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A narrative review on research evidence of homoeopathic treatment in upper respiratory tract infection.

Una revisión narrativa sobre la evidencia de la investigación del tratamiento homeopático en la infección del tracto respiratorio superior.

Dr. Mansi Singh[1*], Dr. Arun B. Jadhav[2]

1- Post Graduate Scholar, Department of Homoeopathic Materia Medica, Bharati Vidyapeeth (Deemed to be University) Homoeopathic Medical College & Hospital, Katraj-Dhankawadi, Pune: 411043, India. Email: mansisingh373@gmail.com ; ORCID:0000-0002-6121-9626

2- Former Principal, PG Guide, Department of Homoeopathic Materia Medica, Bharati Vidyapeeth (Deemed to be University) Homoeopathic Medical College & Hospital, Katraj-Dhankawadi, Pune: 411043, India. Email: drarunbjadhav@gmail.com ; ORCID: 0000-0002-9389-0094

Corresponding Author:

Dr. Mansi Singh, Post Graduate Scholar, Department of Homoeopathic Materia Medica, Bharati Vidyapeeth (Deemed to be University) Homoeopathic Medical College & Hospital, Katraj - Dhankawadi, Pune: 411043, India. Email: mansisingh373@gmail.com ; ORCID:0000-0002-6121-9626

ABSTRACT

Background: In many developing countries, upper respiratory tract infections are a major public health issue, and the leading cause of morbidity and mortality among children and adults. Thus, the purpose of our narrative review was to assess the efficacy of homoeopathic medicines in upper respiratory tract infections.

Methodology: A comprehensive computerized literature search was carried out to find clinical research articles. PubMed, Cochrane, Wiley, Google Scholar, Research Gate, Medline, Science Direct, and the Thieme -E-journal of homoeopathy were searched and relevant articles were used for reviewing purposes. This review only included clinical trials that involved humans. Pilot studies, animal experiments, and article abstracts were excluded. There were complete research articles. All prospective observational clinical research articles that were randomised, double-blind, and placebo-controlled were included.

Results: Sixty articles were found in a preliminary search. Total 43 research articles were studied for the review. Irrelevant and duplicated articles were removed. Total 24 articles were selected for the narrative review. 3 articles were found about acute respiratory tract infections and 21 articles were about upper respiratory tract infection. All the studies were very diverse in the methodology, type of homoeopathy used and outcome measurement. Different types of homoeopathy in terms of individualised, complex syrup and home medication were used in studies. Fourteen studies reported the role of homoeopathy in reducing the severity of symptoms, efficacy beyond placebo, superiority or non-inferiority over conventional medications, in lowering the consumption of antibiotics and as prophylaxis. On the other hand, three studies found little or no effect in reducing symptoms or number of visits.

Conclusion: This systematic review concluded that homeopathic medicines are safe and effective in acute and upper respiratory tract infections. But more randomized placebo controlled studies should be conducted to strengthen the available evidence.

Keywords: Homoeopathy, Randomized clinical trial, Upper respiratory tract infection.

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RESUMEN

Antecedentes: en muchos países en desarrollo, las infecciones de las vías respiratorias superiores son un importante problema de salud pública y la principal causa de morbilidad y mortalidad entre niños y adultos. Por lo tanto, el propósito de nuestra revisión narrativa fue evaluar la eficacia de los medicamentos homeopáticos en las infecciones del tracto respiratorio superior.

Metodología: Se realizó una búsqueda bibliográfica computarizada exhaustiva para encontrar artículos de investigación clínica. Se realizaron búsquedas en PubMed, Cochrane, Wiley, Google Scholar, Research Gate, Medline, Science Direct y Thieme -E-journal of homeopathy y se utilizaron artículos relevantes para fines de revisión. Esta revisión solo incluyó ensayos clínicos en humanos. Se excluyeron estudios piloto, experimentos con animales y resúmenes de artículos. Había artículos completos de investigación. Se incluyeron todos los artículos prospectivos de investigación clínica observacional que fueron aleatorizados, doble ciego y controlados con placebo.

