

## The effect of echinacea in the prevention of upper respiratory infections in children with acute lymphoblastic leukemia

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### Abstract

**Background:** The efficacy of echinacea products to treat upper respiratory tract infections (URTI) has been shown in some studies, however, there are few studies considering the efficacy of echinacea to prevent URTI. Therefore this study aimed to assess the effect of echinacea in the prevention of URTI in these children.

**Materials and Methods:** This retrospective cross-sectional study was conducted on 60 children with ALL in Shahid Sadoughi hospital from September 2020 to September 2021. These Children were divided into two groups (n=30). The case group received immunogen syrup, containing echinacea purpurea root extract (200 mg/ml). This syrup was prescribed in the intervention group as 2 ml for children in the age range of 2-8 years and 0.5 ml for children in the age range of 1-2 years old for 3 months. The control group did not receive echinacea syrup. These patients were followed for 3 months regarding URTI.

**Results:** The frequency of URTI in the case and control groups was 40% and 66.7%, respectively, and a significant difference was noted between the two groups in terms of the frequency of URTI ( $P<0.05$ ). Moreover, 23.3% of patients who received echinacea developed a second URTI, while 53.3% of patients who did not receive echinacea developed a second URTI ( $P<0.05$ ). The mean time for the second URTI in the case and the control groups was  $42.3\pm13.93$ , and  $48.3\pm13.96$  days, respectively ( $P=0.086$ ). Regarding reducing the duration of URTS symptoms, there was no significant difference between the two groups ( $P>0.05$ ).

**Conclusion:** According to the results, echinacea can be effective in decreasing the occurrence of URTI in these children. Therefore, regarding the efficacy of echinacea in decreasing URTI, it is recommended to use echinacea in the prevention of URTI.

**Keywords:** Acute lymphoblastic leukemia, Echinacea, Upper respiratory infections

### Introduction

Acute lymphoblastic leukemia (ALL) is the most prevalent type of leukemia among children (1-4). It occurs due to the interaction of genetic susceptibility as well as endogenous and exogenous factors (3). Major advances in the treatment of childhood ALL have led to a 92% survival rate over the past decades (5), but infection complication is a significant reason for mortality and morbidity in these children (6). Moreover, despite progress in cancer treatment and outcomes during recent years, respiratory viral infections are

barriers to the success of antineoplastic therapy (7-10). Respiratory viral infections and incidence of coinfections are high in pediatric cancer patients (7). On the other hand, respiratory viruses are the main cause of acute respiratory infections in children with cancer and should be considered an important etiology of febrile neutropenia and hospital admissions. The data showed that viral infections are associated with 86.5% of febrile episodes in patients with pediatric cancer (7). Acute respiratory infections are classified into upper respiratory tract infection (URTI) or

lower respiratory tract infection (LRTI) (6). URTIs include acute infections of the pharynx, nose, sinuses, and larynx (11). Echinacea is the family of Asteraceae, known as purple coneflower (12). Three species of echinacea including echinacea purpurea, echinacea Angustifolia, and echinacea pallida, (13) have been applied in the United States and Europe (12). On the other hand, this plant is a herbal medicine used by Native Americans to increase the human immune system. Echinacea was introduced as the most popular herbal supplement in 2012 used by the US adults (14-16) and the annual sale of echinacea in the US alone was in the range of \$10 - \$100 million.

Flavonoids, alkyl amides, polysaccharides, chicoric acid, polyacetylenes, and essential oils are the active components of echinacea (12). Its antiviral and antibacterial activity has been demonstrated in some studies (12). Moreover, it has been applied to preventing and treating URTIs (17). The beneficial effect of echinacea may be due to immunomodulating activity (17). In addition, products of echinacea are the most popular herbal immunostimulants in Europe and North America (12).

There are many studies considering the efficacy of different echinacea products to treat URTI (13, 17). But there are limited data on the prevention of this medicine, especially in pediatric patients with ALL. Therefore, according to these findings and due to the increase of ALL in children in Iran, especially Yazd province (3), and no comprehensive study regarding the effect of echinacea in preventing URTI in children with ALL in our country, this study aimed to assess the effect of echinacea in the prevention of URTI in children with ALL.

