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Evaluation of Effectiveness of Adjuvant Remedies in Treatment of Allergic Rhinitis in Children

ABSTRACT

Background: Homeopathy is one of the most popular of complementary and alternative therapies.

Objective: To evaluate the effectiveness of homeopathic medicine in the treatment of allergic rhinitis in children.

Methods: A prospective follow up study was conducted in National Research Center (NRC) from the first of March till the end of February, Patients aged between 6 and 12 years with allergic rhinitis were treated by homeopathic remedies. Pediatric Rhinoconjuntivitis Quality of life questionnaire (RQLQ), Allergic Rhinitis Nasal Symptoms Score (ARSS), drugs usage and nasal smear eosinophils were done for all Patients at baseline and again after three months.

Results: Fifty-three patients were screened, of whom 30 met the study eligibility criteria (average age 8.30±2.322). The mean RQLQ score was 4.44±1.3 at baseline, after 3 months of treatment, the mean had fallen to 2.10±1.66 (P<0.001). The mean overall total symptoms score decreased significantly from 9.23±2.07 to 5.57±4.07 (P<0.001). Also, significant reduction in number of patients with positive nasal smears to 43.3% after homeopathic treatment (P<0.001)

Conclusions: After homeopathic treatment, patients reported an improvement of their symptoms of allergic rhinitis as reported in Pediatric Rhinoconjuntivitis Quality of life questionnaire (RQLQ), Allergic Rhinitis Nasal Symptoms Score (ARSS) and nasal smear eosinophils.

Recommendation: A formal randomized clinical trial is required.

Keywords: Homeopathy; Allergic rhinitis; quality of life; children

تقييم فاعلية مستحضرات مساعدة فى علاج حساسية الأنف فى الأطفال

الخلفية: تعتبر حساسية الأنف من أكثر الأمراض المزمنة شيوعا بين الأطفال فى العالم وغالبا ما يصاحبها الكثير من المضاعفات التى تؤثر بالسلب على صحة الطفل وادائه المدرسى والاجتماعى ومن اهمهاالربو الشعبى كما انها تشكل عبئا اقتصاديا ولقد أصبح العلاج التكميلى بالهميوباثى من أكثر طرق العلاج شيوعاً فى العالم نظرا لرخص سعره وعدم وجود أى أضرار لاستخدامه.ومن خلال بعض الدراسات على مستوى العالم, ثبت أن للهميوباثى تأثير فعال فى علاج حساسية الانف والتقليل من مضاعفاتها .

الهدف:تقييم فعالية الهميوباثى كوسيلة من وسائل الطب التكميلى كعلاج مساعد في علاج حساسية الأنف فى الأطفال .

خطة البحث: هذه دراسة تدخلية أجريت فى عيادة الطب التكميلى بالمركز القومى للبحوث وقد شملت الدراسة جميع الأطفال الذين تتراوح أعمارهم بين 6-12 سنواتمع وجود تاريخ من التهاب الأنف التحسسى ≥ 1 سنة, تم اختيار المستحضر المناسب لكل حالة بعد تسجيل التاريخ المرضى لكل طفل بالتفصيل وفحصه وتقييمه و تمت المتابعة لمدة ثلاثة أشهر وإعادة التقييم من خلال مقياس أعراض حساسية الأنف واستبيان جودة الحياة لاطفال حساسية الانف ومعدل استخدام الأدوية شهريا وعمل مسحة من الانف لتحليل نسبة eosinophils قبل البدء فى العلاج بالهميوباثى وبعد 3 اشهر من العلاج.

النتائج: وجد ان العلاج بالهميوباثى ادى الى تحسنا ملحوظا فى جميع قياسات جودة استبيان الحياة، وجميع قياسات مقياس اعراض حساسية الانفو كان ذلك ذو دلالة احصائية، وايضا قل عدد المرضى الذين لديهم مسحة الأنف إيجابية من 30(100%) الى 13 (43.3%) وكان ذلك ذو دلالة احصائية. كذلك قل متوسط عدد الادوية المستخدمة لكل مريض من 3.9 الى 2و كان ذلك ذو دلالة احصائية.

