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The effect of Aloe vera syrup on prevention of fever and neutropenia in children with acute lymphoid leukemia

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Abstract

Background: Given that few studies regarding the effect of Aloe vera (A. vera) on prevention of fever and neutropenia on acute lymphoid leukemia (ALL) disease, the aim was to evaluate the effect of A.vera on prevention of fever and neutropenia in children with ALL.

Materials and Methods: This randomized clinical trial study was conducted on 60 children with mean age 5.6± 2.9 years in Oncology department of Shahid Sadoughi hospital during 2018-2019. All these children were underwent chemotherapy. Then, the patients were randomly classified into two groups. The first group received 10 ml A. vera syrup (0.5 mg/ml) for 30 days (case group) and the second group did not receive A. vera syrup (control group). Complete blood count (CBC) tests and frequency of fever, infection, neutropenia, and hospitalization were evaluated in case and control groups before and after intervention. Wilcoxon, T test, and Chi Square test were used for data analysis.

Results: Significant reduction was observed in case group in comparison with control group regarding the frequency of fever (0.19 ±0.107 vs 1.07±0.206), infection (0.81 ±0.2 vs 1.87± 0.236), hospitalization (0.37±0.178 vs 1.33 ±0.187), and neutropenia (0.11± 0.062 vs 0.80 ± 0.2) ($p<0.01$). Moreover, significant increase was observed in case group in comparison with control group considering neutrophil count (2597.5±243.1 vs 1106.53±161.6) and white blood cell (WBC) (4062.96 ± 276.6 vs 2566.67 ±175.5) ($p<0.01$). In addition, recovery of appetite was significantly greater in case group than control group ($p=0.023$). Furthermore, significant difference was observed in case group before and after intervention regarding these parameters ($p<0.05$).

Conclusion: According to findings, A. vera consumption decreased frequency of infection, neutropenia, fever, and hospitalization and increased WBC and neutrophil count. Moreover, appetite was improved in these patients. Therefore, it seems that A.vera can be used for improving quality of life in children with ALL.

Keywords: Acute lymphoid leukemia, Aloe vera, Fever, Neutropenia

Introduction

Leukemia is the main cancer in the body's blood-forming tissues (1-3). Acute lymphoblastic leukemia (ALL) is the most prevalent type of leukemia among children (2, 3). The incidence peak of ALL in children is in age range of 2-5 years old. About 6000 new cases of ALL are diagnosed annually in the United States (1,4,5). This disease occurs due to interaction of endogenous and exogenous and genetic susceptibility (1).

The survival rate of ALL children in the world has been improved approximately 90 % (1, 5). A main complication after intensive chemotherapy in children with

ALL is febrile neutropenia (6). The majority of infections in febrile neutropenia are due to fungal and bacterial infections (7). Viral infections are responsible for 34 % of proven infections in febrile neutropenia (7). There is a significant difference between countries, regions, and centers in terms of involved microorganisms in the etiology of febrile neutropenia (8). Treatment of febrile neutropenia by efficient drugs reduces morbidity and mortality (1). On the other hand, appropriate initiation of therapies have main role in febrile neutropenia attacks (6). Recently, the use of medicinal herbs as a medicinal and nutritional supplement for improving general health and treatment of diseases has taken into consideration (9). Aloe vera (A. vera) plant is originated from arid climates of North Africa (10). It is a succulent cactus like perennial plant with 275 species worldwide. Antiviral, antifungal, and anti-neoplastic activities of A. vera are specified in studies (10). Moreover, A. vera is used against bacteria, including Pseudo-monas, Escherichia coli, Salmonella Staphylococcus, Streptococcus, Klebsiella, Pseudo-monas, etc. In addition, A. vera can have a significant role in the improvement of neutropenia-induced fever as one of the major complications after chemotherapy due to its strong stimulatory effects on the immune system and anti-inflammatory effects (11). Given the high prevalence of ALL in Iran, especially Yazd province(1), the use chemotherapy as the first line of treatment and few studies in this regard, the aim of current study was to evaluate the effect of A.vera syrup on prevention of fever and neutropenia in children with ALL referred to pediatric oncology ward of Shahid Sadoughi hospital.