## Materials and Methods

This retrospective cross-sectional study was conducted on 60 children with a definitive diagnosis of ALL in Shahid Sadoughi hospital from September 2020 to September 2021. These children were

divided into two groups (n=30). The two groups were matched in terms of age, sex, and duration of disease. The first group received immunogen syrup (containing echinacea purpurea root extract, 200 mg/ml) (Kimiagar tos Company). This syrup was prescribed in the intervention group as 2 ml for children in the age range of 2-8 years and 0.5 ml for children in the age range of 1-2 years old for 3 months. Then, they were followed for 3 months in terms of URTI in the two groups (9). URTI symptoms were sneezing, coughing, runny nose, fever, Sore throat, and acute sinusitis. Sometimes these symptoms appeared in combination.

## Inclusion and exclusion criteria

Exclusion criteria included the history of an underlying disease, including chronic heart disease, kidney disease, chronic respiratory disease such as asthma, recurrence of cancer, receiving echinacea during the last 3 months, and the unwillingness of the parents.

## Statistical analysis

Data were entered into SPSS, version 19. The chi-square test and Independent T-test were used for the analysis of data. P-value < 0.05 was assumed significant.

## Ethical consideration

This study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.MEDICINE.REC. 1393.5).

## Results

In the current study, the mean age of patients was  $8.6 \pm 2.4$  years old. In addition, 26, and 24 patients were boys and girls, respectively. As shown in Table I, a significant difference was seen between the two groups in terms of the frequency of URTI ( $P < 0.05$ ). As shown in Table II, a significant difference was seen between the two groups considering the frequency of URTI ( $P < 0.05$ ). Table III shows the average time for the second URTI (after

the first URTI). As shown in Table III, no significant difference was seen between the two groups in terms of the median time for the second URTI ( $P>0.05$ ). The comparison of the two groups in terms of the duration of symptoms is shown in Table 4. As before mentioned, sometimes these symptoms appeared in combination with several symptoms, and sometimes

there were fewer symptoms. As shown in Table 4, no significant difference was seen between the two groups regarding the duration of cold symptoms ( $P>0.05$ ). In addition, acute sinusitis was observed in some patients of the two groups, but its duration was not available in medical records; therefore the comparison was not done.

*Table I: The frequency of patients in terms of URTI in the two groups after intervention*

URTI	Case Frequency (%)	Control Frequency (%)	P-value
No	18 (60)	10 (33.3)	0.03
Yes	12 (40)	20 (66.7)	
Total	30 (100)	30 (100)	

*Table II: The frequency of patients in terms of second URTI in the two groups after intervention*

URTI	Case Frequency (%)	Control Frequency (%)	P-value
No	23 (76.66)	14 (46.7)	0.01
Yes	7 (23.34)	16 (53.3)	
Total	30 (100)	30 (100)	

*Table III: The average time for the second URTI*

Parameter	Case group (day) Mean $\pm$ SD	Control group (day) Mean $\pm$ SD	P-value
The median time for the second URTI (after the first URTI)	42.3 $\pm$ 13.93	48.3 $\pm$ 13.96	0.086

*Table IV: The comparison of the two groups in terms of the duration of symptoms*

Symptoms	Control group (day) Mean $\pm$ SD	Case group (day) Mean $\pm$ SD	P-value
Coughing(day)	7.1 $\pm$ 1.43	6.4 $\pm$ 1.54	0.074
Running noes (day)	5.7 $\pm$ 1.18	5.3 $\pm$ 1.18	0.229
Nasal airway obstruction (day)	4.16 $\pm$ 1.4	4.7 $\pm$ 1.34	0.14
Fever(day)	3.67 $\pm$ 1.09	3.56 $\pm$ 1.13	0.72
Sore throat	...	....	
Sneezing	...	.....	



## Discussion

Immunocompromised patients, including those with hematopoietic stem cell transplantation and cancer, are faced with a higher risk for respiratory infections (19, 20), and these respiratory infections can lead to crucial complications and may be life-threatening, especially regarding the weakened immune system of children with cancer. This study investigated the effect of echinacea in preventing URTI in children with ALL and these findings showed that echinacea could decrease the frequency of patients with URTI after the intervention.

