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Review Article

ROLE OF AYURVEDA IN THE MANAGEMENT OF CHILDHOOD IMMUNODEFICIENCY DISORDERS

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ABSTRACT

'*Swarnaprashana'* as a *lehana chikitsa* and several Ayurveda *Rasayana* drugs can boost the immune system in a specific or nonspecific manner including both innate or adaptive arms of the immune response and enhance the body's overall natural resistance to the disease-causing agent rather than directly neutralize the agent itself in children. **Aim:** To critically review and analyze the role of Ayurveda in the management of childhood immunodeficiency disorders. **Method:** Various Traditional Ayurveda texts and books, magazines, and research journals as well as PubMed, ScienceDirect, Scopus, Web of Science, Ayush research portal, and Clinical Trial Registry, India are used as a source of information about the immune-enhancing effect of Ayurveda drugs useful in childhood immunodeficiency disorders. **Discussion:** Immunodeficiency disorders are a group of heterogeneous disorders with immune system abnormalities characterized by various combinations of recurrent infections, autoimmunity, lymphoproliferation, granulomatous process, etc. '*Swarnaprashana'* as a *lehana chikitsa* and Ayurveda *Rasayana* drug helps the body resist its natural tendency to manage or tolerate the strength, severity, or progression of an illness as well as its natural tendency to prevent the emergence of an illness. '*Swarnaprashana'* and *Rasayana* drugs are used as antioxidants, improving immune status, bactericidal & antimicrobial activity, antiviral, and protectives. It promotes an individual's strength, boosts immunity, and helps to prevent and overcome illness. When the immune system is compromised, it results in immunodeficiency, which leaves the body exposed to a variety of fatal illnesses. '*Swarnaprashana'* and *Rasayana* drugs mentioned in Ayurveda classics are known to boost the immune system. **Conclusion:** The present paper reveals that '*Swarnaprashana'* as *lehana chikitsa* and Ayurveda *Rasayana* drugs are effective in treating childhood immunodeficiency disorders.

INTRODUCTION

Immunodeficiency refers to a compromised or complete absence of a certain immune system's ability because of the malfunction or absence of immune system components, including lymphocytes, phagocytes, and the complement system. Immunodeficiencies can be divided into two types, i.e., primary, or secondary. T-cell deficiency, B-cell deficiency, both T-cell and B-cell deficit, complement deficiency, phagocyte deficiency, and immunoglobulin A deficiency are all subtypes of primary immunodeficiency (PID). [1] These diseases influence both innate and adaptive immunity, and they can cause a variety of symptoms, such as an increased risk of infection, autoimmune disease, inflammation, allergies, and cancer. Contrary to popular belief, PIDs can occur in the general population at prevalence rates as high as 1:1200[2]. Particularly in regions with a high prevalence of infectious diseases, such as most poor nations, the diagnosis of PIDs is frequently delayed or even overlooked entirely.

The more recent understanding of the neuroendocrine-immune axis or the influence of exercise, circadian rhythms, seasonal variations, and different psychological states on the immune system is unfolding many such issues which are bringing the

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modern concept closer to Ayurvedic principles of *Vyadhi-kshamatva*, *Ojas* and *Bala*. *Vyadhi-ksamatwa* (natural resistance) is not of the same order constitutions i.e., it varies with individuals. It also depends upon nutritional, environmental, and individual factors– both physical and mental. The *Vyadhiksamatwa* or *Bala* is stated to be of three types.[3] *Sahaja bala* refers to the genetic and inborn resistance to disease, which exists since birth. It is said to increase with the growth of tissues and does not depend upon any other cause. The term *"Kalaja Bala"* describes the strength a person has developed as a result of the transient effects of aging and seasonal change. It mimics acquired or adaptive immunity in contemporary science. The third type mentioned is *Yuktikrit Bala*. This type of *Sarira Bala* refers to the modulation of the body's resistance against diseases by resorting to an appropriate *Ojovardhak* diet, physical exercise, rest, restorative, and *Rasayana*, therapies in keeping with seasonal needs. *Chakrapanidatta* has interpreted the term *Vyadhi-kshamatwa* as *Vyadhi Bala Virodhitwa* i.e., antagonistic to the strength and virulence of the disease, and *Vyadhyutpada Pratibandhakatwa* i.e., the capacity to inhibit and bind the causes and factors of the disease.[4] The concepts of *Ojas* and *Bala*, of the inherent immunological capabilities including innate immunity and acquired immunity in terms of *Sahajabala* and *Yuktikritabala,* etc., playing a key role in health and disease must be understood and appreciated by modern immunologists. In Ayurvedic practice, the objective of immune enhancement of children is achieved using the '*Swarnaprashana'* as a *Lehana chikitsa* and several Ayurveda *Rasayana* drugs, following *Vyadhi-ksamatwa*, as it is understood in Ayurveda has much wider implications than the term "Immunity" used in modern medicine.

