Original Article

Effect of Glucantime on blood factors in patients with cutaneous leishmaniasis

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Abstract

Background

Glucantime is the first line agent for treatment of cutaneous leishmaniasis (CL). It has adverse effects on blood elements. This research has been done to evaluate the blood complications of this medicine in patients with cutaneous leishmaniasis.

Methods

This clinical trial was done at Nikpour clinic, Yazd, Iran. Blood samples were collected from patients diagnosed with CL before treatment and after receiving 20 mg/kg intramuscular glucantime. Injection every day for 20 days. Full cell blood count was done for all patients. Statistical analysis of data was achieved by paired-T-test using SPSS software (version 13).

Results

The blood tests results showed glucantime significantly decreased RBC, PLT, WBC (except monocytes), Hb and Hct ($P< 0.05$).

MCH and PMN decreased but not significantly. MCV, MCHC and eosinophil count increased but not significantly. No correlation was seen between laboratory test results and patients' age and sex.

Conclusion

Glucantime affected the blood indices and it was suggested to use other alternating therapy. Future study with bigger sample size should be done for the more clear results.

Keywords

Glucantime, Cutaneous leishmaniasis, Blood

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Introduction

Cutaneous leishmaniasis (CL) causes by Leishmania Tropica and is common in tropic and subtropic areas and in southern Europe (1). More than 90% of the world's cases of cutaneous leishmaniasis occur in Afghanistan, Algeria, Iran ,Iraq, Saudi Arabia, Syria, Brazil an Peru (2). In urban areas of Iran such as Mashhad, Neishapour, Shiraz, Kerman, Qom, Saveh, Isfahan, Kashan and Sabzevar, this disease is common. In some rural areas of Isfahan, Sarakhs, Torkaman Sahra, Lotfabad, Espherein, Ahwaz, Desful, Shoosh, Soosangerd and Abadan also it is commom. Leishmania Tropica transmits to human by sand fly (3). Treatment of this disease is medical therapy, cryotherapy, heat therapy, surgery and cauterization (4-6). The drug of choice used in medical therapy are pentavalent antimony compounds like pentostam and glucantime (7-8). These medicines could cause not only changes in blood indices also renal, hepatic, cardiac, gastrointestinal and pancreatic side effects (9). In order to indicate the side effect of glucantime on blood indexes, this study was conducted in patients referred to Nikpour clinic.

Materials and Methods

This clinical trial was done at Nikpour clinic, Yazd, Iran. Blood samples were collected from patients diagnosed with CL before and after treatment in order to compare any blood indices changes. Final diagnosis of Cl was done by histopathological finding of the ulcer. Blood samples were collected from patients before treatment and each patient received 20 mg/kg intramuscular injection of the glucantime every day for 20 days. On the last day of therapy, blood test was done again and the result was compare with result of the test before treatment. The variables considered in this research were age, sex and blood indices. The exclusion criteria were patients with diabetes mellitus, other infectious diseases, corticosteroid therapy and other known hematological diseases. Cell blood count and cell differentiation were done before and after treatment for all patients, and they were compared by paired t-test.

Results

Out of 30 patients, 18(60%) were male and 12(40%) female with an the mean age of 26.72 years old (9 to 42.5 years). The results of present study indicated that the number of RBC, PLT, WBC, Monocytes and PMN decreased. Hb, Hct and MCH also decreased. However, MCV and MCHC increased and the number of Lymphocyte and eosinophils also increased .The mean changes of indices for RBC, PLT, WBC, monocyte, HB, and HCT were significantly decreased ($PV<0.05$). However, PMN and MCH were not significantly decreased. The lymphocytes were increased significantly ($PV<0.05$). However, MCV, MCHC, eosinophil were not increased significantly.

Table 1 showed blood indices before and after treatment. Table 2,3 showed the blood indices change according to the age and sex of the patients.

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Table 1: Changes of blood indices after treatment with Glucantime

Stage / Blood factors	Before treatment		After treatment		Changes		P.value
	SD	X	SD	X	CI95%	Median	
RBC $\times 10^6$ /µl	0.6	5.1	0.5	4.9	-0.13-0.24	- 0.19	0.000
PLT $\times 10^3$/µl	33.1	230.4	33.4	222	-6.3- -10.4	- 8.4	0.000
WBC $\times 10^3$/µl	1.1	7.3	0.8	6.5	0.61-0.98	- 8.4	0.000
MONO%	1.1	5.1	1.5	4.4	0.49-0.97	-0.8	0.000
POLY %	4.2	59.2	4.6	57	0.05- 0.71	- 0.33	0.086
Hct%	4.9	41.4	2.5	40.08	0.3-2.3	- 1.3	0.013
Hb g/dl	2.1	14.65	2	13.99	0.53-0.78	- 0.6	0.000
MCH /pg	1.8	28.8	1.7	28.7	0.11-0.21	- 0.05	0.528
MCHCg/dl	1.3	33.2	1.3	33.2	0.23-0.06	- 0.08	0.274
MCV / fl	7.6	82	4.7	84	4.2-0.22	2	0.076
EOS %	1.5	3	1.5	3.1	0.4-0/13	0.1	0.326
LYMPH %	4.9	32.2	3.9	34.9	3.4-1.9	2.6	0.000