الاستنتاج: ان العلاج بالهميوباثى ادى الى تحسنا ملحوظا فى اعراض مرض حساسية الانف كما اتضح من خلال قياسات جودة استبيان الحياة ومقياس اعراض حساسية الانف واختبار مسحة الانف

الكلمات الدالة: هميوباثى,حساسية الانف,استبيان جودة الحياة,الاطفال

Introduction:

Allergic rhinitis is described as a symptomatic disease of the nasal mucous membranes resulting from IgE-dependent inflammation after exposure of nasal membranes to allergens (Hendaus et al., 2016).

AR is a major chronic respiratory disease because of its prevalence, its effect on quality of life, productivity and performance at work/school, its economic impact on society and its relation to asthma (Solelhac and Charpin, 2014).

Homeopathy is one of the leading complementary therapies used in treatment of this disease (Wassenhoven,2013). Worldwide, homeopathic medicine is one of the most popular of complementary and alternative modalities. About 40% of clinicians in England recommend homeopathy and more than 60% of the French people use homeopathic medicine (Ernst, 2007).

Objective:

This study was performed to evaluate the effect of an individualized homeopathic prescription in the treatment of allergic rhinitis in children.

Subjects And Methods

A follow up study was conducted on all eligible children (aged 6-12 years) attending the Homeopathic Clinic at the National Research Center, Cairo, Egypt during the period from the first of March 2014 till the end of February 2015, Patients were referred to us from ENT outpatient clinic of Al-Azhar university. Children having history of allergic rhinitis ≥ 1 year with Presence of rhinitis symptoms at the time of the clinic visit ± AR co-morbidities were included in the study. Children who were suffering from acute respiratory infection were excluded, as well children with negative nasal smear. Also, children who were suffering from systemic disease or congenital anomalies were excluded.

After obtaining written informed consent from the parents and explanation of all details about enrollment in the study, demographic data and medical data were recorded. Physical examination was done to all patients with focusing on signs of AR.

Assessment of severity of illness by:

1) Pediatric Rhinoconjuntivitis Quality of life questionnaire (RQLQ) (Juniper et al.,1998). RQLQ is a standard and established method of evaluating quality of life in patients with allergic rhinitis. The measure consists of 23 questions in five domains. The children recalled their experiences from previous week and responded to each question using a 7-point scale ranging from0 (not impaired at all) to 6 (severely impaired).

2) Allergic rhinitis nasal symptoms score (Bousquet et al., 2008). It evaluates nasal symptoms by grading them according to a 4-point symptom severity scale.

3) Nasal smear eosinophils: it was done at baseline and after 3 months of treatment. The smears were collected by scraping the mucous membrane of the inferior meatus with a cotton swab, air-dried, stained with Giemsa (MGG) stain and rinsed in tap water. Discoloration with alcohol was done followed again by rinsing in water. After drying, they were examined under light microscopy, all smears were coded and read by a single investigator. A finding of more than 5 eosinophils in 3 to 5 fields of view or a single finding of 20 to 30 cells was considered a positive finding for nasal eosinophilia .

Homeopathic Prescription

Ten different homeopathic remedies were available for use: Natrum Muriaticum, Silicae, Calcarea Carbonica, Phosphorus, Sulphur, Pulsatilla, Allium Cepa, Lycopodium, Veratrum album, Nux vomica. Each patient received the remedy that most closely matches his symptoms picture, Choice of remedie swas done twice: 1st: manually (using Murphy’s Homeopathic Medical Repertory) and 2nd: Radar Homeopathic Software to ensure a uniform homeopathic management. These remedies were in the form of sugar pellets imported from Helios homeopathic pharmacy (Tunbridge Wells, UK) The homeopathic remedies were prepared by dissolving 3 tablets of each remedy in 15 ml distilled water in dark brown glass bottles. Mothers were informed about handling of bottles and dosage and also were instructed to report any reactions after starting treatment and to come for follow-up within the first week to ensure proper choice of the selected remedy, then, follow-up will be monthly over the course of 3 months plus extra visits and telephone consultations as necessary, according to normal practice.

Allergic rhinitis symptoms score (ARSS), Pediatric Rhinoconjuntivitis Quality of life questionnaire (RQLQ), nasal smear eosinophils and drugs usage. These measures were done at baseline and after the course of 3 months.

