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A Review on Homoeopathy and Immunology

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Abstract

The current research examines numerous studies that consider the role of homoeopathy as an immunological modulator. Both homoeopathy and immunology are theoretically related. Homoeopathy is clearly useful in increasing immune responses in illnesses ranging from allergies to neoplasms. Homoeopathic treatment has been shown to have stimulatory and co-stimulatory effects in immunological processes such as haematological parameters such as total and differential leukocyte count proliferation, haemoglobin count with hematopoietic parameters such as bone marrow cellularity, inflammatory processes, CRP value, phagocytises, fibrosis, CD4+ & CD8+ count as well as a boost in immunoglobulin tit Several research studies indicate that homoeopathic immunotherapy has an immunological modulator impact on endogenous molecules such as thymulin, cytokines, histamines, and immunoglobulins (endoisotherapy). Homoeopathic preparations derived from common allergens, influenza agents, Leptospirosis, Tuberculosis, Vibrio parahemolyticus and Vibrio alginolyticus, and cancer cells have also been shown to be useful in eliciting an immune modifying response. Homoeopathic medications affect the immune system by altering gene expression, stimulating macrophages, chemo taxis of polymorph nuclear cells, and producing cytokines.

Keywords: *Cytokines, Homoeopathy, Immuno-modulation, Immunotherapy*

INTRODUCTION

In recent years, there has been a rebirth of scientific studies in homoeopathy, particularly in relation to the notion of 'ultra-dilution/dynamization' of medicines, their mode of operation, and the dependability of its primary principles, the'simile.' Several research have been conducted to demonstrate the underlying mechanisms of action of homoeopathic drugs. The number of preclinical (in vitro and in vivo) research examining their pharmacological efficacy has increased. On the basis of current immunological and pathological understanding, some clarity on its methods of action is expected.

The current research examines numerous studies that consider the role of homoeopathy as an immunological modulator. Both homoeopathy and immunology are theoretically related. The function of membrane bound toll-like receptors is to recognise pathogen-associated molecular patterns of invading microorganisms and, upon activation, mount rapid, nonspecific innate responses and trigger sequential delayed specific adaptive cellular responses, which are mediated by complex signal transduction pathways involving adaptor molecules, co stimulatory ligands and receptors, kinases, transcription factors, and modulated gene expression. [1]

Immunological processes comparable to homoeopathy follow the principle of similarity, which is reflected in the nonlinearity of the dose-response relationship. One example is cytokine, which may be healing in tiny doses but lethal in big doses. In homoeopathy, for example, low dosages of the same drug show harmful effects while large amounts have a paradoxical protective or therapeutic effect. [2]

In Multiple Sclerosis the conventional therapeutic system opts for drugs like natalizumab which suppresses the immune response and later on withdrawal of the drug the disease is relapsed as the rebound effect of the secondary action also called as Immune reconstitution inflammatory syndrome (IRIS). Whereas in Homoeopathic management the Law of similar is followed wherein due to the administration of a drug similar in disease condition in its action, creates a paradoxical or biphasic action (rebound effect) in the organism as therapeutic response.[3]

HOMOEOPATHIC THERAPEUTIC ACTION THROUGH THE REVELATION OF IMMUNOLOGY

Arndt-Schulz Law states that weak stimuli slightly increase biological responses, medium strong stimuli markedly raise them, strong ones suppress them and very strong ones arrest them. A well tested phenomenon of immunology states that a wide variety of substances exert opposing effects (inhibitory or stimulating) at low or high doses.[4] A study conducted by researchers at the Harvard Medical School in Boston observed auto reactivity of T cells is managed by the immune system in at least two different ways depending upon the concentration of self-antigens they encounter, if high concentrations are present then they are killed. When low dose of self- antigen then they undergo active inhibition (called 'bystander suppression'). This reactive pattern of immunological cells can be the medium to explain the therapeutic effects of Homoeopathic pharmaceuticals.[5]