Table 2: Comparison changes of blood indices in two age groups

Age group / Blood indices	N=17 > 25 years		N=13 ≤ 25 years		P.value
	SD	M	SD	M	
PLT $\times 10^3$/µl	4.8	-8.7	6.3	-8	0.713
WBC $\times 10^3$/µl	0.51	-0.76	0.49	0.84-	0.667
MONO%	- 0.77	0.70	0.42	0.76	0.793
POLY %	1.1	- 0.29	0.96	0.38	0.816
Hct%	2.7	-1.04	2.8	-1.6	0.553
Hb g/dl	0.16	0.54	0.42	-o.8	0.053
MCH /pg	0.53	-0.13	0.19	0.06	0.177
MCV / fl	6.5	2.9	5.9	0.81	0.350
MCHC g/dl	0.48	0.11	0.28	0.04	0.651
EOS %	0.69	0.11	0.8	0.15	0.896
LYMPH %	1.3	2.7	2.3	2.6	0.896

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Table 3: Comparison changes of blood indices in two sex group

Sex / Blood indices	N=18 male		N=12 female		P.value
	SD	M	SD	M	
Diff-PLT×10³/µl	6.1	-8.8	4.4	-7.8	0.631
WBC×10³/µl	0.6	-0.86	0.26	0.7-	0.315
MONO%	0.59	0.66	0.71	0.8	0.494
POLY %	1.02	- 0.11	0.98	0.66	0.150
Hct%	2.8	-1.01	2.5	-1.8	0.451
Hb g/dl	0.11	0.6	0.49	-o.74	0.371
MCH /pg	0.45	-0.11	0.38	0.04	0.348
MCV / fl	5.6	1.6	6.6	2.5	0.713
MCHC g/dl	0.32	0.005	0.5	0.2	0.256
EOS %	0.73	0.22	0.73	0.00	0.434
LYMPH %	1.1	3	2.5	2.1	0.227

Discussion

The relation between age, sex and the changes of blood indices were not statistically significant. In 1997, one study by Talari in Kashan, Iran showed that in WBC, RBC, PLT, monocyte, Hb, Hct and neutrophile decreased (6). Variables that increased were ESR, MCV, MCH, MCHC, and eosinophil and basophil, lymphocyte.

The decrease in Hb and Hct in this study compared to prior studies was statistically significant. Unlike the previous study, a decrease in PMN, and MCH was seen, yet both studies were unremarkable. In 1992, Alkhawaya and et al in Saudi Arabia (7) conducted a similar study in laboratory mice and they found out that the decrease of Hb ant Hct, yet there were no data showing changes with in MCH, MCHC and RBC (7) .A year later, Soto et al. in Spain and in 1992 Berman et al. in England studies the side effect of the Glucantime on leukocyte of the patients diagnosed cutaneous leishmaniasis. The result from these studies showed a decrease in some blood elements (10, 11). Mechanism of action of glucantime is inhibition of phosphofructokinase enzyme which has specific role in glycolytic activities in neutrophils which stays active temperature of 37c (36$\pm$2). Blockage of this enzyme can result in decrease of ATP production, which lowers the WBC half-life and decrease the number WBC in the period of treatment with Glucantime (12). In addition, the main cause of leukocyte decrease can be due to the concurrent decrease of monocyte within treatment. Since the role of monocyte plays a controlling aspect within this disease, it is predictable that there will be an increase prior to treatment and decrease after treatment. RBC decrease seems to be because of the phosphofructokinase inhibition resulting glycolytic metabolic disorder as a ATP main source of energy. The hereditary deficiency of this enzyme can cause hereditary non spherocytic hemolytic anemia(6).

In the study conducted in Kashan-Iran, the reason why the was not an decrease in Hb and Hct can be due to the other mechanism such as RBC releasing as reticulocytes(high MCH & MCV).However, our study showed a decrease in Hb & Hct, which was scientifically significant without any reasonable mechanism . In the Kashan study, the increase in ESR was not high enough to make a significant different in the final results of the study, and in the case of lymphocytes, there was an increase but not as much where we can categorize it as lymphocytosis, where as in our study, lymphocyte increase where at the level that it was significant with a unknown reason.

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Conclusion

Although we included a limited number of samples in our study, it can be said that glucantime can effect the blood indices during the 20 days of therapeutic period and our recommendation would be using different approaches such as cryotherpy, heat therapy and other alternating drugs for the patients with hemotologic underline disease.

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