Statistical Analysis:

All statistical tests were two-sided with statistical significance declared at the0.05 probability level. Paired t-tests were performed between baseline and three months of treatment. The SPSS Ver. 12 program was used for statistical calculations.

Results:

A total of 53 patients with allergic rhinitis who met the inclusion criteria were enrolled in the study. The flow of patients through the study is shown in (Figure 1).

Figure 1: Flow chart of patients included in the study.

Table 1 shows the demographic characteristics of the 30 included patients.

|  |  |
| --- | --- |
|   | (Mean ± Sd) |
|  Age (Years)  | 8.30±2.322 |
| Weight ( Percentile) | 44.60±22.291 |
| Height ( Percentile) | 56.10±21.729 |
| Mean duration of illness(years) | 6.32±2.143 |
| Average Number Of Visits  | 5.30±1.26 |
| Average Weeks Of Response | 4.39±2.06 |

Table 2 shows statistically significant improvement in all parameters of Allergic Rhinitis Symptoms Score after homeopathic treatment. The average ARSS at baseline was 2.32±0.607, after treatment it became 1.14±1.05 (P<0.001) and the mean overall total symptoms score decreased significantly from 9.23±2.07 to 5.57±4.07 (P<0.001).

Table 2: Allergic Rhinitis Symptoms Scores (ARSS) before and after homeopathic treatment

|  |  |  |  |
| --- | --- | --- | --- |
| ARSS | Before (Mean±SD) | After (Mean±SD) | P\_Value |
| -Rhinorrhea Score | 2.47±0.507 | 1.30±1.022 | 0.001 |
| Sneezing Score | 2.13±0.681 | 0.901.125 | 0.001 |
| Nasal Congestion Score | 2.43±0.504 | 1.30±1.022 | 0.001 |
| Nasal Itching Score | 2.23±0.679 | 1.07±1.048 | 0.001 |
| Eye Itching Score | 1.73±0.740 | 0.87±0.776 | 0.001 |
| Average Symptomscore | 2.32±0.607 | 1.14± 1.05 | 0.001 |
| Total Symptoms Score | 9.23±2.07 | 5.57±4.07 | 0.001 |

Table 3 shows that at baseline 56.7% of patients were classified as moderate allergic rhinitis and 43.3% as severe with no mild cases according to ARSS. But after homeopathic treatment, most patients (63.3%) became mild with reduction in number of patients with severe allergic rhinitis to 16.7% and with moderate AR to 20% which is statistically significant. It shows also significant reduction in number of patients with positive nasal smear eosinophils from 100% at baseline to 43.3% after homeopathic treatment.

Table 3: Classification of severity according to total score of ARSS and Nasal smear eosinophils before and after homeopathic treatment

|  |  |  |
| --- | --- | --- |
|  | treatment | P Value |
| before | after |
| Mild | 0 | 19 (63.3%) |  |
| Moderate | 17 (56.7%) | 6 (20.0%) | 0.022\* |
| severe | 13 (43.3%) | 5 (16.7%) | 0.059 |
| +Venasaleosinophilia | 30 (100%) | 13(43.3%) | 0.001\* |

Table 4 shows statistically significant improvement in all parameters of Pediatric Rhinoconjuntivitis Quality of life questionnaire (RQLQ) after 3 months of homeopathic treatment. RQLQ: has 23 questions in five domains (activity limitation, nose symptoms, eye symptoms, other symptoms, practical problems) and each question will be scaled from0 (not impaired at all) to 6 (severely impaired) .The highest RQLQ score at baseline was 5.77±0.430, the lowest was 2.90±1.242, the mean was 4.44±1.31 . After 3 months of treatment, patients reported statistically significant improvement in RQLQ scores, the highest score became 2.90±1.539 (P<0.000), the lowest1.10±1.447 (P<0.001).the mean had fallen to 2.10±1.66 (P<0.001) with mean reduction percent 52.7%.

