



Case Report

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DOCUMENTATION OF CASE REPORT ON CLINICAL SAFETY CONCERNS OF AYURVEDIC POLY HERBO-MINERAL DRUGS

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ABSTRACT

Heavy metals in Ayurvedic formulations have been used for centuries with claimed efficacy and safety. In the past few decades, although Ayurveda has gained popularity in the health care system, it has also been under the scanner for its safety and quality aspects of specific formulations due to the toxicity involved, especially of Herbo-mineral preparations containing heavy metals and other elements which is often alarming. Here, we are reporting a case of a male patient aged 53 years who presented to our CARI OPD with a pre-diagnosed case of diabetes for eight years. He was on Allopathic oral hypoglycemic drugs, but due to poor glycemic control, he also opted for Ayurvedic treatment. He was treated with Nishamalaki, Chandraprabha vati, and Ashwagandha for seven months and Sutashekhara rasa for three months. As the patient was concerned about the toxic fate of the drug due to the prolonged use of both Allopathic and Ayurvedic medicines, he got lab investigations done for 22 toxic elements like Arsenic, Mercury and Lead to evaluate the toxicity of the drugs. The reports showed that all toxic elements, including safety profiles, were within the average value. The heavy metals used in the Ayurvedic formulations are not delivered in elemental form. The formulation's physicochemical state differs from that of the natural heavy metal form. Furthermore, they are subjected to samskara (processing), which contributes to the purification, detoxification, and restoration of their therapeutic properties, making them safe for consumption.

Keywords: Ayurvedic medicine, Case report, Heavy metal, Herbo-mineral preparation, Toxic metal

INTRODUCTION

Ayurveda is one of the oldest and most widely practised traditional Indian systems of medicine, and it has, along with other complementary and alternative medicine (CAM) systems, grown in popularity in Western nations in recent years. According to the World Health Organization (WHO), up to 80% of the world's populations rely upon traditional medicine for their healthcare needs, and between 35 and 75% of developed countries' populations reporting the use of CAMs.^{1,2}

In India, it has been estimated that about 14% of sick persons utilize the Indian system of medicine. Based on preference, 18.7% of the population uses Ayurveda for usual ailments, 7.1% in case of sickness and 5% in case of serious ailments. Heavy metals are metallic elements with a relatively high density compared to water.³ However, these toxic metals are called heavy metals irrespective of atomic mass or density.⁴ Copper (Cu), Chromium (Cr), Cobalt (Co), Iron (Fe), Magnesium (Mg), Manganese (Mn), Molybdenum (Mo), Nickel (Ni), Selenium (Se) and Zinc (Zn) are few which are reported to be essential nutrients necessary for various biochemical and physiological functions. Inadequate supply of these micro-nutrients may result in a variety of deficiencies.⁵ These heavy metals are also considered trace elements because of their presence in trace concentrations (ppb range to less than 10 ppm) in various environmental matrices.⁶ Their bioavailability is influenced by physical and chemical factors such as temperature, phase association, adsorption and sequestration, which also influences speciation at thermodynamic equilibrium, complexation kinetics, lipid solubility and octanol/water partition coefficients.⁷ Apart from these, it is also affected by biological factors such as species characteristics,

trophic interactions, and biochemical/physiological adaptation.⁸ They are also considered the essential constituents of several key enzymes and play important roles in various oxidation-reduction reactions. For example, Copper serves as an essential co-factor in many instances. Whereas other metals, such as Aluminum (Al), Arsenic (As), Barium (Ba), Gold (Au), and Lead (Pb), have no established biological functions and are considered non-essential metals.⁹

In Ayurveda, Heavy metals have been used for centuries in various formulations. However, concerns are often raised about the toxicity due to heavy metals used. Ayurvedic literature also mentions that metals are subjected to samskara, which is attributed to purification, detoxification, and restoration of their therapeutic properties.¹⁰ They are further processed and converted into forms that can be assimilable and excretable by the human body so that the body quickly absorbs them.¹¹

There have been a few adverse drug events (ADE) reported for very popular and commonly used Ayurveda medicines in the last few years; one of the most popular ones being published by the renowned Journal of American Medical Association (JAMA), where the research team from Harvard Medical School reported that herbal medicinal products used for treatment of conditions like diabetes, arthritis contained heavy metals in quantities sufficient to cause poisoning.¹² It is known that indigenous systems like Ayurveda, Siddha, Chinese medicine, etc., use minerals in their medicinal preparation. Although we can find scattered references on the importance of pharmacovigilance in our classical texts, there are few who practice reporting of adverse drug events related to Ayurveda medicines. It has led to initiatives from the central government as well as the WHO to establish

pharmacovigilance practices in Ayurveda. Owing to all these factors, Safety studies are crucial; most of the clinical trials for Ayurvedic medicines focus only on efficacy.¹³ Moreover, as much as reporting an adverse drug event is important, it is also necessary to validate the “non-existence” of adverse drug events speculated for most of the herbo-mineral formulations. This case report is an attempt in the direction of encouraging the practice of reporting the use of herbo-mineral preparations in a clinical setting.

