Evaluation of eosinophil, immune-globulin E and Interleukin 6 levels in bronchial asthmatic children after management with needle and laser acupuncture

Inas E M. Ahmed Kamel[a], Hala H. Shaaban[b], Emad N Zikri[a]

[a]Department of Complementary Medicine, National Research Centre, [b]Department of Pediatric, Cairo University, Cairo, Egypt

Correspondence to Dr. Inas EM Ahmed Kamel, (PhD), Complementary Medicine Department, 33rd EL Bohouth Street, Dokki, Giza 12622, Egypt. Tel: +002 0120 091 1112; e-mail: inasmahfouz83@gmail.com

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Background/aim
Bronchial asthma is a disabling disease causing interruption with the daily activities of children. Acupuncture proved to be beneficial in improving the symptoms of the disease and decreasing the dose of conventional medications that must be taken and may have serious side effects. This study aims to evaluate the variations of some inflammatory and immunity markers such as Eosinophil, immune-globulin E (IgE), and Interleukin 6 (IL6) in bronchial asthmatic children after treatment with needle and laser acupuncture.

Patients and methods
In this randomized controlled clinical trial, we included 75 patients divided into three groups. Each group has 25 children. The patients in the first group received laser sessions three times a week for 4 weeks. Those in the second group were treated by needle acupuncture during the same period of time, while the children in third group received only conventional medications and were used as control. Complete blood cell count, which reveals eosinophilic count, was determined, as well as serum IgE and IL6 were measured using Elisa techniques at baseline and after one month of treatment.

Results
All the patients in the three groups showed significant improvement concerning their symptoms and laboratory parameters number of attacks/week and night awakens/month all decrease significantly ($P<0.001$) also IgE ($P<0.001$) after 1 month of treatment with needle or laser. However, children receiving needle and laser sessions showed more significant improvement ($P<0.05$) than the control group, with no differences between the two groups. White blood cells, eosinophils, IgE, IL 6 were statistically decreased ($P<0.05$) after the end of the sessions.

Conclusion
Needle and laser acupuncture proved efficient in relieving the symptoms of the bronchial asthma in children more than conventional medications alone, as well as Eosinophil, IgE, and IL6 levels were significantly decreased after the treatment.

Keywords:
acupuncture, asthma, eosinophil, immune-globulin E, Interleukin 6, laser

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Introduction

Bronchial asthma, in childhood, is a disabling respiratory disease-causing interruption of daily child activities and affects the school and sports performance. Adequate and sufficient management of the disease enables the restoration of respiratory normal physiological performance. Acupuncture is a form of stimulation that modulates the activity of the autonomic nervous system [1,2].

Laser acupuncture has superiority over needle acupuncture in the fact that it is less invasive with easier acceptability for both parents and children. Bronchial hyper-responsiveness is affected by the autonomic nervous system interplay between sympathetic and parasympathetic system. Acupuncture causes neuro-modulation that enhances the bronchial tree smooth muscle relaxation. In addition, it causes immuno-modulation that would reduce the allergic response observed in asthma patients [3,4].

Management of asthma in childhood has been largely dependent on bronchodilators and mast cell stabilizers. However, intervention by acupuncture was observed by researchers all over the globe to reduce the medication doses and the immune pathological course of the disease [5,6].

On the other hand, some viruses such as parainfluenza virus or Epstein-Barr virus, can cause triggering of immune-globulin E (IgE) antibodies and Eosinophil and interacting with the viral infection to exacerbate the acute asthma attacks, moreover, Th2 lymphocytes' are responsible to produce cytokines, such as Interleukin 6 (IL4) and IL-5 and IL 6 [6].

This study aims to evaluate the variations of some inflammatory and immunity markers such as Eosinophil, IgE, and IL6 in bronchial asthmatic children after treatment with needle and laser acupuncture.

Patients and methods

Patients

The current research study is a randomized clinical trial study, enrolled 75 asthmatic children aged from 12 to 16 years, males and females, and under conventional medical treatment, visiting the outpatient clinic of Allergy and Asthma Clinic, Pediatrics Hospital, Cairo University and the Laser and Acupuncture Clinic in the Centre of Excellence at National Research Centre, Cairo, from September to November 2023.