Resultados: Sesenta artículos fueron encontrados en una búsqueda preliminar. Se estudiaron un total de 43 artículos de investigación para la revisión. Se eliminaron los artículos irrelevantes y duplicados. Se seleccionaron un total de 24 artículos para la revisión narrativa. Se encontraron 3 artículos sobre infecciones agudas del tracto respiratorio y 21 artículos sobre infección del tracto respiratorio superior. Todos los estudios fueron muy diversos en cuanto a la metodología, el tipo de homeopatía utilizada y la medición de los resultados. En los estudios se utilizaron diferentes tipos de homeopatía en términos de jarabe complejo individualizado y medicación domiciliaria. Catorce estudios informaron el papel de la homeopatía en la reducción de la gravedad de los síntomas, la eficacia más allá del placebo, la superioridad o no inferioridad sobre los medicamentos convencionales, en la reducción del consumo de antibióticos y como profilaxis. Por otro lado, tres estudios encontraron poco o ningún efecto en la reducción de los síntomas o el número de visitas.

Conclusión: esta revisión sistemática concluyó que los medicamentos homeopáticos son seguros y efectivos en las infecciones agudas y de las vías respiratorias superiores. Pero se deben realizar más estudios aleatorios controlados con placebo para fortalecer la evidencia disponible.

Palabras clave: Homeopatía, Ensayo clínico aleatorizado, Infección del tracto respiratorio superior.

INTRODUCTION

Upper respiratory tract infection (URTI) has been recognized as one of the most common medical problems in the daily lives of people worldwide. It is one of the leading causes of morbidity worldwide especially in the paediatric age group. URTI has been regarded as a nonspecific term that is used to describe acute infections involving the nose, paranasal sinuses, pharynx, larynx, trachea, and bronchi (Spurling GK et al., 2013, Kho BP et al., 2013). URTI mainly includes Common cold, laryngitis, pharyngitis or tonsillitis, acute rhinitis, acute rhino sinusitis and acute otitis media are the infections of upper respiratory tract.

Clinically, all these infections more or less present with similar symptom complex and are hence considered under one umbrella of URTI. Nasal stiffness, sore throat, headache, malaise, hoarseness usually accompanied by low-grade fever, anorexia and myalgia are the principal symptoms. URTI infections, on the other hand, have been suggested to be mild and self-limiting, but they have also been linked to life-threatening complications. Furthermore, the cause of URTIs has been attributed to viruses, but studies have suggested that the cause is bacterial. The most common viruses that cause URTIs are rhinovirus, parainfluenza virus, coronavirus, adenovirus, respiratory syncytial virus, coxsackievirus, and influenza virus, whereas the most common bacteria that cause URTIs are beta-hemolytic streptococci, Corynebacterium diphtheriae, Neisseria gonorrhoeae, Arcanobacterium haemolyticum. (Poole MD et al., 2005, Fendrick AM et al.,2003)

While bacterial infections are severe in presentation, abrupt in onset, and typically mucopurulent in nature, viral infections are milder in presentation, gradual in onset, and watery in nature. Hand-to-hand contact

(Cotton M et al., 2004) or self-inoculation of the conjunctiva or nasal mucosa are the two main methods of transmission (Belser JA et al.,2013).

These diseases place a huge health burden not only on individuals, but also on society as a whole. Chronic obstructive pulmonary disease, asthma, acute lower respiratory tract infections (pneumonia), tuberculosis, and lung cancer are the most common causes of high mortality worldwide, and URTIs such as rhinitis, pharyngitis, and tonsillitis have lower mortality but high morbidity (Levine SM et al.,2022). On an average, adults have two to four episodes annually, and young children may have as many as six to eight episodes which make acute URTI the second most common diagnosis in physicians' office (Renati S et al.,2016).