Table 4: PRQLQ before and after homeopathic treatment

| PRQLQ | Before(Mean±SD) | After(Mean±SD) | P Value |
| --- | --- | --- | --- |
| Nose Symptoms | Blocked Nose | 5.23±0.971 | 2.60±1.632 | 0.001\* |
| Sneezing | 4.20±1.297 | 1.83±1.315 | 0.001\* |
| Runny Nose | 5.43±1.040 | 2.80±1.827 | 0.001\* |
| Itchy Nose | 4.97±1.351 | 2.33±1.826 | 0.001\* |
| Mean Of All Nasal Symptoms | 4.96±1.25 | 2.39±1.68 | 0.001\* |
| Eye Symptoms | Itchy Eyes | 4.30±1.418 | 1.97±1.650 | 0.001\* |
| Watery Eyes | 3.50±1.333 | 1.47±1.456 | 0.001\* |
| Puffy Eyes | 3.00±1.259 | 1.17±1.177 | 0.001\* |
| Sore Eyes | 2.90±1.242 | 1.10±1.447 | 0.001\* |
| Mean Of Eye Symptoms | 3.43±1.41 | 1.43±1.46 | 0.001\* |
| Practical Problems: | Rub Nose And Eyes | 4.40±1.276 | 2.07±1.660 | 0.001\* |
| Blow Nose | 5.33±1.028 | 2.67±1.688 | 0.001\* |
| Carry Tissues | 5.70±0.596 | 2.87±1.655 | 0.001\* |
| Take Medications | 5.77±0.430 | 2.90±1.539 | 0.001\* |
| Feel Embarrassed | 3.97±1.033 | 1.90±1.729 | 0.001\* |
| Mean Of Practical Problems | 4.37±1.08 | 2.03±1.66 | 0.001\* |
| Other Symptoms: | Thirst | 4.60±1.133 | 2.17±1.704 | 0.001\* |
| Don’t Feel Well All Over | 4.57±0.935 | 2.20±1.710 | 0.001\* |
| Irritable | 4.27±1.048 | 2.00±1.661 | 0.001\* |
| Tired | 4.37±0.850 | 2.17±1.704 | 0.001\* |
| Headache | 3.90± 1.322 | 1.77±1.569 | 0.001\* |
| Scratchy/Itchy Throat | 4.07± 1.311 | 1.80±1.400 | 0.001\* |
| Mean Of All Other Symptoms | 4.29±1.11 | 2.04±1.62 | 0.001\* |
| Activities: | Playing Outdoors | 4.27±0.907 | 2.17±1.704 | 0.001\* |
| Hard to get to sleep at night | 4.80±0.997 | 2.27±1.596 | 0.001\* |
| Hard To Pay Attention | 4.00±1.050 | 1.73±1.596 | 0.001\* |
| Wake Up During The Night | 4.80±0.997 | 2.27±1.741 | 0.001\* |
| Mean Of Activities  | 4.37±1.08 | 2.03±1.66 | 0.001\* |
| Mean Rqlqscore | 4.44±1.31 | 2.10±1.66 | 0.001\* |

Table 5 shows statistically significant reduction in using some conventional medicines usually prescribed for allergic rhinitis {decongestants (P<0.001), oral steroids (P<0.035), antibiotics (P<0.001)}, it showed also reduction in using other drugs but it is not statistically significant. Patients used an average of 3.9 medications before homeopathic treatment and 2 after (P<0.001).

Table 5: Comparison before and after homeopathic treatment as regards to medications

|  |  |  |  |
| --- | --- | --- | --- |
|  | before | after | P- Value |
| decongestants | 16 (53.3%) | 2 (6.6%) | 0.001\* |
| Nasal Irrigation | 21 (70%) | 20 (66.6%) | 0.879 |
| singular | 5 (16.6%) | 4 (13.3%) | 0.739 |
| zaditen | 2 (6.6%) | 1 (3.3%) | 0.564 |
| Oral\_Steroids | 9 (30%) | 2 (6.6%) | 0.035\* |
| Antibiotics | 23 (76.6%) | 5 (16.6%) | 0.001\* |
| Cough\_Drugs | 15 (50.0%) | 10 (33.3%) | 0.317 |
| antihistamine | 21 (70%) | 17 (56.6%) | 0.516 |
| Nasal\_Steroid | 11 (36.6%) | 6 (20%) | 0.225 |
| Average N. of drugs for each patient | 3.9 ±1.11 | 2± 1.17 | 0.001\* |

Discussion:

In the current study, the outcome measures for the 30 patients for whom there were complete follow- up data showed positive response to homeopathic treatment in most of patients as represented by statistically significant improvement in all parameters of RQLQ and ARSS after 3 months of homeopathic treatment (P<0.001). At baseline 56.7% of patients were classified according to ARSS as moderate allergic rhinitis and 43.3% as severe with no mild cases. But after homeopathic treatment, most patients (63.3%) became mild with reduction in number of patients with severe allergic rhinitis to 16.7% and with moderate AR to 20% which is statistically significant (P<0.02). In (2009) Goossens et al. conducted a prospective, open, non-comparative study in Belgium. Patients with SAR were treated by one of seven homeopathic physicians. Patients completed the RQLQ at baseline and again after three and four weeks of homeopathic treatment. Patients reported an alleviation of their symptoms of allergic rhinitis as reported in the RQLQ. The highest RQLQ score at baseline was 5.50, the lowest 1.21, the mean was 3.40 ±0.98 at baseline. After three and four weeks of treatment, patients reported significant improvement in the HRQL. After three weeks of homeopathic treatment it was 1.97 ±1.32 (P <0.0001) and after four weeks of treatment 1.6 ±1.28 (P <0.0001) .Patients reported an improvement of 38% after three weeks of homeopathic treatment in HRQL. After four weeks of homeopathic treatment the improvement was 52% (Goossens et al., 2009). In agreement with our study, the highest RQLQ score at baseline was 5.77±0.43, the lowest was 2.90±1.242, the mean was 4.44±1.31 at baseline. After 3 months of treatment, patients reported statistically significant improvement in RQLQ scores, the highest score became2.90±1.539 (P<0.000), the lowest1.10±1.447 (P<0.001), the mean 2.1±1.66 with mean reduction percent 52.7%. This study like our study, both of them used Individualized homeopathic treatment, in which each patient was prescribed either a single remedy or multiple remedies based on the totality of each patient's symptoms.

An open-label, 3-arm, parallel group, multicenter study to evaluate the efficacy and safety of nasal steroid (ciclesonide) in comparison to both levocetirizine alone, and a ciclesonide/levocetirizine combination in patients with seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR). Subjects exhibiting moderate to severe allergic rhinitis for longer than 1 year received 200 μg cicle­sonide, 5 mg levocetirizine, or a combination of both. Changes from baseline until the end-of-study visit (2 weeks following) were evaluated by re­flective total nasal symptom scores (rTNSSs) and rhinoconjunctivitis quality-of-life questionnaires (RQLQ). Mean RQLQ [SD] at baseline was 4.1+/-0.9, 3.8+/-0.9, 4.1+/-1.1 for nasal steroid (ciclesonide) group, levocetirizine alone group and a ciclesonide/levocetirizine combination group respectively. After 2 weeks of treatment, all groups showed statistically significant improvement of RQLQ . Mean RQLQ [SD] was 2.7+/-1.0, 2.7+/-1.0, 2.5+/-1.2 for nasal steroid (ciclesonide) group, levocetirizine alone group and a ciclesonide/levocetirizine combination group respectively (Pvalue<0.010) (Kim et al., 2015). In comparison to our study, the mean RQLQ at baseline was 4.44±1.31, after treatment it had fallen to2.1±1.66 (P<0.001).Mean(rTNSSs) at baseline was 7.5±1.5, 7.3±1.2, 7.6±1.4 for nasal steroid (ciclesonide) group, levocetirizine alone group and a ciclesonide/levocetirizine combination group respectively. After 2 weeks of treatment, all groups showed significant improvement of rTNSS,with superiority of ciclesonide group over the levo­cetirizine group in rTNSS . A similar de­gree of improvement was seen in the combination treatment group . Mean (rTNSS) after treatment was 3.6±2.2, 3.0±2.1, 3.9±2.6 for nasal steroid (ciclesonide) group, levocetirizine alone group and a ciclesonide/levocetirizine combination group respectively (Kim et al., 2015) . In comparison to our study, the mean ARSS total score at baseline was 9.23±2.07, after treatment it had fallen to4.57±4.07 (P<0.001).In agreement with our results, the above study showed that homeopathy is not inferior to conventional treatment for improving clinical symptoms and quality of life in patients with allergic. Frenkel and Hermoni conducted a retrospective analysis of patients with respiratory allergies who had received individually chosen homeopathic medicines. The clinic’s database revealed that when evaluating drug usage three months before homeopathic treatment and three months after, 27 of 31 patients who used conventional allergy medications (antihistamines, steroids, and decongestants) reduced usage of these drugs after homeopathic treatment; two patients experienced an increase in drug usage, and two patients showed no change. A 60% reduction in drug costs was observed after homeopathic treatment, amounting to an average savings of $24 per patient in a three-month period. Patients used an average of 3.1 medications before homeopathic treatment and 1.6 after (p<0.001) (Frenkel and Hermoni, 2002).In agreement with our study, it showed statistically significant reduction in using allergic rhinitis medications. Patients used an average of 3.9+/-1.1medications before homeopathic treatment and 2.0+/-1.2 after (P<0.001) with mean percent reduction 48.72%.In contrast to our study, a double-blind, randomized, placebo-controlled trial was conducted to determine if the homeopathic medicine Betula 30c is more effective than placebo at reducing symptoms of pollen allergy in patients sensitive to birch pollen. Tablets were given both as a prophylactic agent, once a week four weeks before the pollen season and as an acute remedy during the pollen season. The study involved 73 children, adolescents and young adults from 7 to 25 y of age. Allergy-symptoms were assessed on a visual analogue scale (VAS) by patients or parents. Main outcome measure was the median of the symptom scores for all the treated patients, each day during a 10-day period. Homeopaths might attribute the findings to a putative aggravation response, but the results certainly do not lend support to the usefulness of the tested homeopathic approach (Aabel, 2000).