Need of Study

The main problem facing medical science now is antibiotic resistance. Children are more vulnerable as a result of the inappropriate use of antibiotics, thus great care must be made when screening the medications and formulations. Ayurvedic medicines are to enhance the body's overall natural resistance to the disease-causing agent rather than directly neutralize the agent itself. Ayurveda drugs are usually involved in managing any infections that are already present and preventing future infections and replacing or boosting the parts of the immune system that are damaged or missing. These *Swarnaprashan* and herbal *Rasayana* drugs have wide scope for application in the normal population for the enhancement of their immune status and prevention of various communicable and infectious diseases, and as an adjunct in the therapy in the immunocompromised disease states.

AIM

To critically review and analyze the role of Ayurveda in the management of childhood immunodeficiency disorders.

METHOD

Various Traditional Ayurveda texts and books, magazines, and research journals as well as PubMed, ScienceDirect, Scopus, Web of Science, Ayush research portal, and Clinical Trial Registry, India are used as a source of information about the immune-enhancing effect of Ayurveda drugs useful in childhood immunodeficiency disorders.

DISCUSSION

Immunodeficiency is a state in which the immune system's ability to fight infectious disease is either compromised or completely absent. The enhancement of the immune responsiveness of an organism against a pathogen is done by nonspecifically activating the immune system using immunomodulatory agents. With the help of Ayurvedic medicines, there is the enhancement of the overall natural resistance of children against disease-causing agents rather than directly neutralizing the agent itself. The Ayurveda drugs which are useful for immunodeficiency disorders in children are '*Swarnaprashana'* as a *Lehana chikitsa* and several Ayurveda *Rasayana*, describe below-

'Swarnaprashana'* as a *Lehana Chikitsa

'*Swarnaprashana'* is a crucial recipe for promoting a child's growth, improving their memory, and extending their lifespan[5]. *Madhu* being *yogvahi*, along with *Ghrita*, which can imbibe the quality of drugs combined with it, enhances the therapeutic properties of gold like immunomodulatory action, anti-oxidative and anti-stress activity, etc. The *Madhu-Ghrita* combination has a very strong immuno-potentiating effect in the pharmacological investigation, both in terms of humoral antibody production and cell-mediated immunity. The only combination having an impact on humoral antibody production is *Madhu-Ghrita-Swarna-Vacha*. In the clinical study, *Madhu-Ghrita* and *Madhu-Ghrita-Swarna-Vacha* both act as equivalent immunomodulators for neonates. They have definite action on the immune system as evidenced by triggering the immune system's response by inducing an increase in the total proteins and serum IgG levels as compared to its decrease in the control group[6].

Another pharmacological clinical research was performed on gold nanoparticles, which showed that when faced with an inflammatory threat, gold nanoparticles modulate the immunological response. The therapeutic application of nanoparticles in diseases involving inflammatory problems is demonstrated by these findings[7].

Its immunomodulatory activity was evaluated in male mice. *Kushtha Tila Kalan* (KTK) was orally administered to animals at dosages of 6.25, 12.5, 25, and 50mg/kg body weight for 10 days. Besides general immuno-pathological parameters, cell-mediated immunity was evaluated by measuring delayed type of hypersensitivity response (DTH) while humoral immunity was assessed using plaque-forming cell (PFC) assay.[8]

The clinical study "Immunological, Biochemical, and Infant-Toddler Quality of Life Parameter-Based Study of *Swarnaprashan* (a Herbo-Mineral Ayurveda preparation) in Infants" showed a statistically highly significant increase in all the anthropometrical measurements of infants and did not hamper normal growth of the infants[9].