Homoeopathy is a medical system developed by German physician Dr. Christian Friedrich Samuel Hahnemann (10th April, 1755–2nd July, 1843). The main principle of homoeopathy is 'Similia similibus curantur,' which means 'let likes be treated by likes'. Another principle, individualisation, refers to a holistic approach to health, disease, and treatment that takes into account the sick individual on physical, mental, social, and spiritual levels (Pingel S et al., 1992)

Homeopathic medicines are effective? Still a topic of debate due to lack of sufficient evidences. To answer this question, more scientific and evidence based research is the need of time. Homoeopathy not only gained enormous popularity worldwide for its use in a variety of clinical conditions, but it also drew criticism for its highly diluted, minimum doses and therapeutic efficacy in some conditions. We conducted a thorough search for available evidence in homoeopathy for treating URTI in children. Thus our narrative review was aim to evaluate the efficacy of homeopathic medicines in upper respiratory tract infections.

MATERIAL AND METHODS

A comprehensive computerized literature search was carried out to find clinical research Articles. Pub med, Cochrane controlled register of trials (CENTRAL) and two specialty databases called Core-Hom and Cam-Quest, Medline, Google scholars, science direct and Thieme-E- journal of homeopathy was searched extensively. Only human based clinical trials were included in this review. Animal trials, abstracts of articles and pilot studies were not included. Full length research articles were included. Controlled clinical trials (randomised or non-randomised), observational studies and case series describing adequate number of cases (more than 20) were eligible for the inclusion. All randomized double blind placebo-controlled prospective observational clinical research articles were included. We also excluded the articles which were not relevant to our study. Opinion papers and articles without any solid conclusion were also excluded from review.

Total 60 articles were searched through different database. 43 articles were remained after duplication removal. Two reviewers independently screened the articles. 20 articles were not included in this review due to exclusion criteria. 23 full length articles were included in this review. 3 articles were found on acute respiratory tract infections and 20 articles were on upper respiratory tract infections. No single article was found on lower respiratory tract infections.

RESULTS

Total 43 research articles were studied for the review. Irrelevant and duplicated articles were removed. Total 23 articles were selected for the systematic review. The descriptions and principal findings of the included studies were included for review (►Table 1).

(Haidvogl, et al. 2007), conducted a comparative study and concluded that homoeopathic medicines are as effective as conventional treatments. In a case series of URTI in children below 5 years of age illustrated that recurrent episodes of URTI decrease following 6 months of treatment with individualised homoeopathic medicines. [16]