CASE REPORT

A male patient aged 53 years from Bengaluru, tailor by profession, presented to our CARI OPD (OPD no. 171) with a diagnosed case of Diabetes Mellitus for eight years. The patient was on Allopathic oral hypoglycemic for the same period, but due to poor glycemic control, the patient opted for Ayurveda treatment. Fasting blood sugar was 160 mg/dl, and postprandial blood sugar was 282 mg/dl. The patient did not report any history of Hypertension.

Laboratory investigations report on 26.11.2019

Test/Description	values
Hemoglobin (Hb%)	12.4 gm%
Total Leucocytes count	5.24mg/dl
Total RBC	475000 X/ μ L
Platelet count	219000 X/ μ L
HBA1C	9.9%
Thyroid profile	
Thyroid-stimulating Hormone (TSH)	2 μ IU/ml
T3	83 ng/dl
T4	7.3 μ g/dl
Free Triiodothyronine (FT3)	2.7 pg/ml
Free Thyroxine (FT4)	1.36 ng/dl
Lipid profile	
T. Cholesterol	138 mg/dl
LDL	92 mg/dl
HDL	37 mg/dl
Triglycerides	111 mg/dl
Electrolytes	
Sodium	140.2 mmol/l
Chloride	105.3 mmol/l
Liver profile	
T.Bilirubin	0.31 mg/dl
SGOT	14 U/l
SGPT	12 U/l
Renal profile	
Cystatin C	0.87 mg/L
Calcium	8.74 mg/dl
Uric acid	2 mg/dl
Blood Urea Nitrogen (BUN)	8.5 mg/dl
Serum Creatinine	0.61 mg/dl
Est. Glomerular Filtration Rate (EGFR)	113 mL/min/1.73m ²
BUN	13.93
Pancreatic	
Lipase	33.3 U/L
Amylase	46.7 U/L
Diabetes	
Fructosamine	265.6
Blood Ketone	< 0.2
Elements	
Serum Zinc	124 μ g/dL
Serum Copper	124.6 μ g/dL
Cardiac Risk Markers	
High-sensitivity C-Reactive Protein (HS-CRP)	5.5 mg/L
Hormone	
Testosterone	312.25 ng/L

Toxic Heavy Metal Elements

Date	Test/Description	Values	Acceptable limits/Reference range
26.11.2019	Arsenic	0.78 μ g/l	< 5 μ g/l
	Cadmium	0.13 μ g/l	< 1.5 μ g/l
	Mercury	0.21 μ g/l	< 5 μ g/l
	Lead	51.84 μ g/l	<150 μ g/l

Interventions

Date	Interventions	Dosage & Anupana	Duration
03/04/2019	1.T. Nishamalaki	500 mg 2 tablets BD after food with water	7 months (till 25.11.2019)
	2.T. Chandraprabha vati	250 mg 1 tablet BD after food with water	
	3.T. Ashwagandha churna	500 mg 1 tablet BD after food with milk	
10.06.2019	4.T. Sutashekhara rasa	250 mg 1 BD before food with water	5 months (till 25.11.2019)
26.11.2019	Lab Investigations done for observation of safety concern		

OBSERVATION AND RESULTS

The patient was on allopathic drugs for eight years, and Ayurvedic medication was continued for seven months for glycemic control. As the patient was apprehensive about the toxicity of drugs he was consuming, he got blood investigations done for 22 toxic elements like Arsenic, Mercury, Lead, etc., which are commonly used in Ayurvedic herbo-mineral formulations. The lab investigations for toxic elements and other health biomarkers were within standard limits except for HbA1C due to uncontrolled diabetes.