Materials and Methods

This randomized clinical trial study was conducted 60 children hospitalized in Oncology department of Shahid Sadoughi hospital, Yazd, Iran, during 2018-2019. These children were underwent chemotherapy with a treatment protocol. After taking consent from parents of children, this study was approved by Shahid Sadoughi University of Medical Sciences (number: IR.SSU.MEDICINE.REC.1396.187). Then patients were randomly classified into two groups. The first group (group 1) received 10 ml A. vera syrup (0.5 mg/ml) for 30 days (case group) and the second group (group 2) did not receive A. vera syrup (as control group). Complete blood count (CBC) tests were done by Sysmex cell counter (k-21, Japan) in all patients. Moreover, parameters such as frequency of fever, infection neutropenia, and hospitalization were evaluated in case and control groups. Moreover, these parameters were assessed before and after intervention. Children's appetite was assessed in all patients.

Statistical analysis

Data were entered SPSS, version 19. Wilcoxon Test, T test, and Chi Square test were used for analysis of data. $P < 0.05$ was considered statistically significant.

Results

The mean age of patients in case and control groups was 5.5 ± 1.975 and 5.37 ± 3.404, respectively ($p=0.882$). Comparison of two groups in terms of frequency of fever, infection, hospitalization, sever neutropenia, neutrophil, and WBC count is shown in Table I. As shown in Table I, a significant reduction was observed in case group in comparison with control group regarding frequency of fever, infection, hospitalization, and neutropenia ($p<0.01$). Moreover, a significant enhancement was seen in case group compared to control group regarding neutrophil and WBC count ($p<0.01$). Table II shows comparison of each group before and after treatment in terms of the frequency of fever, infection, hospitalization, sever neutropenia, neutrophil, and WBC count. As shown in Table II, a significant reduction was observed after intervention regarding the

frequency of fever, infection, hospitalization, and neutropenia ($p<0.01$). Moreover, a significant enhancement was seen after intervention regarding neutrophil and WBC count ($p<0.01$). Comparison of patients in second group (end of first and second month), in terms of frequency of fever, infection, hospitalization, sever neutropenia, neutrophil, and WBC count, is shown in Table III. As shown in Table III, there was no significant difference at end of first and second months in terms of frequency of fever, infection, hospitalization, sever neutropenia, neutrophil, and WBC count ($p> 0.05$).

Comparison of two groups in terms of appetite is shown in Table IV. As demonstrated in Table IV, a significant difference was observed between two groups regarding appetite ($p<0.05$). In this regard, recovery of appetite was significantly greater in case group than control group.

Table I: Comparison of two groups in terms of frequency of fever, infection, hospitalization, sever neutropenia, neutrophil, and white blood cell (WBC) count

Parameters	Group	Mean ± SD	P-value
Fever	Case	0.19 ±0.107	≤ 0.001
	Control	1.07±0.206	
Infection	Case	0.81 ±0.2	0.002
	Control	1.87± 0.236	
Hospitalization	Case	0.37±0.178	≤ 0.001
	Control	1.33 ±0.187	
Sever Neutropenia	Case	0.11± 0.062	0.001
	Control	0.80 ± 0.2	
Neutrophil count	Case	2597.5±243.1	≤ 0.001
	Control	1106.53±161.6	
WBC count	Case	4062.96±276.6	0.001
	Control	2566.67 ±175.5	

Table II: Comparison of case group before and after treatment in terms of the number of fever, infection, hospitalization, sever neutropenia, neutrophil and WBC count

Parameters	Group	Mean ± SD	p-value
The number of fever	Before intervention	0.96 ± 0.136	≤ 0.001
	After intervention	0.19 ±0.107	
The number of infection	Before intervention	1.56 ±0.209	0.002
	After intervention	0.59 ± 0.2	
The number of hospitalization	Before intervention	1.15±0.205	≤ 0.001
	After intervention	0.37±0.178	
The number of sever Neutropenia	Before intervention	0.78± 0.111	≤ 0.001
	After intervention	0.11± 0.062	
The number of neutrophil count	Before intervention	1609.07 ±179.4	≤ 0.001
	After intervention	2597.59 ±3243.1	
The number of WBC count	Before intervention	2862.9±184.1	0.001
	After intervention	4062.96±276.6	