The randomized open-label control study aimed to observe the demographic status of morbidity in children in a defined population, to decrease the morbidity status in children with *Swarnaprashan,* and to observe the immunomodulatory effect of *Swarnaprashan. Swarnaprashan* works as an immunomodulatory which decreased/lowered the morbidity rate and therefore can be a simple remedy to bring down the morbidity rate in children. [10]

Ayurveda *Rasayana* drugs

Rasayana refers to nutrition, natural resistance, and geriatrics. The functions of *Rasayanas* are to improve the state of nourishment, which in turn upholds increased immunity and youthfulness. *Rasayana* can be a drug, diet, or even a lifestyle and conduct i.e., Achar, which may help achieve the above goal. The *Rasayanas* are supposed to strengthen *Ojas* and *Bala* i.e., vitality and bio strength with a natural resistance against aging and disease. It is stated to contribute to the integrity of body tissues and thus increase longevity. The other benefits of this therapy are the promotion of memory and intelligence, and the preservation of youth, luster, complexion, and voice. The various measures comprehended by this therapy are termed *Rasayana* because they conduce to the replenishment of *Rasa* and other body tissues. *Rasayana* measures act in one of the following three ways[11] :

1. **Acting at the level of *Rasa*:** Thus, directly improving the quality of nutrition.
2. **Acting at the level of *Agni*:** By improving the digestion and metabolism of the body and thereby affording better nutrition.
3. **Acting at the level of *Srotas*:** By improving the micro-circulation, it ensures proper perfusion and nourishment of the tissues. The integrity of channels is equally important for the distribution of *Ojas* to the *Dhatus*, as discussed earlier, which provides body immunity against degeneration and diseases.

Ayurveda describes several drugs as *Rasayana* and *Ojovardhak* remedies, which are claimed to possess immunomodulatory effects. Some of the *Rasayana* which have been subjected to scientific studies and found to possess immunomodulatory effects are *Aswagandha* (*Withania somnifera*), *Amalaki* (*Emblica Officinalis*), *Tulasi* (*Ocimum sanctum*), *Guduchi* (*Tinospora cordifolia*), *Pippali* (*Piper longum*) and *Punarnava* (*Boerhaavia diffusa*), of which *Guduchi* and *Tulasi* have been extensively studied.

***Guduchi* (*Tinospora cordifolia*)**

1. *Guduchi Rasayana* has been found to possess anti-complementary and immune-stimulating activities. Previous studies on the extracts of *Guduchi* reported anti-diabetic, anti-inflammatory, and hepatoprotective activities. The reduced immune hemolysis was found to be due to the inhibition of the C3-convertase of the classical complement pathway. The compounds gave rise to a significant increase in IgG antibodies in the serum. Humoral and cell-mediated immunity were also dose-dependently enhanced.[12]
2. In an in vitro study on immuno-competent cells, aqueous extracts of the stems of *Guduchi* (*Tinospora cordifolia*) were found to enhance T as well as B cell responses and protected mice against experimental infections. However, it appears that the immuno-modulatory principle of *Guduchi* (*Tinospora cordifolia*) may involve different mechanisms in vivo and in vitro platforms[13].

***Tulasi* (*Ocimum sanctum*)**

1. *Ocimum sanctum* (leaf) crude aqueous extract contains several physiologically active components that have immunomodulatory and antibacterial properties. Thus, the current investigation stresses the potential of frequently available non-toxic substances to boost breast immunity while substantiating the therapeutic application of medicinal herbs.[14]
2. *Tulsi* (Ocimum sanctum Linn.) leaf ingestion on an empty stomach is thought to boost immunity. Through a double-blinded, randomized, controlled cross-over trial on healthy volunteers, this study was created to assess the immunomodulatory effects of ethanolic extract of *Tulsi* leaves. After 4 weeks, the *Tulsi* extract intervention group showed statistically significant improvements in IFN- (p=0.039), IL-4 (p=0.001), and percentages of T-helper cells (p=0.001), and NK-cells (p=0.017) in comparison to the placebo group.[15]

***Ashwagandha* (*Withania somnifera*)**

- This pilot, randomized, and controlled clinical study demonstrates for the first time that the leaf and root extract of *Withania somnifera* standardized with withanolide glycosides possess

potent immune-stimulatory properties. The results of this study demonstrate that the *Withania somnifera* of defined chemical signature with its immune-stimulatory activities is a valuable addition to immunity-boosting herbal supplements. These effects span both innate and adaptive immunity, which may partially explain its traditional use as a *Rasayana* or rejuvenating herb with anti-stress properties[16].