EVIDENTIAL IMMUNOLOGICAL EXPERIMENTS WITH HOMOEOPATHIC REMEDIES

An experimental study was conducted to evaluate the Homoeopathic remedies with antineoplastic properties (Thuja 1M, Carcinosin 200C, Ruta 30C) having immune-modulator effects on Balb/c mice. Results reveal that Homoeopathic medicines significantly enhanced the haematological parameters like total and differential WBC count, haemoglobin count, hematopoietic parameters like bone marrow cellularity and α-esterase positive cells along with enhanced immune parameters for antibody (titer) response and enhanced B & T lymphoid cell proliferation. This positive immunological response was significant when compared with other group with exposure to antibiotics and other placebo group, thus depicting efficacy of homoeopathic medicines through parameters of various immune responses.[6]

A comparative study to investigate effect of Canova on normal and sarcoma 180 bearing mice shown that the group administered with homoeopathically prepared Canova on histological examination revealed a delay in the development and a reduction in size of the tumors. Also on flow cytology observations there was increased infiltration by lymphoid cells, granulation tissue and fibrosis surrounding the tumor. Moreover all animals survived in the intervention group, whereas, 30% of animals in observational group died. A total regression of tumor was observed in 30% of intervention group whereas no regression of tumor was

noticed in observational group. Treatment with Canova increased total number of leukocytes and lymphocytes and thus it proves to enhance immune response of the host.[7]

An experiment was performed to investigate the effect of Echinacea, Aconitum, Lachesis and Apis extracts, and their combinations on phagocytises of human granulocytes after incorporation of latex microspheres. Result reflected that only vitamin C, Lip polysaccharide and Echinacea Angustifolia were able to enhance the rate of phagocytises. Whereas Aconitum, Apis mellfica, Lachesis individually failed to stimulate phagocytises but showed an enhanced effect when combined with one another or with Echinacea. A combination of Aconitum and Lachesis was able to stimulate phagocytises up to 390%.[8] A study was conducted to evaluate the gene expression modifying effect of homoeopathic complex medication Canova. Outcome revealed decrease in interleukin – 2 and interleukin – 4 productions and a differential expression in 147 genes from Canova group. These genes are mainly involved in transcription/translation, cell structure and dynamics, immune response, cytoprotection enzymatic process and receptors/ligands. Thus affirming that Canova provokes a reaction that involves modifying gene expression.[9] A study was conducted to evaluate the immune modulator effect of Homoeopathic commercial compound product Engystol upon antigenic challenge in mouse model. Results revealed that Engystol alone did not alter immunity of mice in pre antigenic challenge, but with post antigenic challenge it decreased CD4(+)/CD8(+) ratios, altered select cytokines/chemokines, and anti-H5N1 HA IgG titers were increased in comparison to control group. Thus this study finding is suggestive that Engystol can modulate immunity upon antigenic challenge.[10]

A double-blind randomized control trial conducted to investigate the cardio protective immune modifying effect of Phosphorus 13C after artificial inoculation of Trypanosome Cruzi in rat model. It revealed that rats treated with Phosphorus 13C yielded higher concentrations of interferon – gamma on the 5^{th} day of infection with significant decrease on the 10^{th}& 24^{th} day. Also high concentration of tumor necrosis factor alpha was observed on 5^{th} and 10th days of infection with decrease on 24^{th} days of infection. In comparison to control group, intervention group reflected significant hike in interferon gamma and tumor necrosis factor alpha on 5th day of infection. Also the experiment group had 52.5% less number of myocarditis focuses in heart, relatively on 10th day of infection. The significant increase in cytokines on 5^{th} day resulted in significant 10^{th} day reduction in the number of inflammatory foci in cardiac tissue.[11] A case control study was conducted to investigate the

immune modulator and neuro digestive effect of Lycopodium Clavatum 13C in rats artificially inoculated with Trypanosoma Cruzi infection. Results revealed that the cytokines, its dosage, quantification and morphometry of myenteric neurons were raised. Experiment group showed increase in interferon – gamma on 10th day after infection & on 24th day interleukin - 12 surged along with decrease in interleukin – 10 concentrations on 10th day after infection and thus increase in cytokines and interleukin – 4 on day 24th resulting in huge number of myenteric neurons relatively. Thus Lycopodium Clavatum 13C promotes a beneficial immunomodulatory action reducing the pathogenic progression in rats infected with Trypanosoma Cruzi.[12] A study suggests that Homoeopathic drug Canova seems to be beneficial in stabilizing platelet morphology and thus can be effective as an immune modulator.[13]

