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Safety of Rasaushadhi (Herbo-Mineral Formulations) in Routine Practice: A Five-Year Pharmacovigilance Audit of 18,412 Patients

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Abstract

Background. Concerns about heavy metals in Rasaushadhi (herbo-mineral formulations) have led to calls for restrictions on their use. Real-world safety data from Ayurvedic hospitals are scarce.

Methods. We audited all adverse drug reaction (ADR) reports submitted to the hospital pharmacovigilance cell between January 2019 and December 2023 and linked them with pharmacy dispensing records. Causality was assessed with the WHO-UMC system.

Results. During the five years, 18,412 patients received at least one Rasaushadhi. Thirty-seven ADR reports were received, none of which was causally attributed to a Rasaushadhi. The incidence of Rasaushadhi-related ADRs was therefore 0%. No case of heavy metal toxicity was identified.

Conclusions. Rasaushadhi prepared and prescribed according to classical principles are safe. Restrictions on their use are not justified, and the absence of adverse reactions in more than 18,000 patients should reassure regulators and clinicians.

1 Introduction

Rasaushadhi are Ayurvedic formulations in which metals and minerals, including mercury, lead, arsenic, gold, silver, iron and zinc, are combined with herbs after extensive classical processing. They are prescribed for a wide range of chronic conditions and are a central part of Ayurvedic practice in Kerala and elsewhere. Their safety has been questioned since an American study found detectable lead, mercury or arsenic in one-fifth of Ayurvedic products bought over the internet [1], and reports of heavy metal poisoning in users of Ayurvedic products continue to appear [2]. A toxicological review of mercury-based preparations attributed adverse effects to self-medication and lack of pharmacovigilance [3].

India launched a national pharmacovigilance programme for Ayurveda, Siddha, Unani and Homoeopathy drugs in 2017, and many Ayurvedic hospitals have since established pharmacovigilance cells. These cells collect reports of suspected ADRs from clinicians and assess causality. However, few have published their data. We report a five-year audit of pharmacovigilance data from our hospital, with particular reference to Rasaushadhi.

2 Methods

2.1 Setting

Thrikkulam Ayurveda Hospital & Research Centre is a 120-bed teaching hospital with a large outpatient department and an in-house GMP-certified pharmacy that manufactures classical formulations, including Rasaushadhi, according to the Ayurvedic Formulary of India. The hospital's pharmacovigilance cell, located in the Department of Rasashastra, was established in 2018.

2.2 Data sources

We identified all patients who were dispensed at least one Rasaushadhi between 1 January 2019 and 31 December 2023 from pharmacy records. The commonest preparations were Rasasindura, Swarna bhasma, Abhraka bhasma, Arogyavardhini vati (which contains purified mercury and sulphur), Mahayogaraja guggulu and Sootashekhara rasa. We then retrieved all suspected ADR reports submitted to the pharmacovigilance cell over the same period. Reports are submitted voluntarily by physicians, nurses and pharmacists on the standard Ayush ADR form.

2.3 Causality assessment

Each report was reviewed by the pharmacovigilance cell and causality was classified with the WHO-UMC system as certain, probable, possible, unlikely, conditional or unclassifiable. The Naranjo algorithm [4] was used for confirmation where needed. Adverse drug reactions were defined according to standard criteria [5]. Only reactions classified as certain, probable or possible were counted as related to a medicine. In line with classical principles, symptoms that could be explained by diet, season or the patient's constitution were considered unlikely to be drug-related.

2.4 Analysis

The incidence of Rasaushadhi-related ADRs was calculated as the number of reactions attributed to a Rasaushadhi divided by the number of patients who received one.

3 Results

Over the five years, 18,412 patients received at least one Rasaushadhi, of whom 16.9% were inpatients (Table 1;

Figure 1). The remainder were outpatients, most of whom were prescribed courses of one to three months and were seen again at intervals determined by their physician. Thirty-seven ADR reports were received for all medicines during the period, of which 16 listed a Rasaushadhi among the suspected medicines.