Clinical and experimental observations have shown that the presence of eosinophils and their products in the airways is strongly correlated with disease severity and the development of airway hyperreactivity. A cross sectional study of 50 Children with allergic rhinitis, aged 5 to 18 years was conducted, nasal smear eosinophilia was carried out and graded as I-V, The correlation between the class of allergic rhinitis and grade of nasal smear eosinophilia, obtained using Spearman correlation, was significant (r=0.82, P<0.001) (Amperayani and Kuravi, 2011). The reduction in number of patients with positive nasal smear eosinophils from 100% at baseline to 43.3% after homeopathic treatment, is matching with the significant improvement in other clinical parameters (ARSS and RQLQ) But our study is lacking the grading of nasal smear eosinophils, which may be the cause of undetected improvement in eosinophilic count after homeopathic treatment. Our results suggest that homeopathic therapy could be effective as adjuvant therapy for treating allergic rhinitis in children.

Conclusions: After homeopathic treatment, patients reported an improvement of their symptoms of allergic rhinitis as reported in PRQLQ, ARSS and nasal smear eosinophils.

Recommendation: A formal Randomized Clinical Trial (RCT) is required.

References:

Aabel S. No beneficial effect of isopathic prophylactic treatment for birch pollen allergy during a low-pollen season: a double-blind, placebo-controlled clinical trial of homeopathic Betula 30c. Br Homeopath J. (2000 Oct);89(4):169-73.

Amperayani S and Kuravi N. Correlation of nasal smear eosinophilia with class of allergic rhinitis. Indian Pediatr. (2011 Apr);48(4):329-30.

Ernst E: The truth about homeopathy. British Journal of Clinical Pharmacology. (2007);65(2):163-164.

Goossens M, Laekeman G, Aertgeerts B, et al. ARCH study group. Evaluation of the quality of life after individualized homeopathic treatment for seasonal allergic rhinitis. A prospective, open, non-comparative study. Homeopathy.(2009 Jan);98(1):11-6.

Hendaus MA, Jomha FA and Ehlayel M. Allergic diseases among children: nutritional prevention and intervention. Therapeutics and Clinical Risk Management. (2016);12:361-372.

Juniper EF, Howland WC, Roberts NB, et al. Measuring quality of life in children with rhinoconjunctivitis. J Allergy ClinImmuno l(1998);2: 163-170.

Kim CH, Kim JK, Kim HJ, et al. Comparison of intranasal ciclesonide, oral levocetirizine, and combination treatment for allergic rhinitis. Allergy Asthma Immunol Res.(2015 Mar);7(2):158-66.

Solelhac G and CharpinD . Management of allergic rhinitis. F1000Prime Reports (2014), 6:94.

Wassenhoven MV: Priorities and methods for developing the evidence profile of homeopathy. (2005);94:107-124.