Few studies were conducted regarding the prevention role of echinacea in URI and most studies were done regarding the effect of echinacea in the treatment of URI (21). Rahmati et al. assessed the role of echinacea in the prevention of acute respiratory infection and observed that the rate of acute respiratory infections was decreased in the intervention group than in the control group (21). The finding of the current study was consistent with our study. Ogal et al. evaluated the role of echinacea in the prevention of respiratory tract infections in children and observed that echinacea led to prevent respiratory tract infections by up to 32.5% (22). According to these findings, the use of echinacea was useful for the prevention of respiratory tract infections. Werber et al. evaluated the effect of echinacea purpurea in the prevention of URTI in 524 children with the age range of 2-11 years. Children were checked for URTIs over 4 months and the findings demonstrated that echinacea purpurea may be effective in decreasing the occurrence of URTIs in children (13). The finding of this study was also consistent with our study.

Dieter et al. used echinacea extracts for the prevention of URTS. In this regard, the extract from echinacea purpurea, echinacea Angustifolia, or placebo was given to patients for 12 weeks and revealed that 36.7% of individuals in the placebo group had an infection, but 32% of individuals in

the E angustifolia group and 29.3% in the E purpurea group had an infection (25).

Islam et al. reported that echinacea was used for the prevention or treatment of URTI. Moreover, according to the findings of this study, the principal action of echinacea was done through immunostimulation (23). Guinning et al., also reported that echinacea did not have any direct antiviral and antibacterial activity. It seems that the beneficial effect of echinacea was via the modulation of the immune system; therefore, it indirectly provided an anti-infective effect (24).

Tylor et al. assessed the efficacy of echinacea in children with cancer. In this regard, 337 children with UTRIs were treated with echinacea and 370 children with a placebo. The median duration of UTRIs was 9 days. The findings showed no difference in duration between placebo and UTRIs treated with echinacea. No significant difference was seen between the two groups in terms of the severity of URI symptoms (17). Moreover, no significant difference was seen between the two groups regarding the adverse effect. In this regard, rash occurred in 7.1% of patients with UTRIs treated with echinacea and 2.7% of patients in the placebo group. The difference between the two studies is that we did not evaluate the adverse effect of echinacea.

Although most studies revealed the beneficial role of echinacea in the prevention of cold and respiratory infection, Barret et al., evaluated the effect of echinacea in the treatment of the common cold and reported that echinacea than placebo provided no detectable harm or benefit in the treatment of a common cold. It is believed that further research is necessary to assess whether echinacea is an effective therapy for the common cold (26). Therefore, the findings regarding the effect of echinacea are controversial. It seems that several factors, including the dose of medicine, duration of use, age, the type of disease, etc may play.

In addition, in the current study, there was a significant difference between the two groups regarding the occurrence of a second URTI. Few studies were conducted considering the occurrence of a second URTI. Werber et al. revealed that 69.2% of patients who received a placebo developed a second URTI, while 55.8% of patients who received echinacea developed URTI (13). The finding of this study was consistent with our study regarding the occurrence of more occurrence of second URTI. Furthermore, regarding reducing the duration of URTS symptoms, there was no significant difference between the two groups. Rahmati et al. also conducted a study in this regard and reported that there was no significant difference between those receiving echinacea and those receiving a placebo regarding the duration of URTS symptoms (21). This finding was consistent with our study.

## Conclusion

According to this finding, it seems that echinacea can be effective in decreasing the occurrence of URTI in pediatric cancer. Therefore, with regard to the efficacy of echinacea in decreasing URTI, it is recommended to use echinacea in the prevention of URTI in these children.

## Conflict of interest

The authors declare no conflict of interest.