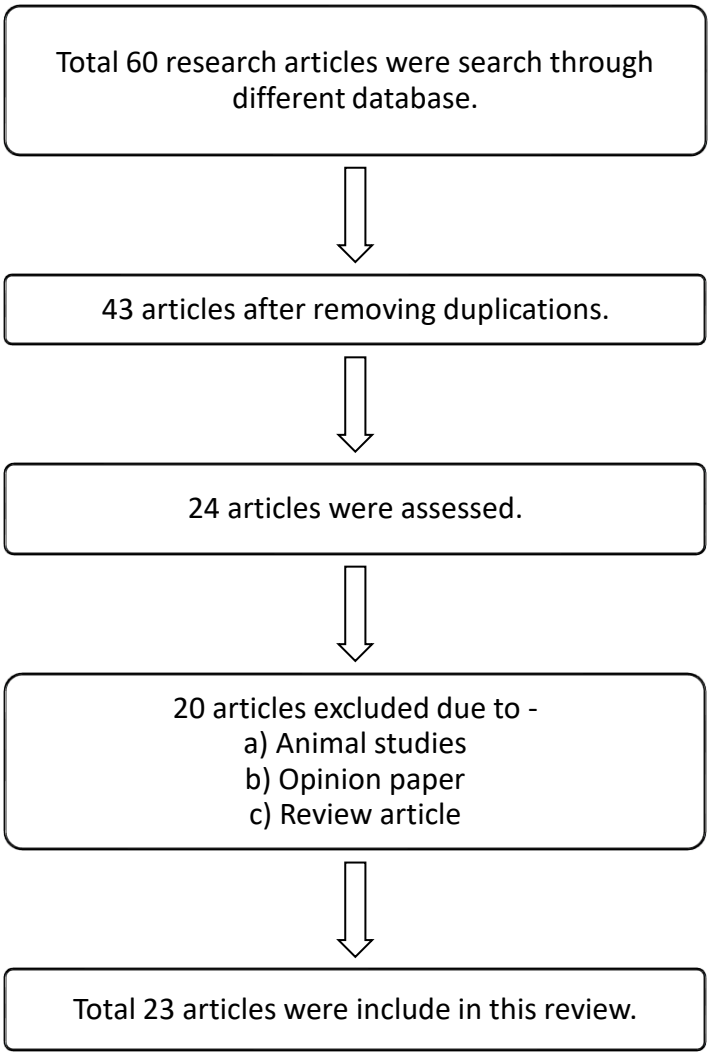

Fig 1: over view of study

(Michalsen et al. 2015), was investigated that, in acute respiratory tract infections homeopathic medicine is safe and effective for both children and adult. The study was prospective non-interventional study . Another trial was conducted by (Siqueira, et al.2016), and the design of this trial was randomized, blind, placebo controlled. Results of this trial was that homeopathic medicines are very effective in reducing the severity of flue and acute respiratory tract infections.

The main findings of this trial was that homeopathic medicines are efficacious in the management of acute rhinitis (Nayak C et al., 2010). One study was conducted on 134 patients of chronic sinusitis. It was a prospective multi-centric observational study and the conclusion of this study was that good improvement was seen in patients after the use of homeopathic medicines (Witt CM et al.,2009). On seasonal allergic rhinitis a study was conducted by (Goossens et al.2009). The study design was prospective open label and comparative. The major finding of study was that after homeopathic treatments, patients reported an alleviation of their symptoms in allergic rhinitis. Randomized double blind placebo controlled trial was conducted in patients with acute viral tonsillitis. After the use of homeopathic complex, a good improvement was seen in patients. No patient reported any adverse effect (Malapane E et al.,2014). Aslaksteinsbekk et al.,2005, conducted a clinical trial for the evaluation of individualized homeopathic treatment in upper respiratory tract infections. He

concluded that homeopathic treatment is efficacious in the prevention of URTI. For recurrent tonsillitis an international pragmatic, randomized controlled trial was conducted in 2017. SilAtro-5-90 and standard treatment was used in 256 patients (Palm J et al., 2017). Van Haselen et al., 2016 conducted a clinical trial on safety and effectiveness of homeopathic medicine in lower respiratory tract infections with fever in pediatrics and positive result was obtained. (Zabolotnyi et al., 2007) conducted a clinical trial in patients with maxillary sinusitis to evaluate the safety and efficacy of homeopathic medication (Sinfrontal). As it was prospective, randomized double blind placebo controlled study and he concluded that complex homeopathic medication is safe and effective. One clinical trial was conducted to evaluate the impact of homeopathic medication on upper respiratory tract infections in COPD patients. This was prospective observational multi-center study. Main findings of this study was that homeopathic medication use during the influenza-exposure period may have a beneficial impact at reducing URTIs number and duration in COPD patients (Diez SC et al., 2019).

One study was conducted on upper respiratory tract infections associated with cold. The trial design was non-randomized observational. Major findings of trial was that homeopathic medicines may be effective for this condition (Schmiedel V et al., 2006). Alessandro Zanasi worked on newly formulated homoeopathic syrup for the patients suffering from acute cough in upper respiratory tract infections and acute bronchitis and study design was randomized double blind placebo controlled. Main findings of this trial were that, homeopathic syrup helps in reducing the symptoms severity of cough and sputum viscosity (Zanasi A et al., 2014). Aslak Steinsbekk carried out a randomized double blind placebo controlled clinical trial among children to investigate the effect of self-treatment with one of three self-selected ultra-molecular homeopathic medicines for the prevention of childhood upper respiratory tract infections (Steinsbekk A et al., 2005). Jennifer Jacobs also conducted a randomized controlled trial of homeopathic syrup in the treatment of cold symptoms in young children and major findings of this trial was that homeopathic syrup appeared to be effective in reducing the severity of cold symptoms (Jacobs J et al.,2016).