A study was conducted to affirm the immune modulatory effect of homeopathically prepared Engystol – N of potency between 4X to 8X, on isolated leukocytes and in whole blood counts. It reveals that Engystol stimulates the production of cytokines with inhibiting action on superoxide anion generation of neutrophils, thus confirming its immune modulatory effect.[14] A study to evaluate the immune modulatory response of homoeopathic medicines in Rheumatoid Arthritis revealed that along with clinical improvement Pulsatilla produced significant reduction in ESR value and in patients treated with Rhus tox and Medorrhinum compared to control arm there was significant reduction in IL 6 levels. Thus with the mentioned outcomes it can be suggested that Homoeopathic medicines indulge positively in immune modulation mechanism.[15]

In vitro studies effects of homoeopathic medicines on immunological & inflammatory cells suggest that they have stimulatory and co – stimulatory effects on cytokines, antibody production (basophils, lymphocytes, granulocytes and fibroblasts) and activation of immune competent cells and macrophages.[16] A study was conducted to test the immune response modifying potential of a Homoeopathic complex Canova. The result revealed that, on encountering with macrophages lymphocytes underwent higher number of proliferations by Canova treatment, in comparison to the lymphocytes without Canova treatment. This Canova action causing lymphocyte proliferation was observed due to presence of Interferon gamma and interleukin – 5 cytokines.[17]

A study conducted to evaluate the immune-stimulatory activity of Rhus Tox in different potencies depicted that Rhus Tox was found to affect the immune response; however the crude form, mother tincture, 6cH, and 30cH dilutions appeared to be more potent in comparison to higher potencies. In vitro studies all the dilutions demonstrated stimulation of phagocytosis, candida-cidal activity and chemo taxis of human polymorph nuclear cells. Also, oxidative processes in the polymorph nuclear cells were accelerated in the presence of Rhus Tox.[18] A case control study conducted to examine the existence of positive biological effect of high dilutions of histamine on activation of basophils. Result revealed that there was significant reproducible inhibition of human basophil activation by high dilutions of histamine in comparison to effects observed with water controls at same dilution levels. The potency with peak effect was observed in the range of 15 – 17CH. Absence of significant biological effect was seen when histamine was replaced with histidine (a histamine precursor).[19]

A study was performed in order to test the Immune modulation effect of Mercurius Solubilis in 6, 12, 30, 200 centesimal high dilutions potencies on mice peritoneal macrophages. It revealed that macrophages showed activated morphology in both in vivo (Mercurius solubilis added to drinking water of mice) and in vitro studies (Mercurius Solubilis added directly to mice peritoneal macrophages). Depending upon the dilutions of Mercurius Solubilis immunological cells stimulated by macrophages are interferon release at lower dilutions and production of Interleukin – 6 at higher dilutions.[20] An in vitro study conducted to test two Homoeopathic preparations (Phase 6 & Flu Terminator) effect in immune modulation by stimulation of cytokines to produce leucocytes. In comparison to the carrier solvent (20% ethanol), both the Homoeopathic preparations have showed that they stimulated the production of pro and anti-inflammatory cytokines by human leukocytes, also it was observed that low doses generate a stronger response in comparison to high doses of homoeopathic preparations. Whereas, the carrier solvent 20% ethanol failed to elicit any form of cytokine synthesis.[21] Homoeopathic treatment in cases of HIV revealed significant improvement in immunological parameters, CD4 & CD8 cell counts.[22]