Study design

Seventy five asthmatic children were divided randomly into three equal groups, as follows:

Group A: 25 children were subjected to laser acupuncture sessions, three times/week for 4 weeks with conventional medications.

Group B: 25 patients using needle acupuncture sessions for 1 month (three times/week) with conventional medications.

Group C: 25 patients were given conventional medical treatment only and were used as control group.

All Cases have been followed-up and assessed for 1 month.

Inclusion criteria

According to GINA (2023) [7], the patients had partially controlled or uncontrolled asthma for at least 3 months and were diagnosed more than 6 months before the study. The peak expiratory flow rate (PEFR) was 60–80%, within one month before the application of the research.

Exclusion criteria

The cases excluded from the study are those having heart failure, tuberculosis, and genetic disorders such as Down syndrome and cystic fibrosis.

Ethical consideration

The present study was conducted with the Code of Ethics of the World Medical Association, according to the principles expressed in the Declaration of Helsinki. This study has been approved by the local Ethics Committee of National Research Centre, Cairo, Egypt with approval number 17 152, a written informed consent was provided by each participant before their inclusion in the study.

Methods

All the cases had been subjected to history taking and full clinical examination IL 6, IgE, and leucocytic count were tested in all the patients before the therapy (baseline) and after one month (just after the last session).

Laser device

Laser device used was diode (semiconductor laser), low power (cold laser). The machine used aculaser point with 100 mW power and 3000 HZ frequency. It has two probes, one shower that was not used in this study, the other one have tunable wave length ranging from 650 to 860 nm. In this study, we used the wavelength of 860 nm, the power of 100 mW for 20 s over each acupoint giving power density of 3 Joules/Cm^2. (The laser wave was continuous) to stimulate acupuncture points: DU20 (BaiHui), BL23 (ShenShu), BL28 (Pang Guang Shu), SiShen Cong (3 cm from the point BaiHui), RN6 (QiHai), GB20 (FengChi) and Du16 (FengFu).

Needle acupuncture

We used fine sterile disposable acupuncture needles (0.25 × 25 mm) to stimulate acupuncture points: DU20 (BaiHui), BL23 (ShenShu), BL28 (PangGuangShu), SiShenCong (3 cm from the point BaiHui), RN6 (QiHai), GB20 (FengChi) and Du16 (FengFu), as shown in Fig. 1.

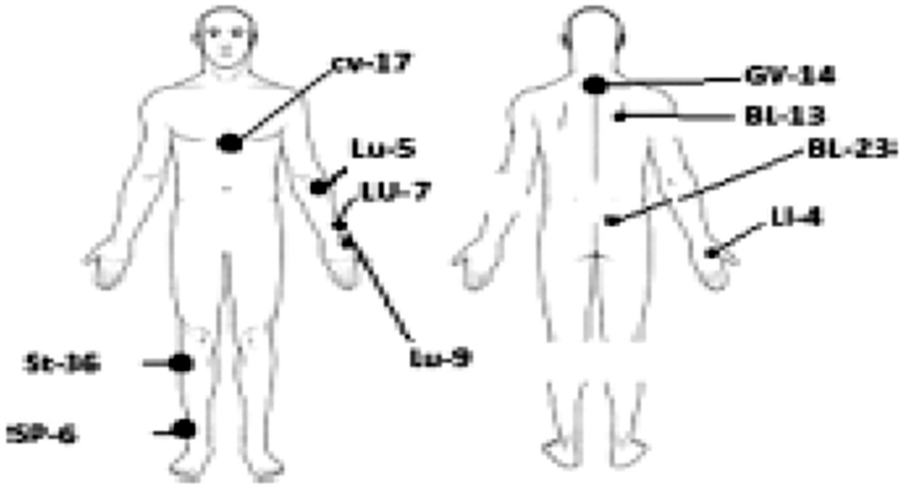
Sites of needle on skin of children had been sterilized on by alcohol swab before its application. Needles were entered till its ¼ th of their length.

Laboratory investigations

Complete blood count with differential white blood cell count, that reveals eosinophilic count, was determined using Blood Coulter of Mindari Co. (Germany).

