Comparing of total leucocyte count, absolute neutrophil count and platelet count of group A1 and B1 at 1, 2, 3, 4, 8, 12, 16, 20 and 24 weeks, there is no significant difference found. Comparing of total leucocyte count and platelet count of group A2 and B2 at 4, 8, 12, 16, 20 and 24 weeks, there is no significant difference found.

Conclusion: No dose-limiting toxicities were seen in group-A for curcumin. Derangement of liver function tests occurred in 1 (5%) patients from group-A1 and 2 (10%) patients from group-B1. No renal toxicity was encountered in group-A1 and B1.

Keywords: Neutrophil, Leucocyte, Haemoglobin

Introduction

Acute lymphoblastic leukemia (ALL)¹ is a neoplasm of hematopoietic cells of the lymphoid lineage. Clonal expansion of aberrant T- or B-lymphoblasts manifests in the bone marrow, peripheral blood, & extramedullary sites. Rudolf Virchow was the first to use the term leukaemia in 1847, J.H Bennett and D. Craigie from Scotland, had first described cases of the disease². Leukemia comprises 32% of malignancies in children under 15. The majority are ALL. Each year approximately 2,400 children in the United States are diagnosed with ALL. An incident peak is seen between 2 - 5 years among children living in the Western world³. The annual incidence is 3.9 children under 15 years per 100,000⁴. Adult ALL is less common. The incidence decreases from age 15 until 50, when there is a 2nd, minor increase in new cases. A 3rd peak appears at age 80.

Curcumin decrease blood cholesterol; prevents low-density lipoprotein oxidation, inhibits platelet aggregation, reduces thrombosis and myocardial infarction; reduces symptoms associated with type II diabetes, rheumatoid arthritis, multiple sclerosis and Alzheimer's disease; inhibits HIV replication; improve wound healing; protects from liver injury; prevents cataract formation; protects from pulmonary toxicity and fibrosis, has therapeutic effects in leishmaniasis; and has antiatherosclerotic activity. Curcumin has potential in the prevention and treatment of various cancer.⁵

Material and Methods

The study population consisted of male and female patients of Haematological Malignancies & patient of solid tumours (stage 3 & 4 lung, breast, head & neck, ovary Cancer) selected from patients attending medical, radiotherapy and Birla Cancer OPD and medical in-patient wards.

Study type/ design: Hospital based Randomized control trial pilot study

Study place: Medical OPD and wards, Leukaemia Lymphoma Clinic at Birla Cancer Centre, S.M.S. Hospital, Jaipur.

Duration of study: 12 months

Case: Newly diagnosed 20 patient of Haematological Malignancies & 20 patient of solid tumours (stage 3 & 4 lung, breast, head & neck, ovary Cancer) of both sex receiving myelo-suppressive chemotherapy.

Controls: Newly diagnosed, age, sex, stage of carcinoma and type of carcinoma matched 20 patient of Haematological Malignancies & 20 patients of solid tumours.

Sample size: Expecting 20% decreasing in common side effect experienced by cases, (eg. 100% control v/s 80% case). The sample size required detecting this difference in

side effect at 95% confidence interval and 80% power is 40 in each group (40: 40).

• **Inclusion criteria :**

1. Newly diagnosed, chemo-naive Patients of haematological malignancies (acute leukemia, high-grade NHL, Hodgkin's lymphoma) and solid tumours planned to be given myelo-suppressive chemotherapy.

• **Exclusion Criteria:**

1. Patients of haematological malignancy and solid tumours of both sexes already completed chemotherapy/ radiotherapy.

2. Patients unable to give informed consent.

3. Patients who are allergic/intolerant to curcumin.

4. Patients with severe systemic CV, hepatic or renal disease or uncontrolled infection.

Curcumin will be started in dose of 250 mg/day

• Patients will be randomized by computer generated random number table to receive standard chemotherapy or standard chemotherapy plus oral curcumin.