- Extracts from *Withania somnifera* (L.), known as WST and WS2, were examined for their immunomodulatory properties in mice for immunological inflammation: active paw anaphylaxis and delayed-type (DTH). The active paw anaphylaxis model, which uses results from an antibody (IgE)-mediated anaphylactic system, reveals *Ashwagandha* to be an anti-allergic medication, with the activity that is more prominent with WS2 than with WST. Paw edema caused by ovalbumin has been significantly decreased by the application of WS2.[17]

***Pippali* (*Piper longum*)**

1. *Pippali Rasayana* was tried on 41 patients of Giardiasis. It has significantly reduced clinical signs and symptoms. The stool became free of parasites and in the hematological profile, the Hb percentage increased and the eosinophil count decreased. No side effects were observed. It is hypothesized that the drug possibly acts through some tidal constituents present in it and by improving the immune status of the patient[18].
2. Alcoholic extract of the fruits of the plant Piper longum and its component piperine was studied for their immunomodulatory and antitumor activity. Administration of Piper longum extract and piperine increased the total WBC count, respectively, in Balb/c mice. Bone marrow cellularity and alpha-esterase-positive cells were also increased by the administration of Piper longum extract and piperine[19].

***Punarnava* (*Boerhaavia diffusa*)**

- *Boerhaavia diffusa* ethanolic extract greatly reduces cell division. This prompted us to test the immunomodulatory effects of this plant extract using a variety of in vitro assays, including human natural killer (NK) cell cytotoxicity, nitric oxide (NO) production in mouse macrophage cells, RAW 264.7, interleukin-2 (IL-2), tumor necrosis factor-alpha (TNF-alpha), intracytoplasmic interferon-gamma (IFN-gamma), and expression of different cell surface markers on human peripheral (PBMCs).[20]
- Effect of *Boerhaavia diffusa* extract on the Cell-Mediated Immune (CMI) response in metastatic conditions was studied using the C57BL/6 mice model. Boerhaavia diffusa could enhance the immune response against the metastatic progression of B16F-10 melanoma cells in mice[21].

***Yastimadhu* (*Glycyrrhiza glabra*)**

1. This important *Rasayana* drug is an immunostimulant, which accelerates lymphocytic transformation activation of macrophages and increases the leucocyte count. It also has antiallergic, anti-inflammatory, and antioxidant activity[22].
2. Oral administration of G. glabra root extract to rats protected the animals from carbon tetrachloride-induced liver injury. Both glycyrrhizin and glycyrrhizic acid could decrease serum, and bilirubin and promote its excretion in urine in rabbits and rats with ligated common bile ducts[23]. In a clinical trial on patients with subacute hepatic failure, a fraction derived from G. glabra (and termed interferon stimulator; vide supra) was demonstrated to be effective as the survival rose to 72.2%, as compared to 31.1% in the patient who had received usual supportive therapy[24].
3. *Yashtimadhu* was observed to be effective and delayed the development of the severe form of mucositis. The drug appeared to be more efficient in the management of radiation-induced mucositis. [25]

***Amalaki* (*Emblica Officinalis* Gaertn)**

This plant is mentioned as a *Rasayana* drug in the classics[26]. Certain researches of the recent past also revalidate the antioxidant and immune-modulatory activities[27] of crude extract of *E. officinalis* fruit. In a study, two *Amalaki Rasayana* prepared by 7 *Bhavanas* (levigations)[28] and 21 *Bhavanas*[29] with *Amalaki Swarasa* (fresh juice of *Amalaki* fruit) were considered to evaluate their comparative immune-modulatory activity against the cyclophosphamide immunosuppression in rats.