Determination of Serum IgE and IL6 were performed by the enzymatic immunoassay method using the kits supplied from DRG International, Inc. (Springfield, NJ 07081, USA), according to manufacturer's instructions.

Figure 1



The sites of acupuncture points.

Sample size calculation

It was depending on who found that the Mean±SD of VC% before and after LASER acupuncture were 62.7 ±14.2 and 75.2±12.3 respectively. Assuming that the correlation between before and after LASER acupuncture levels was 0.500, power= 0.80 and α=0.05, and by using G*Power 3.1.9.4 release the minimal sample size to detect a significant statistical change in VC% is 17 cases. We will recruit 25 cases for possible attrition, additional equal samples were recruited in the needle group and control group [8].

Statistical methods

The collected data were coded, tabulated and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 28.0, IBM Corp., Chicago, USA, 2021. Quantitative data were tested for normality using Shapiro-Wilk test, then described as mean±SD and then compared using independent t-test (two independent groups) and ANOVA test (three independent groups), Bonferoni test were used for post hoc comparisons, as well as paired *t*-test (paired data). Qualitative data were described as number and percentage and compared using χ^2 test as well as Fisher's Exact test according to expected numbers in cells (independent groups), as well as marginal homogeneity test (paired ordinal data). The level of significance was taken at *P* value less than 0.05 was significant, otherwise was nonsignificant [9].

Results

The data presented in Table 1 showed that insignificant statistical difference between the different asthmatic children groups treated with laser, needle, or control groups, regarding age, sex, weight, asthma severity, and antiasthma treatment.

Table 1 Demographic and clinical history between the study groups

Variables	Laser group (Group A)	Needle group (Group B)	Control group (Group C)	*P value*
Age (y)	13.6±1.3	13.2±1.2	13.5±1.3	^0.447
Sex				
Male	16 (64.0%)	16 (64.0%)	14 (56.0%)	#0.799
Female	9 (36.0%)	9 (36.0%)	11 (44.0%)	
Weight percentile	73.6±7.0	74.5±8.6	74.8±5.9	^0.817
Asthma severity				
Intermittent	4 (16.0%)	3 (12.0%)	3 (12.0%)	¤0.942
Mild persistent	4 (16.0%)	5 (20.0%)	7 (28.0%)	
Moderate persistent	13 (52.0%)	11 (44.0%)	10 (40.0%)	
Severe persistent	4 (16.0%)	6 (24.0%)	5 (20.0%)	
Treatment				
SABD	25 (100.0%)	25 (100.0%)	25 (100.0%)	NA
LABD	16 (64.0%)	14 (56.0%)	13 (52.0%)	#0.678
Montelukast	25 (100.0%)	25 (100.0%)	25 (100.0%)	NA

LABD, Long acting bronchodilators; NA, Not Applicable; SABD, Short acting bronchodilators. ^ANOVA test. #χ^2, Chi square test, ¤Fisher's Exact test.

Table 2 shows that insignificant statistical difference between the study groups regarding baseline number of attacks/week and number of night awakens/month. However, number of attacks/week and number of night awakens/month 1 month after treatment were significantly higher in control group ($P<0.05$) with no significant difference between the Laser and Needle groups. Reductions in number of attacks/week and number of night awakens/month were significantly lowest ($P<0.05$) in the control group with no significant difference between the Laser and Needle groups. The number of attacks/week and number of night awakens/month significantly decreased ($P<0.05$) than baseline, in all the study groups.

Table 3 showed that insignificant statistical difference between the study groups regarding baseline on hemoglobin, Leucocytes, Eosinophil, IgE, and IL-6. One month after treatment, there was no significant difference between the study groups regarding the hemoglobin level and its change. One month after treatment were significantly highest ($P<0.05$) in control group, while insignificant difference was reported between the Laser and Needle groups. Reductions in Leucocytes, Eosinophil, IgE, and IL-6 were significantly lowest ($P<0.05$) in control group while insignificant difference was reported between the Laser and Needle groups. Hemoglobin exhibited insignificant changes in the study groups. Leucocytes, Eosinophil, IgE, and IL-6 showed significant decreases ($P<0.05$) in all the study groups.