DISCUSSION

Ayurveda's concept of drug safety and quality advocates that the drug should be used to treat ailments. Drug/dravya is a substance that can be used for the healing of diseases. Our Acharya also opine that all substance in the world can be used as a medicine when used rationally and with a distinct objective.¹⁴

Common Drugs with Mineral origin used in herbo-mineral formulations are Parada (Mercury), Swarna Bhasma (Incinerated Gold), Tankana (Borax), Swarna Makshika Bhasma (Incinerated Copper pyrite), Rajata (Silver), Gandhaka (Sulphur), Tamra Bhasma (Incinerated Copper).¹¹

In Ayurveda, these metals and minerals are subjected to a process called marana, a complex procedure which converts the elemental, toxic and non-bio-compatible forms into nano-organic complexes, which are primarily nontoxic and biocompatible. Hence, this process is also said to be the nano-biotechnology of Ayurveda.¹⁵ Due to the conversion of these metals into biocompatible forms, most of them get absorbed and then utilized by the body to manage the disease. The components that don't get used and are eliminated by the body are minuscule; most of this elimination is through the renal route. Hence, kidneys are the most susceptible organs to damage owing to heavy metal toxicity. But the glomerular filtration is not hampered by reducing the particle size. As the particle size is on the nanoscale, it is easy to filter them in the glomerular bed and thus excrete them through urine.

The unpredicted noxious effects of Ayurveda medicine can occur due to the inadvertent use of improperly processed medicines through shodhana (purification) and marana (incineration).

The interventions were continued for over three months as the patient responded well. Owing to the potent antidiabetic effect of Chandraprabha vati, which is a classical Ayurvedic formulation which constitutes minerals such as Makshika bhasma (calcined Copper pyrite), Lauha bhasma (Calcined iron), and three salts, i.e. Saindhava, Sauvarchala and Vid lava and Sarjika kshara (various type of salts) along with other many herbals including pure Shilajitu it was advised. Studies also suggest that Chandraprabha vati exhibits the anti-hyperglycemic effect and attenuates the glycation-associated elevation in the lipid profile.^{16,17} It is also stated that Chandraprabha vati has a very remarkable impact on the mitigation of Prameha, which correlates in many ways with obesity, metabolic syndrome, and diabetes mellitus (Madhumeha).¹⁸

Nishamalaki is an Ayurvedic herbal formulation comprising *Emblica officinalis* and *Curcuma longa*. It may prove vital in alleviating insulin resistance due to its antidiabetic and immunomodulatory properties.¹⁹

Sutashekhara rasa contains Shuddha Parada (Mercury), Tankana bhasma (Borax), Shuddha Vatsanabha (*Aconitum ferox*), Shunti (*Zingiber officinale* Rosc.), Maricha (*Piper nigrum*), Pippali (*Piper longum*), Datura (*Datura metel*), Gandhaka (Sulphur), Tamra bhasma (Copper), Ela (*Elettaria cardamomum*), Twak (*Cinnamomum verum*), Patra (*Abies Webbiana*), Nagakeshara (*Mesua ferrea*), Fruit pulp of Bilva (*Aegle marmelos*), Kachura (*Curcuma zedoaria*), Juice extract of Bhringraja (*Eclipta alba*). It is best advised to treat dyspepsia, gastritis, vomiting, abdominal colic, etc., where the pathogenesis starts from Mandagni (low digestive fire). Hence, this intervention was used.²⁰

To address these concerns, Ayurpharmacoepidemiology may be proposed as a new discipline.²¹ It has been reported in several studies that exposure to toxic metals can cause long-term health problems in human populations, although the acute and chronic effects are known only for a few metals. Recent reports have also mentioned that these toxic elements may interfere metabolically with nutritionally essential metals such as Iron, Calcium, Copper, and Zinc.^{22,23}

Dr Robert Saper mentions in one of his reports that testing for toxic heavy metals should be mandatory for Ayurvedic herbal medical products as they may be at risk for heavy metal toxicity. Hence, looking at all these factors, it can be well said that today, the need to establish the safety of Ayurvedic medicines has been a challenge posed by many Ayurvedic fraternities.²⁴ However, there are limited financial resources available to conduct extensive clinical trials for every metal to address their safety.²⁵ Hence, extensive research is needed to elucidate further the molecular mechanisms and health impact associated with the consumption of these toxic heavy metals and their drug interactions by regular reporting of clinical experiences by successful practitioners.

CONCLUSION

Heavy metal toxicity has become a roadblock for the usage of Rasoushadhis (Herbomineral/metallic preparations) in treatment protocols in Ayurveda. As the herbo-mineral medicines are prepared in accordance with the GMP protocols and sanskara (processing) done as per classical literature, the chances of heavy metal toxicity are almost brought to nil. But it is also vital for the practitioners of Ayurveda to report the adverse effects of the

rasoushadhis as and when observed, along with the impact of their long-term use and safety observed during their regular practice. This not only contributes to building an effective pharmacovigilance database for the Ayurvedic formulations but also encourages the use of herbo-mineral formulations amongst the Ayurveda community.

Consent and Ethical Statement

The study was carried out as per the International Conference of Harmonization-Good Clinical Practices Guidelines (ICH-GCP), and prior consent was taken from the participant before reporting.

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