Prospective comparative observational trial was conducted in childrens of otitis media. Patients were randomly assigned to group 1 or group 2. No permanent sequels were found in both groups (Friese K et al., 1997). Another study was conducted in 1994 by Weiser and Clasen. It was a randomized double blind trial. Euphorbium compositum S nasal spray was used in sinusitis patients. Euphorbium compositum S nasal spray had shown reliable efficacy and good tolerance in sinusitis patients (Weiser M et al.,1994). Homeopathic ear drops were used as an adjunct to standard therapy for the treatment of acute otitis media in 119 patients. It was a randomized clinical trial. It was concluded that homeopathic ear drops moderately effective in this condition (Taylor JA etal., 2011).

A multicentre open, comparative, randomized controlled clinical trial was conducted to assess the effectiveness, safety and tolerability of a complex homeopathic medicinal product in the prevention of recurrent acute upper respiratory tract infections in children. Conclusion of this study was that, a comparable reduction of Upper Respiratory Tract Infections in both treatment groups observed. Randomized parallel trial was conducted Aslak Steinsbekk in 2007. Patients were randomly assigned to homeopathic care or one of three self-prescribed homeopathic medicines. No relevant effect of homeopathic care and homeopathic medicines was seen (Jong MC et al., 2016). In 2018, a prospective observational study was conducted with the aim of understanding the choice of Pharmacists in prescribing cough syrups in 414 children (Voß HW et al.,2018). Regarding the two homeopathic syrups, the results - were recorded by pharmacists were as follows: “Drosetux” (Drosera 3C, Arni-ca montana 3C, Belladonna 3C, Cina 3C, Coccus cacti 3C, Corallium rubrum 3C, Cuprum metallicum 3C, Ferrum phosphoricum 3C, Ipeca 3C, Solidago virga aurea 1C) or “Stodal” (Antimonium tartaricum 6C, Bryonia 3C, Coccus cacti 3C, Drosera MT, Ipeca 3C, Myocardium 6C, Pulsatilla 6C, Rumex crispus 6C, Spongia tosta 3C, Sticta pulmonaria 3C, Tolu syrup, Polygala syrup). Authors assessed the evolution of the cough, tolerance and satisfaction with the treatment, administering a questionnaire after 5 days of treatment. Two-third of parents showed satisfaction; both with homeopathic or allopathic medicines, and adverse effects were higher in children treated with allopathic drugs. Based on these observations, the authors suggested that homeopathy may have a positive role to play in the treatment of cough in children (Voß HW et al., 2018).

Table 1: Table of Included Studies

S.N.	Author's & Year	Intervention	No. of subject	Conditioned studied	Study Type	Key Results
1.	Haidvogl, *et al*.	Homoeopathy / conventional therapy	1,577	Acute upper respiratory and ear complaint	Comparative study	Homoeopathic treatment was equally effective to conventional treatment
2.	Ramchandani 2010	Individualized homoeopathic medicine	30	Upper respiratory tract infection	Prospective observational study	Decrease of episodes of URTI after homoeopathic treatment.
3.	Michalsen, Uehleke *et al*. 2015	Complex homeopathic drug	1050	Acute respiratory tract infections	Prospective non-intervention al study	Homeopathic complex drug was shown to be safe and effective forchildren and adults likewise.
4.	Siqueira, *et al*. 2016	Group1:Homeopathic complex, group2: placebo group3: InfluBio	445	Influenza and acute respiratory tract infections	RCT	Use of homeopathic medicines minimizes the severity of influenza and acute respiratory tract infections
5.	Nayak, et al. 2010	Homoeopathic medicines	784	Acute rhinitis	Multi-centric open clinical trial	Major findings of this study was that homeopathic medicines are effective in the management of acute rhinitis
6.	Witt, et al. 2009	Homeopathic medicines	134	Chronic sinusitis	Prospective multi-centric observational trial	This observational study showed relevant improvements that persisted for 8 years in patients seeking homeopathic treatment because of sinusitis.
7.	Goossens, et al. 2009	Individualized homeopathic medicines	74	Seasonal allergic rhinitis	prospective, open, non-comparative	After homeopathic treatment, patients reported an alleviation of their symptoms of allergic rhinitis
8.	Malapane, Solomon et al. 2014	1-Homeopathic complex (Atropabelladonn	30	Acute viral tonsillitis	Randomized double blind placebo	The homeopathic complex used in this study exhibited