Results

Table 1: Compare total leucocyte count in group A1 and B1

Group	1 st week	2 nd week	3 rd week	4 th week
Group A 1	5.26	3.13	2.94	4.25
Group B1	6.82	3.44	3.34	4.69

Table 2: Compare total leucocyte count in group A 1 and B 1

Group	4 th week	8 th week	12 th week	16 th week	20 th week	24 th week
Group A1	4.25	6.02	5.25	6.47	5.08	4.73
Group B1	4.69	5.68	3.96	4.66	4.07	4.24

Table 3: Compare Absolute Neutrophil Count (ANC) In Group A1 and B1

Group	1 st week	2 nd week	3 th week	4 th week
Group A 1	1.27	1.25	1.05	2.4
Group B 1	1.76	1.51	1.49	2.42

Table 4: Compare platelet in group A1 and B1

Group	1 st week	2 nd week	3 rd week	4 th week
Group A 1	1.03	1.07	1.27	1.96
Group B 1	0.69	0.88	1.15	1.61

Table 5: Compare total leucocyte count in Group A2 and B2

Group	4 th week	8 th week	12 th week	16 th week	20 th week	24 th week
Group A 2	6.65	7.15	7.12	7.27	7.1	7.27
Group B 2	6.04	6.4	6.87	6.67	6.61	5.88

Table 6: Compare platelet count in Group A2 and B2

Group	4 th week	8 th week	12 th week	16 th week	20 th week	24 th week
Group A 2	2.75	2.71	2.97	2.79	2.93	2.92
Group B 2	2.59	2.83	2.68	2.64	2.53	2.45

No dose-limiting toxicities were seen in group-A for curcumin. Derangement of liver function tests occurred in 1 (5%) patients from group-A1 and 2 (10 %) patients from group-B1. No renal toxicity was encountered in group-A1 and B1.

Discussion

The present study was a hospital based, randomized, open label, comparative pilot study, conducted over the period of one year. The study consisted of 40 patients of Acute

lymphoblastic leukemia and 40 patients of solid malignancy (lung carcinoma and breast carcinoma). All the cases were further divided into two groups, by computer generated random number generator, one receiving curcumin plus chemotherapy in group A and the other receiving chemotherapy only in group B. All the cases were evaluated in follow-up visits by routine blood investigations, quality of life questionnaire- FACT-leu & EQ-5. Out of 80 patients, 20 patients in group A 1 (Acute lymphoblastic leukemia receiving curcumin plus chemotherapy), 20

patients in group A 2 (solid malignancy receiving curcumin plus chemotherapy) , 20 patients in group B1(Acute lymphoblastic leukemia receiving chemotherapy only) and 20 patients in group B 2 (solid malignancy receiving chemotherapy only). Of 20 patients in each group, males were 60% in group-A 1 and 75% in group-B1.

In this study we compared haemoglobin, total leucocyte count, absolute neutrophil count and platelet count of group A1 and B1 at 1, 2, 3, 4, 8, 12, 16, 20 and 24 weeks, and no significant difference was found. After 1 weeks, comparison of mean scores between both groups were – haemoglobin (8.44 vs. 7.89), total leucocyte count (5.26 vs. 6.82), absolute neutrophil count (1.27 vs. 1.76), platelet count (1.03 vs. 0.69). After 2 weeks, comparison of mean scores between both groups were – haemoglobin (8.8 vs. 8.02), total leucocyte count (3.13 vs. 3.44), absolute neutrophil count (1.25 vs. 1.51), platelet count (1.07 vs. 1.61). After 3 weeks, comparison of mean scores between both groups were – haemoglobin (8.82 vs. 8.46), total leucocyte count (2.94 vs. 3.34), absolute neutrophil count (1.05 vs. 1.49), platelet count (1.27 vs. 1.15). After 4 weeks, comparison of mean scores between both groups were – haemoglobin (9.65 vs. 8.94), total leucocyte count (4.25 vs. 4.69), absolute neutrophil count (2.4 vs. 2.42), platelet count (1.96 vs. 1.61). After 8 weeks,; comparisons of mean scores between both groups were – haemoglobin (10.5 vs. 9.88), total leucocyte count (6.02 vs. 5.68), absolute neutrophil count (3.85 vs. 3.27), platelet count (2.4 vs. 2.45). After 12 weeks, comparison of mean scores between both groups were – haemoglobin (10.65 vs. 9.88), total leucocyte count (5.25 vs.3.96), absolute neutrophil count (3.03 vs.2.49), platelet count (2.47 vs.2.49). After 16 weeks, comparison of mean scores between both groups were – haemoglobin (10.53 vs. 10.1), total leucocyte count (6.47 vs. 4.66), absolute neutrophil count (4.23 vs. 2.8), platelet count (2.68 vs. 2.49). After 20 weeks, comparison of mean scores between both groups were – haemoglobin (10.43 vs. 10.5), total leucocyte count (5.08 vs. 4.07), absolute neutrophil count (2.79 vs. 2.46), platelet count (2.73 vs. 2.46). After 24 weeks, comparison of mean scores between both groups were – haemoglobin (11.41 vs.10.8), total leucocyte count (4.73 vs. 4.24), absolute neutrophil count (2.17 vs. 2.05), platelet count (2.88 vs. 2.09).