A case control study was conducted to evaluate immune modulator effect of Homoeopathic drug Metodo Canova. Mice peritoneal macrophages were cultivated with (Case) and without (Control) Homoeopathic medicine Metodo Canova. Outcome was a marked difference in

morphology and molecular distribution (alpha5 and beta 1 integrins, actin filaments and Fc receptors). Results reveal that control group macrophages had the morphology of resident cells and in intervention group macrophages were more spread, had many cellular projections and a substantial increase in cytoplasmic volume. Also in comparison to control group, macrophages culture with 2 doses of Metodo Canova showed decreased production of tumor necrosis factor – alpha.[23]

A research paper published, states conclusions drawn from three different experiments aimed commonly towards investigating the effect of highly diluted solutions of silica on mice macrophages, on stimulation with 50 and 200 microgram zymosan per milliliter. First experiment includes three groups, group 1 of mice receives 1.66 X 10-11 M Silica in drinking water for 25 days, group 2 of mice receives 1.66 X 10-19 M Silica for same period and group 3 was untreated. They resulted in production of 44.2 and 30.8% respectively more paf-acether by group 1 mice peritoneal macrophages and 67.5 and 38% respectively more paf-acether by group 2 mice peritoneal macrophages, in comparison to the third observation group mice. Second experiment includes 3 groups of mice; group 1 consists of mice receiving 1.66 X 10-19 M of Silica and group 2 mice received normal saline subjected to the same dilution procedure, while group 3 mice remained untreated. They resulted in 55.5 and 33.5% respectively more paf-acether synthesis by group 1 mice peritoneal macrophages, in comparison to group 2 mice. Third experiment includes 3 groups of mice, group 1 mice was administered 1.6 X 10-19 M of silica, group 2 mice received normal saline or lactose subjected to the same dilution procedure and group 3 was left untreated. The result was 61.3 and 28.6% respectively more paf- acether synthesis in group 1 mice peritoneal macrophages in comparison to group 2 mice. In all the three experiments, the difference between the control group and the group receiving the Silica treatment were statistically significant.[24]

A study was conducted to evaluate the stimulatory activity of lymphocytes by co cultured macrophages against the melanoma, when intervened by a complex homoeopathic medication. Results revealed that in comparison to controlled lymphocytes, the group where a complex homoeopathic medication is introduced to lymphocytes co cultured with macrophages there was a greater anti melanoma activity observed. It was demonstrated by reducing melanoma cell density and increasing the number of lysed tumor cells, along with higher proportion of activated CD25+ lymphocytes with increased viability. Thus by

Homoeopathic complex medication lymphocytes destroyed growing cancer cells more effectively than control lymphocytes.[25]

A study was conducted to investigate the activity of a homoeopathic formulation Traumeel S and its individual component in blood induced inflammations in rats. After triggering the edema development process and local administering the Traumeel S and its individual components, observations were rapid reduction in paw edema in rats treated with Traumeel S in comparison to control group rats. Similar effects were noticed when rats were tested with individual drug components of Traumeel S. The efficacy of Traumeel S together was more in comparison to its individual components. Traumeel S proved effective not only on administering it locally an hour before the experiment but also proved effective when administered after the edema induction. This therapeutic effect of Traumeel S was associated with a significant decrease of systematic interleukin-6 production.[26]

ROLE OFHOMOEOPATHIC IMMUNOTHERAPY (HIT)

A study was conducted to estimate the immune modulator effect of endogenous substances like thymulin, cytokines and other hormones, prepared according to Homoeopathic methods. Thymulin 5CH when administered to mice reflected enhanced phagocytic activity when experimentally exposed to different viral, bacterial and parasitic infections.[27] Another study with same medicine when administered in a mice who is inoculated with murine Leishmaniosis showed more exuberant inflammatory response at the site of infection and decrease in number of parasites inside the primary lesion with no difference seen in local lymph node histology.[28]