Table 4 showed that continued clinical improvement one month after medical treatment discontinuation significantly was significantly least frequent in

Table 2 Changes in the clinical condition between the study groups

Variables	Laser group (Total=25)	Needle group (Total=25)	Control group (Total=25)	^*P value*
Number of attacks per week				
Baseline	6.4±3.1	6.7±3.9	6.7±4.2	0.933
Month-1	1.8±2.7a	2.0±2.6a	4.3±4.0b	0.011*
§*P value*	<0.001*	<0.001*	<0.001*	
Number of night awakens per month				
Baseline	7.4±4.6	8.6±3.9	8.0±6.4	0.693
Month-1	1.6±2.2a	2.6±2.2a	5.0±5.2b	0.003*
§*P value*	<0.001*	<0.001*	<0.001*	

All data are expressed as mean + SD. All data with different letters (a, b, c) are significant using ^ANOVA test. *Significant difference using ^ANOVA or § Paired t-test at *P* less than 0.05.

Table 3 Changes in the laboratory findings between the study groups

Variables	LASER Group (Total=25)	Needle Group (Total=25)	Control Group (Total=25)	^*P-value*
Hemoglobin (gm/dL)				
Baseline	12.3±1.6	12.0±1.7	11.9±1.4	0.730
Month-1	12.3±1.5	12.1±1.7	11.7±1.4	0.295
§*P value*	0.581	0.357	0.054	
Leucocytes (x103/mL)				
Baseline	7.1±1.8	7.2±1.3	7.3±2.2	0.947
Month-1	5.7±2.0a	5.7±1.5a	7.0±2.1b	0.015*
§*P value*	<0.001*	<0.001*	0.038*	
Eosinophil (%)				
Baseline	13.7±2.9	13.6±3.8	13.8±2.7	0.975
Month-1	10.9±2.8a	10.8±3.2a	13.2±3.3b	0.010*
§*P value*	<0.001*	<0.001*	0.013*	
IgE (IU/mL)				
Baseline	1027.9±174.4	1005.8±157.3	1017.0±151.3	0.889
Month-1	248.1±119.2a	240.9±210.0a	514.4±173.1b	<0.001*
§*P value*	<0.001*	<0.001*	<0.001*	
Il-6 (pg/mL)				
Baseline	14.5±5.4	14.1±7.0	15.0±7.2	0.899
Month-1	7.2±3.9a	7.4±6.0a	13.2±7.4b	<0.001*
§*P value*	<0.001*	<0.001*	<0.001*	

All data are expressed as mean + SD. All data with different letters (a, b, c) are significant using ^ANOVA test. *Significant difference using ^ANOVA or § Paired *t*-test at *P* less than 0.05.

Table 4 Improvement one month after medical treatment discontinuation between the study cases

Improvement	Laser group (Total=25)	Needle group (Total=25)	Control group (Total=25)	*P* value
Continued	19 (76.0%)a	18 (72.0%)a	9 (36.0%)b	#0.006*
Discontinued	6 (24.0%)	7 (28.0%)	16 (64.0%)	

All data are expressed as number and percentage. *Significant difference using χ^2, Chi square test at *P* less than 0.05.

control group with no significant difference between Laser and Needle groups.

Discussion

The present research has revealed that acupuncture could simplify the management of asthma via its anti-inflammatory influences. Acupuncture whether laser or needle at specific acupoints has proved to affect Th1/Th2 balance, block the inflammatory cell activities and immune mediator production, improve bronchial tree remodeling and adjust hypothalamic–pituitary–adrenal axis function. Acupuncture therapy was revealed by prior research efforts to have multiple pathways in managing asthma pathological pathway development [10].

The current study has revealed that reductions in the number of attacks/week and the number of night awakens/month were lowest within the control group without any significant difference concerning Laser and Needle groups. The number of attacks/week and the number of night awakens/month significantly decreased in all the study groups. These research findings are justified by the fact that as long as the respiratory functions are not interrupted during sleep the sleep pattern wouldn't be affected. In addition, it was shown that acupuncture enhances the large, medium and small sized bronchi modeling and reduces bronchial constriction. So, when conjugated with medication, acupuncture leads to augmented improvement in the symptom profile during the disease course. Interestingly, those findings were revealed in a similar fashion in a prior research effort in which it was shown that there is a correlation between bronchial asthma and sleep disorders. Uncontrolled asthma enhances sleep disorders. Also, troubles in sleep, when left without treatment, prevent good management of asthmatic patients [11].