Table III: Comparison of patients in second group (after two months) in terms of frequency of fever, infection, hospitalization, sever neutropenia, neutrophil, and WBC count

Parameters	Months	Mean ± SD	p-value
Fever	End of first month	0.93 ± 0.182	0.48
	End of second month	1.07 ±0.206	
Infection	End of first month	1.80 ±0.262	0.78
	End of second month	1.87 ± 0.236	
Hospitalization	End of first month	1.40±0.235	0.70
	End of second month	1.33 ±0.187	
Sever neutropenia	End of first month	0.80± 0.175	1
	End of second month	0.80 ± 0.2	
Neutrophil count	End of first month	1010.8 ±158.6	0.86
	End of second month	1106.53 ±161.6	
WBC count	End of first month	2593.33 ±181.9	0.9
	End of second month	2566.67 ±175.5	

Table IV: Comparison of two groups in terms of appetite

Group	Recovery of appetite	Not recovery of appetite	p-value Chi-Square test
Case	16 (59.3 %)	11 (40.7 %)	0.023
Control	3 (20 %)	12 (80 %)	
Total	19 (45.2 %)	23 (54.8 %)	

Discussion

Fungal infections and febrile neutropenia are the most common causes of mortality in children with ALL (6). Among these infections, bacterial infections are the most common than others. However, other studies reported that fungal infections were seen in 50% of cases of blood malignancies (12,13). In children with ALL receiving treatment, the mortality related to infection decreased using appropriate antibacterial agents (12,13). Increasing incidence of bacterial resistance to antibiotics and the side effects of these drugs were factors in the expansion of research on medicinal plants in recent years. Despite various studies on the different properties of A. vera, few studies were performed on the antimicrobial properties of this plant in our country (14). A. vera was widely used in herbal medicine as antifungal, antibacterial, antiviral, and anti-inflammatory agents.

In the current study, the use of A. vera decreased infection, neutrophil count, and WBC count. Recently, several studies have been conducted to investigate the role of A. vera for treating blood disease and cancer associated with low WBC (10). Olatunya et al., assessed the effect of A. vera on HIV infection. In this regard, patients consumed antiretroviral drugs with 30–40 mL of A. vera and findings revealed that consumption of A. vera may be useful for HIV-infected individuals (15). Ghadiri et al., revealed antibacterial effects of A. vera on bacterial pathogens of human and animals (16). In addition, Puch et al., reported that the antibacterial component of A. vera was effective against Escherichia coli, Aureus, Streptococcus pyogenes, and P. aeruginosa (17). Sadr et al., also demonstrated that the aqueous extract of A. vera had an equivalent or better effect than common antibiotics on important infectious bacteria isolated from patients (14). Channa et al., reported that A. vera extraction increased the lymphocyte concentration in rabbit. Lymphocytes play a main role in

developing T cell immune and humorai response against foreign antigens, such as viral and bacterial antigens. It seems that acemannan molecule in the aloe gel stimulates the body to produce WBC to fight disease, especially macrophages. These compounds digest unwanted substances, including viruses and bacteria (10).

Other studies revealed that phagocytic activity of recticuloendothellial system was activated in the presence of A. vera (18). Moreover, A. vera increased the cellular and humoral immunity via different mechanisms (19). In addition, improvement of B lymphocyte which is responsible for organization of immunoglobulins M and G has been seen in the presence of A. vera. Furthermore, A. vera can enhance CD8 and CD4 receptor (20). Therefore, increase of lymphocyte may be due to the presence of proteins and glycoproteins with low molecular weight and mitogenic effect, causing proliferation of immune cells (10).

In addition, we observed significant increase in appetite in case group. Mahdavi et al., achieved the same result and reported that A. vera extraction stimulated appetite (21). Chatterjee et al., reported that A. vera was used in treatment of patients with poor appetite (22). Furthermore, fever was decreased in case control compared to control group. Sharma et al., revealed that A. vera reduced fever (23).

Conclusion

According to these findings, A. vera consumption decreased frequency of infection, neutropenia, fever, and hospitalization and increased WBC and neutrophil count. Moreover, appetite was improved in these patients. Therefore, it seems that A.vera can be used for improving quality of life of children with ALL. In addition, there was no significant difference between these parameters at end of first and second months.

Conflict of interest

Authors declared no conflict of interest.

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