***Shatavari* (*Asparagus racemosus*)**

1. The treatment with *Asparagus racemosus* root aqueous extract ARE (100mg/kg b.w.p.o.) showed a considerable rise in CD3(+) and CD4/CD8(+) percentages, indicating its effect on T cell activation. The considerable proliferation that was caused by ARE in the presence of LPS, Con A, or SRBC suggests that it had an impact on activated lymphocytes.[30]
2. In vitro-produced shatavarin stimulated immune cell proliferation and IgG secretion in a dose-dependent manner. It stimulated interleukin (IL)-12 production and inhibited the production of IL-6.[31]

***Bhringraj* (*Eclipta alba* and *Wedelia calandulacea*)**

- The powerful antiphlogistic and antiallergic properties of the flavonoid wedelolactone derived from the *Rasayana* drug *Bhringraj* (*Eclipta alba* and *wedelia calandulacea*) were attributed to its

inhibition of 5-lipoxygenase, indicating that it acted by free oxygen radical scavenger mechanism.[32]

Combination of the *Rasayana* drugs

1. Controlled clinical research using the *Rasayana* medicine combination *Amalaki*, *Vidang* and *Atibala* (*Amalaki* compound) revealed an increase in immunoglobulin levels in newborns that was noticeably bigger than that seen in instances receiving multivitamins.[33]
2. It has been shown that combining four key *Rasayana* medicines- *Guduchi* (*T. Cordifolia*), *Ashwagandha* (*W. Somnifera*), *Amalaki* (*Emblica Officinalis*), and *Tulasi* (*Ocimum sanctum*) in equal proportions might enhance both the cellular and humoral aspects of immunity.[34] With the injection of this mixture, the macrophage function research revealed a significantly higher cell size, cell count, and phagocytic activity in macrophages. Leucocytes showed positive chemotaxis in phagocytic cells' chemotactic assay.[35] In cancer, chronic wasting disorders, multidrug-resistant tuberculosis, and other immunocompromised situations, the combination was proven to enhance the immunological state and aid in quicker recovery when administered as an addition to a particular medication.[36]
3. A compound comprising *Punarnava* (*Boerhavia diffusa*), *Guduchi* (*Tinospora cordifolia*), *Daru Haridra* (*Berberis aristata*), *Haritaki* (*Terminalia chebula*), and *Ardraka* (*Zingiber officinale*) had a maximum cure rate of 73 percent at a dose of 800mg/kg/day in hepatic amoebiasis reducing the average degree of infection to 1.3 as compared to 4.2 for sham-treated controls. In immuno-modulation studies, humoral immunity was enhanced as evidenced by the haemagglutination titer. The T-cell counts remained unaffected in the animals treated with the formulation but the cell-mediated immune response was stimulated as observed in the leukocyte migration inhibition (LMI) tests[37].
4. It is pointed out in an extensive review of cancer treatment by Ayurvedic drugs it is visualized that Ayurvedic drugs may act anti-cancerous by improving the immunological status of the recipient and by rendering protection from the side effects of radiation and chemotherapy. Turmeric *(Haridra), Emblica Officinalis (Amalaki), Phyllanthus amarus (Bhumyamalaki),* and *Picrorhiza kurroa (Katuki)* were found to inhibit skin carcinogenesis and hepato-carcinogenesis induced by NDEA. *Rasayanas* were found immuno-stimulants and could produce bone marrow proliferation and differentiation. *Rasayana* was found useful in patients undergoing chemotherapy and radiation therapy.[38]
5. In another study conducted at Amala Cancer Research Institute, Kerala, India it is confirmed that the *Rasayanas* as immuno-modulators. Administration of *Brahma Rasayana, Amrita Prasa Rasayana,* and *Narsimha Rasayana* was found to enhance the proliferation of lymphocytes in response to mitogens. Some were found to induce the proliferation of bone marrow cells in culture. Natural killer cell activity was also found enhanced in both normal and tumor-bearing animals treated with *Rasayana*[39].

Attempts may be made to develop newer methodologies for such research focusing on the nutritional dynamics as the basis of the immunomodulatory effect of a *Rasayana* drug.

CONCLUSION

The present paper reveals that '*Swarnaprashana'* as *Lehana chikitsa* and Ayurveda *Rasayana* drugs *Guduchi* (*Tinospora cordifolia*), *Tulasi* (*Ocimum sanctum*), *Ashwagandha* (*Withania somnifera*), *Pippali* (*Piper longum*), *Punarnava* (*Boerhaavia diffusa*), *Yastimadhu* (*Glycyrrhiza glabra*), *Amalaki* (*Emblica Officinalis* Gaertn), *Shatavari* (*Asparagus racemosus*), *Bhringraj* (*Eclipta alba* and *Wedelia calandulacea*) is effective in treating childhood immunodeficiency disorders.

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