In our study Curcumin **dose** was **125 mg BD** but oral bioavailability of the curcumin is less, so low dose may be a possibility of insignificant result.

Song WB et al⁵. The experiment was carried out using 4 groups of rats, namely the normal control group, enteritis model group, sulfasalazine (SASP) group and curcumin group. Exception of the rats in the normal control group, all rats were subjected to intraperitoneal injection to induce

enteritis and received subsequent daily intragastric administration of SASP (100 mg/kg), curcumin (100 mg/kg), or normal saline for 5 days. Methotrexate induces increased mucosal permeability of the small intestines in rats, and curcumin may offer protective effects against MTX-induced rat enteritis by lowering the intestinal mucosal permeability.

Hussain AR et al⁶ investigated the effect of curcumin on the activation of apoptotic pathway in T-cell acute lymphoblastic leukemia (T-ALL) malignant cells. They demonstrate that curcumin causes dose dependent suppression of proliferation in several T cell lines. Treatment of T-ALL cells with curcumin down-regulated the expression of inhibitor of apoptosis protein (IAPs). This study suggest that curcumin suppresses constitutively activated targets of PI3'-kinase (AKT, FOXO and GSK3) in T cells leading to the inhibition of proliferation and induction of caspase-dependent apoptosis.

Conclusion

Comparing of total leucocyte count, absolute neutrophil count and platelet count of group A1 and B1 at 1, 2, 3, 4, 8, 12, 16, 20 and 24 weeks, there is no significant difference found.

References

1. Bennett JH (1980) Classics in oncology. Two cases of disease and enlargement of the spleen in which death took place from the purulent matter in the blood. *CA Cancer J Clin* 30: 59-62
2. Greaves M (2006) Infection, immune responses and the aetiology of childhood leukaemia. *Nat Rev Cancer* 6: 193-203
3. Gustafsson G, Schmiegelow K, Forestier E, Clausen N, Glomstein A, Jonmundsson G, Mellander L, Makiperna A, Nygaard R, Saارينen-Pihkala UM (2000) Improving outcome through two decades in childhood ALL in the Nordic countries: the impact of high-dose methotrexate in the reduction of CNS irradiation. *Nordic Society of Pediatric Haematology and Oncology (NOPHO). Leukemia* 14: 2267-2275
4. Prescott S. Is cyclooxygenase-2 the alpha and the omega in cancer? *J Clin Invest.* 2000;105: 1511-3.
5. Aggarwal S, Ichikawa H, Takada Y, Sandur SK, Shidhodia S, Aggarwal BB. Curcumin (diferuloylmethane) down-regulates expression of cell proliferation and antiapoptotic and metastatic gene products through suppression of I kappaB-alpha kinase and Akt activation. *Mol Pharmacol.* 2006; 69:195-206.