		a D4, Calcarea phosphoricum D4, Hepar sulphuris D4, Kalium bichromat D4, Kalium muriaticum D4, Mercurius proto iodid D10, and Mercurius bin iodid D10) 2-Placebo			controlled study	significant anti-inflammatory and pain-relieving qualities in children with acute viral tonsillitis. No patients reported any adverse effects
9.	Steinsbekk, Fønnebø et al. 2005	Individualized homeopathic treatment	169	Upper respiratory tract infections	Open, pragmatic, randomized, parallel group trial	Major findings of this study was that individualized homeopathic treatment is effective for the prevention of URTI
10.	Palm, et al. 2017	SilAtro-5-90 standard treatment	256	Recurrent tonsillitis	International, Pragmatic, randomized, controlled clinical trial	SilAtro-5-90 is given alongside Mainstream symptomatic treatment may bring therapeutic benefit to patients suffering from recurrent tonsillitis
11.	van Haselen, et al. 2016	1.Standard treatment 2.IFC is the combination of 6 homeopathic medicines (Aconitum D3, Bryonia D2, Eupatorium perfoliatum D1, Gelsemium D3, Ipecacuanha D3, and Phosphorus D5),	261	Upper respiratory tract infections with fever	Randomized controlled clinical trial	IFC as add-on treatment in pediatric URTI reduced global disease severity, shortened symptom resolution, and was safe in use
12.	Zabolotnyi, et al. 2007	Complex homeopathic medication(28) and placebo	113	Acute maxillary sinusitis	Prospective, randomized double blind placebo controlled	This complex homeopathic medication was safe and appeared to be an effective treatment for acute maxillary sinusitis.
13.	Diez, et al. 2019	Group 1: conventional and homeopathic medication	219	Upper respiratory tract infections in COPD patients	Prospective observational study	Homeopathic medication use during the influenza-exposure period may

		Group 2: conventional treatment only				have a beneficial impact at reducing URTIs' number and duration in COPD patients
14.	Schniedel, et al. 2006	Complex Homeopathic medicines compared with conventional therapies	397	Upper respiratory infections associated with cold	Non-randomized observational trial	Homeopathic treatment may be a useful component of an integrated symptomatic therapy for the common cold
15.	Zanasi, et al. 2014	Homeopathic syrup	80	Acute cough in URTI and acute bronchitis	A randomized, double-blind, placebo-controlled trial	This homeopathic syrup helps in reducing the symptoms severity of cough.
16.	Steinsbekk, et al. 2005	1-Ultra-molecular homeopathic medicines (Calcareacarb ,Pulsatilla, Sulphur) 2-Placebo	251	Upper respiratory tract infections	Double-blind, randomized parallel group placebo controlled design	In this study there was no effect over placebo for self-treatment with one of three self-selected, ultra-molecular homeopathic medicines in preventing childhood URTI
17.	Jacobs, et al. 2016	Homeopathic cold syrup and placebo	261	Cold	Randomized controlled trial	Homeopathic cold syrup appeared to be effective in reducing symptom severity
18.	Friese, et al. 1997	Group 1: Aconite napellus, Apismellifica Belladonna Capsicum Chamomilla Kaliumbichromicum Lachesis Group 2: Nasal drops Antibiotics Antipyretics	131	Otitis media in children's	Prospective comparative observational trial	No permanent sequels were found in either groups

19.	Weiser and Clasen 1994	Euphorbium compositum S nasal spray	155	Sinusitis	Randomized double blind trial	This study revealed a reliable efficacy and good tolerance of euphorbium compositum S nasal spray in the therapy of sinusitis
20.	Taylor and Jacobs 2011	Homeopathic ear drops as an adjunct to standard therapy	119	Acute otitis media	Randomized clinical trial	Homeopathic drpos are moderately effective in treating acute otitis media in children
21.	Jong, et al. 2016	CalSuli-4-02 and comparator homeopathic product	200	Recurrent acute upper respiratory tract infections	Prospective, multicenter, randomized, open, comparative clinical trial	A comparable reduction of URTIs in both treatment groups observed. However, CalSuli-4-02 led to significantly less URTI-related complaints and higher treatment satisfaction.
22.	(Steinsbekk, Lewith et al. 2007	Self-prescribed Homeopathic medicines vs homeopathic care	208	Upper respiratory tract infections	Randomized parallel study	The main findings of this study that there is no relevant effect of homeopathic care and Homeopathic medicines given by child's parents.
23.	Allaert 2018	Management of cough with two homoeopathic syrups or with allopathic drug by pharmacists.	414	Upper respiratory tract infections	Prospective observational study, without control group	Better improvemts with homoeopathic syrupa and same satisfaction.