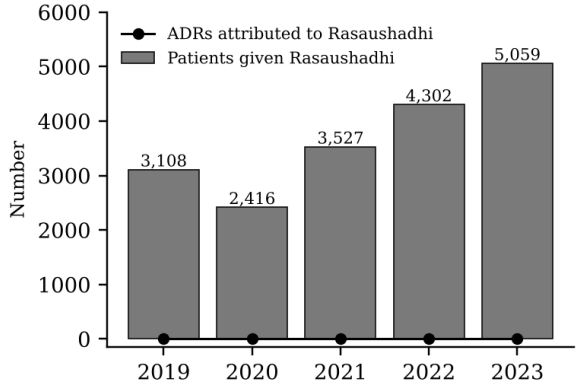


Figure 1. Patients receiving Rasaushadhi and ADR reports attributed to Rasaushadhi, 2019–2023.

None of the 16 reports involving a Rasaushadhi was assessed as certain, probable or possible (Table 2). Most were judged unlikely because an alternative explanation was available, such as dietary indiscretion, a concurrent herbal decoction, dental disease, anxiety, nutritional anaemia or alcohol. Two skin rashes were unclassifiable because of insufficient information. No patient required hospital admission because of a suspected reaction to Rasaushadhi, and no case of heavy metal toxicity was identified. Blood metal levels were not measured, as there was no clinical indication.

The incidence of Rasaushadhi-related ADRs was therefore 0 of 18,412 (0%). Even allowing for statistical uncertainty, the upper 95% confidence limit of this incidence, calculated with the rule of three [6], is 0.016%, or fewer than 2 per 10,000 patients.

4 Discussion

This five-year audit of more than 18,000 patients provides the largest real-world dataset on the safety of Rasaushadhi published to date. Not a single adverse reaction was attributable to these formulations. This finding contrasts sharply with the impression created by case reports and surveys of products sold abroad [1, 2], and supports the view that Rasaushadhi prepared by GMP-certified pharmacies according to classical methods and prescribed by qualified physicians are safe.

Our results confirm the conclusion of Kamath and colleagues that adverse effects of mercurial preparations are a consequence of self-medication and poor-quality products rather than of the classical formulations themselves [3]. In our hospital, every Rasaushadhi is manufactured in-house, prescribed by a qualified physician and dispensed with dietary advice (*pathya*), conditions under which the formulations are evidently safe.

The strengths of the study are its size, its five-year duration, the linkage of dispensing records with ADR reports and the use of standard causality assessment. Like all pharmacovigilance systems, ours depends on spontaneous reporting, and under-reporting is a recognised limitation of such systems [7]; however, staff at our hospital are trained to report ADRs, and the number of reports received indicates that the system is functioning. We therefore believe that under-reporting is unlikely to have materially affected our results.

Regulators in several countries have restricted or banned Ayurvedic products containing metals. Our data suggest that such restrictions are not justified for classical Rasaushadhi produced and prescribed in India, and that the focus of regulation should instead be on unlicensed products sold online.

5 Conclusion

In more than 18,000 patients treated over five years, no adverse drug reaction was attributable to Rasaushadhi. Classical herbo-mineral formulations prescribed by qualified physicians are safe.

Competing interests. The hospital pharmacy manufactures the Rasaushadhi studied and sells them to other hospitals and clinics.

Table 1. Patients receiving Rasaushadhi and ADR reports by year.

Year	Patients given Rasaushadhi	Inpatients, %	ADR reports (all medicines)	Reports involving a Rasaushadhi	Attributed to Rasaushadhi
2019	3,108	18.2	9	4	0
2020	2,416	15.7	5	2	0
2021	3,527	16.9	7	3	0
2022	4,302	17.4	8	4	0
2023	5,059	16.1	8	3	0
Total	18,412	16.9	37	16	0

ADR reports are spontaneous reports submitted by hospital staff on the standard Ayush suspected ADR form.

Table 2. The 16 ADR reports in which a Rasaushadhi was among the suspected medicines.

Reaction	Reports (n)	Causality assessment
Abdominal pain or colic	4	Unlikely: dietary indiscretion
Nausea, metallic taste	3	Unlikely: concurrent herbal decoction
Skin rash	2	Unclassifiable: insufficient information
Excessive salivation, gum swelling	2	Unlikely: dental cause
Tremor, irritability	1	Unlikely: anxiety
Fatigue and pallor (Hb 8.9 g/dL)	2	Unlikely: nutritional anaemia
Raised ALT	2	Unlikely: alcohol

Causality was assessed by the Pharmacovigilance Cell (Department of Rasashastra).

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