A case control study was conducted to see the effects of homoeopathic dilutions of histamine on basophil degranulation. Study stated that homoeopathic preparation of histamine was associated with a significant inhibition of basophil degranulation against the identically diluted water samples.[29] A study investigates the modifying effect of homoeopathic treatments in immune response to influenza antigen. On administering BALB/c mice, for 21 days with influenzinum (isotherapy) and thymulin (endo isotherapy) Homoeopathic preparation and on 21st day influenza antigen challenge was performed; there was significant changes in T & B cell balance, as per flow cytometry & morphometry.[30]

Different researches to explore effect of high dilution of immuno-allergological substances has been conducted. One of the study revealed that Thymulin has positive immune modulating effect. Rhus tox has an anti-inflammatory activity reflected in different models right from the mother tinctures to high dilutions. In vitro and in vivo studies demonstrated the induction of lymphocyte proliferation, and reduction in the size of tumors and mortality of sarcoma bearing mice. In allergic conditions, high dilution histamine has an inhibitory effect on basophil activation in both multicentre trials and independent trials. However few well examined studies reveal no effect of high dilution histamine.[31]

In an in-vitro single blind study conducted to investigate the effect of highly diluted homoeopathic drugs Lung Histamine and Apis Mellifica on human basophil degranulation. Basophil degranulation induced by M anti – IgE antibody was significantly inhibited in the presence of Lung Histamine 5CH and 15 CH by 28.8% and 28.6% respectively, but it is nearly 100% inhibited when tested with high potency of 18CH and beyond. Basophil degranulation induced by M anti – IgE antibody was significantly inhibited in the presence of Apis Mel 9CH by 65.8%, but it was nearly 100% inhibited when tested with high potency of Apis Mel 10CH and beyond.[32] A total of 83 original studies were noted suggesting significant positive outcomes in allergic conditions with Homoeopathic medicines. Galphimia glauca (low homeopathic dilutions) in allergic oculo-rhinitis, Anas barbariae (high homeopathic dilutions) in influenza-like syndromes, classical individualized homeopathy in otitis, in allergic complaints and in fibromyalgia, and a few low-potency homeopathic complexes in sinusitis, rhino conjunctivitis, arthritis were found effective.[33]

An in vitro isobathic study was conducted to investigate the biological effect of low dose and high potency of Cadmium Chloride on both human primary lymphocytes and human leukemia cell line. The result depicted significantly increased cell viability in primary lymphocytes in comparison to control cells after exposed to toxic challenge, when pre-treated with low concentrations or high potency of Cadmium Chloride. Similar significant observation was noticed by cancerous lymphocytes when pre-treated with low doses of Cadmium Chloride, although response was weaker in comparison to effect observed on normal lymphocytes. There was no effect on cancerous lymphocytes after administration of high potency of Cadmium Chloride.[34]

A double blind case control study was conducted on 40 samples with seasonal allergic rhinitis symptoms, wherein the effect of homoeopathic preparations from common allergens (tree, grass, and weed species) were tested on them. Result shows that in relation to placebo group, significant positive changes were observed in the group administered with homoeopathic medicines.[35]

A double-blind case control study was conducted on 32 study samples and 34 control samples to see the effect of isopathic remedy Betula 30C to patients suffering from birch pollen allergy. Results revealed that there was no statistically significant difference in the study and control group in the initial & last part of the May month and from 8th to 18th May there was significant difference i.e. the group receiving Betula 30C depicted fewer and less severe symptoms relative to the control group.[36] In an experimental study when homoeopathic preparation of anti IgE within the range from 1 X 10(2) to 1 X 10(120), demonstrated basophil degranulation from 40 to 60%, despite absence of any anti – IgE molecules at the highest dilutions, on calculation. Thus by this experiment it can be stated that homoeopathic preparation of anti-serum against IgE can very well generate an immune modulatory response.[37]