24.	Voss 2018	Homoeopathic complex (drosera,cocus cacti, cuprum sulph, Ipecachuana vs placebo)	89	Upper respiratory tract infections	Clinical study	Improvement of symptoms and equal tolerability.

DISCUSSION

This systematic review was carried out to establish the fact that homeopathic medicines are safe and effective. For this purpose, full length articles were studied related to upper respiratory tract infections. All searched articles were about acute respiratory tract infections or upper respiratory tract infections, not a single article found about lower respiratory tract infections. Although efficacy of homeopathic medicines is still a controversial topic but despite this fact majority of patients are highly satisfied with the use of homeopathic medicines (Marian F et al.,2008) due to safety aspect of homeopathic medicines (Pilkington K et al., 2005). As we all knows, Homeopathy was introduced by German physician Samuel Hahnemann. He was the person who established basic principles of homeopathy (Bodeker G et al.,2005). Homeopathic medicines are prescribed according to like cures like and potentization principles (Cooper KL et al., 2010).

Homeopathy is one of the most popular form of complementary and alternative medicines (Pilkington K et al., 2005). Thus the main aim of this review to document the safety and efficacy of homeopathic medicines in respiratory tract infections. In this review total 21 articles were included. 3 articles were related to acute respiratory tract infections and 18 were related to upper respiratory tract infections. All of three studies concluded that homeopathic medicines are effective in acute respiratory tract infections. A comparative study was conducted in 1577 patients with acute respiratory and ear complaints. Homoeopathic treatment was equally effective to conventional treatment were the main findings of study. The main flaws of this study were that patients were not randomly assigned to their respective study groups. Patient's preference for homeopathic medicines was also a big limitation of study. Moreover, the result of two clinical trial was that homeopathic medicines are safe and equally effective in certain disease conditions.

Out of 21 articles, 18 articles were on upper respiratory tract infections. In one study it was concluded that homeopathic medicines were effective in acute rhinitis condition. It was a multi-centric observational study. In chronic sinusitis and seasonal allergic rhinitis two articles were found and the main findings of these articles were that, homeopathic remedies are effective. Although Homeopathic medicines are found to be effective in many respiratory complaints but more refined and strong methodological studies should be conducted to established concreate conclusion.

Overall significant results were found about the safety and efficacy of homeopathic medicines in upper respiratory tract infections.

Only few articles were not reached to any concreate conclusion due to some limitations of clinical trial. Insufficient sample size, high dilutions of homeopathic medicines were the major flaws of the study. But according to Samuel Hahnemann, smallest amount of medicine can produce better result [44].

As conclusion, this systematic review concluded that homeopathic medicines are safe and effective in acute and upper respiratory tract infections. But more randomized placebo controlled studies should be conducted to strengthen the available evidence. In future studies must be conducted in lower respiratory tract infections as we did not found any article related to it.

We have categorised and described the most significant homoeopathic studies in the fields under consideration in this work, and we have proposed a semi-quantitative evaluation criterion that allows evaluating the entire set of results without eliminating any work, as they did in previous meta-analyses. We have the

advantage of including the contribution, albeit partial, of each publication of sufficient validity and thus of having an overall view of literature in a relatively small field like homoeopathy, where scientific research is still in its infancy and there is no consensus on the model validity of different approaches. The use of personalised homoeopathy or homoeopathic medications could be considered as a potential option in the fields reviewed in this work, especially in light of the clinical findings.

Conflict of Interest: The authors declare there is no conflict of interest.

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