## References

1. Sheikhpour R, Hashemi A, Akhondzadeh E, Khanjarpanah Z, Mirakhor M. Evaluation of Immunoglobulin-A Level in Children with Acute Lymphoblastic Leukemia. *IJPHO* 2017; 7(3): 149-153
2. Sheikhpour R, Fazli R, Mehrabani S. Gene Identification from Microarray Data for Diagnosis of Acute Myeloid and Lymphoblastic Leukemia Using a Sparse Gene Selection Method. *IJPHO* 2021; 11(2):1-9.
3. Hashemi A, Kokab M, Elnaz Sheikhpour. The effect of Aloe vera syrup on the prevention of fever and neutropenia in children with acute lymphoid leukemia. *IJPHO* 2020; 1-9
4. Sheikhpour R, Sarram M, Sheikhpour R. Diagnosis of acute myeloid and lymphoblastic leukemia using gene selection of microarray data and data mining algorithm. *J Blood Transfus* 2016;12(4):347-357
5. Pui CH, Pei D, Campana D. A revised definition for cure of childhood acute lymphoblastic leukemia. *Leukemia* 2014; 28(12):2336–2343.
6. Hakim H. Acute respiratory infections in children and adolescents with acute lymphoblastic leukemia. *Cancer* 2016; 122(5):798-805
7. Soudani N, Caniza M, Casals A, Shaker R, Lteif M, Su Y. Prevalence and characteristics of acute respiratory virus infections in pediatric cancer patients. *J Med Virol* 2019; 91: 1191-1201
8. Mendoza Sánchez MC, Ruiz-Contreras J, Vivanco L, et al. Respiratory virus infections in children with cancer or HIV infection. *J Pediatr Hematol Oncol* 2006; 28(3):154-159.
9. Rahmati M, Firouzi R, Houshmandi M, Nazemi A, Hamed Y. Echinacea for prevention of acute upper respiratory infection in children 1 to 5 years old. *J Med Plants* 2016; 15 (58) :176-181.
10. Dizon DS, Krilov L, Cohen E. Clinical cancer advances 2016: annual report on progress against cancer from the American society of clinical oncology. *J Clin Oncol* 2016; 34(9):987-1011.
11. David S. Echinacea for the prevention and treatment of upper respiratory tract infections: A systematic review and meta-analysis. *Complement Ther Med* 2019; 44:11-26
12. Kumar M. Pharmacological importance of echinacea. *Int J Pharma Bioscience* 2011; 2(4):304-309.
13. Werber W. Echinacea purpurea for prevention of upper respiratory tract infections in children. *J Alterna Complementary Med* 2005; 11(6):102-126.

14. Andreas S, Peter K, Johnston S. L. Echinacea Reduces the Risk of Recurrent Respiratory Tract Infections and Complications: A Meta-Analysis of Randomized Controlled Trials. *Adv Ther* 2015; **32**, 187–200.
15. Sachin Sh, Stephen S, White C M. Evaluation of echinacea for the prevention and treatment of the common cold: a meta-analysis. *Lancet Infect Dis* 2007; **7**: 473–480.
16. Roland S, Peter K, Andy S, Johnston S. Echinacea in the prevention of induced rhinovirus colds: A meta-analysis. *Clin Ther* 2006; **28**: 174–183
17. Tylor J. Efficacy and safety of echinase in treating upper respiratory infection in children. *JAMA* 2003; **29**(21): 2824-2830.
18. Sperber S, Shah L, Gilbert R. Echinacea purpurea for prevention of experimental rhinovirus colds. *Clin Infect Dis* 2004; **38**:1367–1371.
19. Benites ECA, Cabrini DP, Silva ACB, et al. Acute respiratory viral infections in pediatric cancer patients undergoing chemotherapy. *J Pediatr Rio J* 2014; **90**(4):370-376.
20. Fazekas T, Eickhoff P, Rauch M. Prevalence and clinical course of viral upper respiratory tract infections in immunocompromised pediatric patients with malignancies or after hematopoietic stem cell transplantation. *J Pediatr Hematol Oncol* 2012; **34**(6):442-449.
21. Rahmati M B, Safdarian F, Hamed Y, Khadem A A, Rezai M S. Efficacy and Safety of Echinacea Root Extracts in the Treatment of Pediatric Common Cold: A Randomized Clinical Trial. *J Mazandaran Univ Med Sci* 2012; **22** (93):12-18
22. Olga M. Echinacea reduces antibiotic usage in children through respiratory tract infection prevention: a randomized, blinded, controlled clinical trial. Ogal et al. *Eur J Med Res* 2021; **26**:33-39.
23. Islam J. Use of Echinacea in upper respiratory tract infection. *South Med J* 2005; **98**(3):311-8.
24. Guining K. Echinacea in the treatment and prevention of upper respiratory tract infections. *WJM* 1999;1-9
25. Melchart D, Walther E, Klaus Linde K. Echinacea Root Extracts for the Prevention of Upper Respiratory Tract Infections. *Arch Fam Med* 1998; **7**:541-549.
26. Barret B. Treatment of the common cold with unrefined Echinacea. *Ann Intern Med* 2002; 1-9