A case control study was conducted independently to re test the evidence from the prior two trials supporting the hypothesis that homoeopathy differs from placebo. Homoeopathic immunotherapy was administered, wherein 28 subjects with allergic asthma were prescribed with homoeopathic immunotherapy to their respective principal allergen or with a contemporary control group. The daily visual analogue scale of overall symptom intensity favoured homoeopathic immunotherapy within a week of homoeopathic treatment and persistently for 8 weeks. In respiratory function and bronchial reactivity tests similar trends were observed. Thus strengthening the evidence that homoeopathy does more than just placebo.[38]

A study was conducted to investigate the immune response of homoeopathic preparation of nosodes, Vibrio parahemolyticus and Vibro alginolyticus (H1) group and commercial homoeopathic medication Phosphoric Acidum and Silicea Terra (H2) group on longfin yellowtail fish juveniles, when challenged with Vibrio Parahaemolyticus. Results revealed that with respect to control group H1 treatment group showcased an over expression of the

interleukin – 1 beta and it's under expression was observed when treated with H2 treatment group. When the fish treated with H1 group and H2 group after getting challenged with Vibrio parahemolyticus resulted in, over expression of Interleukin – 1 beta. The results suggest that the effect of H1 was due to the presence of unknown antigens lower concentrations (hormesis) and the response of H2 treated group after pathogenic challenge may have been due to a stimulating effect of nano structures.[39]

A study was conducted to investigate the effectiveness and safety outcome assessment of specific sublingual immunotherapy (SLIT) against non-specific homoeopathic therapy for treatment of intermittent (IAR) & persistent allergic rhinitis (PAR). Both therapeutic methods presented with symptomatic relief but non-specific homoeopathic treatment lead to an improvement in persistent allergic rhinitis in comparison with specific sub lingual immunotherapy. Thus, results suggest that specific sub lingual immunotherapy was less effective than homoeopathic treatment in children with allergic rhinitis.[40]

A study was conducted to evaluate the effect of homoeopathic Immunotherapy against cancer. Homoeopathic complex medicines coded as M1 & M8 when tested in vivo & in vitro prevented lung and subcutaneous melanoma growth, decreased angiogenesis inside tumors, decreased some extracellular matrix molecules, such as perlecan and hyaluronic acid, decreasing metastasis, activated macrophages that can activate other cells in the immune system as well as endothelial cells and fibroblasts; modulated cytokines such as TNF alpha, IFN gamma, IL 10, increased not only the differentiation of NK cells but also the cytotoxicity of NK cells, modulated reactive oxygen species and nitric oxide production. Thus it can be said that through homoeopathic medicines, individuals self-healing power is stimulated through immune system to firstly identify the target cancer cells and act against it exclusively and thus giving gentle restoration of the individual's immune system.[41]

A study was conducted to evaluate the immune modulator potential of homoeopathic medicine Thymulin 5CH in a BCG induced Granuloma Model. The score of infected phagocytes in the lesion decreased and the number of B1 derived phagocytes, CD4+ and CD8+ T lymphocytes in the local lymph node increased in relation to control group of mice. Thus these results suggest that thymulin 5CH treatment is able to improve the granuloma

inflammatory process and the infection remission, by modulating local and systemic phagocyte differentiation.[42]

Homoeopathic medicines produce modulation of immune function at multiple levels, including gene expression modulation, stimulation of macrophages, expression of receptors on macrophage surface, chemo taxis of polymorph nuclear cells and production of cytokines and reactive nitrogen and oxygen species from the immune cells observed in mice models. Such pre-clinical study results are suggestive of Homoeopathic treatment having a potential for individual specific immune modulation.[43]

There is a need of better study models to assess immune modulatory effects of homoeopathic medicines which can explore molecular mechanism behind modulation of immune function at multiple levels.

CONCLUSION

Homoeopathy is clearly beneficial in increasing immune responses in illnesses ranging from allergies to neoplasms. In immunological processes, homoeopathic therapy appears to have stimulatory and co-stimulatory effects. Homoeopathic medications affect the immune system by modifying gene expression, stimulating macrophages, causing chemotaxis of polymorph nuclear cells, and producing cytokines.

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