Furthermore, we found that the laboratory changes that reflect the immune system activities, have revealed that one month after treatment, leucocytes, eosinophils, IgE and IL-6 were significantly highest in the control group with no significant difference without any significant differences between the group treated by laser and those treated by needle acupuncture. Hemoglobin levels were not changed significantly in the study groups. Leucocytes, eosinophils, IgE and IL-6 significantly decreased in all the study groups.

Eosinophils cause inflammation when allergens attack the bronchi. Eosinophilia triggering airway inflammation and remodeling leads to persistent bronchial airflow obstruction, epithelial lining damage and increase of the mucus secretion. This is associated with deterioration of the asthmatic manifestations and more impairment of the pulmonary functions [12,13].

A study showed that stimulation of acupoints whether by needles or laser beam can decrease eosinophilia thus, improving the symptoms through regulating disorders in mRNA and promoting eosinophil apoptosis [14]. IgE enhances many immune cells responsible for triggering chronic allergic inflammation through receptors expressed by the airway on the mast cells and eosinophils [15–17]. Also, IgE stimulates the activation and the amplification of the allergens leading to the aggravation of allergic asthma. This occurs mostly after viral infection, such as parainfluenza virus or Epstein-Barr virus. IgE antibodies interacting with the viral infection exacerbate the acute asthma attacks [18].

Acupuncture improves the symptoms of allergic bronchial asthma and the pulmonary function tests by decreasing the serum levels of IgE in children with chronic persistent asthma [19]. Those research findings are justified by the fact that acupuncture has immunomodulatory activities in a manner that reduces the bronchial hyper-responsiveness.

It was revealed, by prior research groups, that either needle or laser acupuncture has proved to be beneficial in decreasing the production of Th2 lymphocytes' cytokines, such as IL4 and IL-5 and increasing the cytokines specific to Th1 lymphocytes leading to the reduction of pro-inflammatory cytokines such as IL1b and IL 6 [20,21]. Also, Park *et al.*, in their trial showed that acupoints stimulation leads to the reduction of the blood levels of IL-4, IL-5 and IgE in an asthmatic mouse [22].

Conclusion

The presented study concluded that the needle and laser acupuncture proved efficiency in relieving the symptoms of the bronchial asthma in children more than conventional medications alone, as well as Eosinophil, Ig E and IL6 levels were significantly decreased after the treatment.

Recommendations

Acupuncture is an effective complementary mode that should be integrated in management protocols of asthma in children. However more studies should be performed on larger number of patients to reach more accurate results concerning the anti-inflammatory and immunomodulatory effect of needle and laser acupuncture in asthmatic patients.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Chunfeng H, Xuan W. Study on the drug treatment of bronchial asthma. J Med Inform 2021; 34:63–65. [Google Scholar]

2 Jihe Z, Blagica A, Kristina K. Acupuncture treatment in asthma. European Journal of Pharmaceutical and Medical Research 2019; 7:61–63.

3 Jun S, Bin L, Hong L, Beizhen M, Xingjia Q, Hao Z, *et al.* Clinical study on acupoint application in the treatment of 60 cases of bronchial asthma in the remission stage. Clinical Journal of Chinese Medicine 2017; 9:30–32. [Google Scholar]

4 Yiming W, Xinxin Z, Xinyue Z. Clinical observation on the therapeutic effect of acupoint application of 'winter disease and summer treatment' on preventing and treating pediatric bronchial asthma. J Extern Tradit Chin Med 2019; 28:18–20. [Google Scholar]

5 Jing C, Shasha L, Minfeng Y, Dongdong W, Jinjun S, Wenliang W, Hong L. Observation on the therapeutic efect of acupoint application for winter disease and summer treatment in preventing and treating pediatric bronchial asthma. Chin Pract Med 2020; 15:167–169. [Google Scholar]

6 Asthma group of Chinese Throacic Society. Guidelines for bronchial asthma prevent and management (2020 edition) Asthma group of Chinese Throacic Society. Chinese Journal of Tuberculosis and Respiratory Diseases 2020; 43:1023–1048.

7 GINA (Global Initiative for Asthma) Main Report 2023: Global strategy for asthma management and prevention. July 10, 2023. Available on https://ginasthma.org/2023-gina-main-report/

8 Wang X, Zeng S, Li Z, Li Y, Jia H. A network meta-analysis of different acupuncture modalities in the treatment of bronchial asthma. BMC Pulm Med 2023; 23:35.

9 Reiter J, Ramagopal M, Gileles-Hillel A, Forno E. Sleep disorders in children with asthma. Pediatric Pulmonology 2022; 57:1851–1859.

10 Zeiger RS, Schatz M, Dalal AA, Chen W, Sadikova E, Suruki RY, *et al.* Blood eosinophil count and outcomes in severe uncontrolled asthma: a prospective study. J Allergy Clin Immunology Pract 2017; 5:144–153.

11 Solomon Y, Malkamu B, Berhan A, Eyayu T, Almaw A, Legese B, Woldu B. Peripheral blood eosinophilia in adult asthmatic patients and its association with the severity of asthma. BMC Pulm Med 2023; 23:96.

12 Wu ZL, Li CR, Liu ZL, Zhang QR. Effects of acupuncture at 'Zusanli' (ST 36) on eosinophil apoptosis and related gene expression in rats with asthma. Zhongguo Zhen Jiu 2012; 32:721–725.

13 Maurer D, Fiebiger S, Ebner C, Reininger B, Fischer GF, Wichlas S. Peripheral blood dendritic cells express Fc epsilon RI as a complex composed of Fc epsilon RI alpha- and Fc epsilon RI gamma-chains and can use this receptor for IgE-mediated allergen presentation. J Immunol 1996; 157:607–616.

14 Redhu NS, Gounni AS. The high affinity IgE receptor (FcεRI) expression and function in airway smooth muscle. Pulm Pharmacol Ther 2013; 26:86–94.

15 Sihra BS, Kon OM, Grant JA, Kay AB. Expression of high-affinity IgE receptors (Fc epsilon RI) on peripheral blood basophils, monocytes, and eosinophils in atopic and non atopic subjects: relationship to total serum IgE concentrations. J Allergy Clin Immunol 1997; 99:699–706.

16 Matucci A, Vultaggio A, Maggi E, Kasujee I. Is IgE or eosinophils the key player in allergic asthma pathogenesis? Are we asking the right question?. Respiratory Research 2018; 19:113.

17 Yang YF, Wang XY, Kong LX, Zhang YM, Zhao L. Acupoint thread-embedding as adjuvant therapy for bronchial asthma in children and its effect on pulmonary function, serum IgA and IgE levels] Randomized Controlled Trial. Zhongguo Zhen Jiu 2021; 41:1349–1353.

18 Wei Y, Dong M, Zhang H, Lv Y, Liu J, Wei K, *et al.* Acupuncture attenuated inflammation and inhibited Th17 and Treg activity in experimental asthma. Evidence-Based Complement Alternat Med 2015; 2015:340126.

19 Nurwati I, Purwanto B, Mudigdo A, Saputra K, Prasetyo DH, Muthmainah M. Improvement in inflammation and airway remodeling after acupuncture at BL 13 and ST 36 in a mouse model of chronic asthma. Acupunct Med 2019; 37:228–236.

20 Park MB, Ko E, Ahn C, Choi H, Rho S, Shin MK, *et al.* Suppression of IgE production and modulation of Th1/Th2 cell response by electroacupuncture in DNP-KLH immunized mice. J Neuroimmunol 2004; 151:40–44.

21 Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G Power 3.1: Tests for correlation and regression analyses. Behavior research methods 2009 41:1149–1160.

22 Mohamed NH, Adbel Meguid IEA, Shaaban HH, Kamel IMA. Evaluation of needle acupuncture actions on clinical improvement, pulmonary functions, and cytokines of asthmatic children. Medical Research Journal 2013; 12:43–48.