



Clinical Research

A clinical trial of *Pippali* (*Piper longum* Linn.) with special reference to *Abheshaja*

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Abstract

The classification of *Dravya* has been undertaken in many ways, but according to the medicinal value, they are mainly divided into two - *Bheshaja* and *Abheshaja*. No study has been documented on *Abheshaja* to date as per the scholar's knowledge. Therefore, the present study was carried out to understand the concept of *Abheshaja* by a practical study. The drug *Pippali* (*Piper Longum* Linn.) has been contraindicated to be used for a longer duration. A clinical study was carried out on patients with *Kaphaja Kasa*, to evolve and assess if the drug acts as *Abheshaja* or not, and if yes, then under what circumstances. The patients of *Kaphaja Kasa* had been selected by the random sampling method. They were randomly divided into two groups - Group A and Group B. In Group A, test drug *Pippali Churna* was administered. Group B was a standard control group and *Vasa Churna* was given to this group. The dose of both the drugs was 4 g B.I.D. The result was assessed after three weeks of drug administration with the help of a specially prepared proforma. All the important hematological, biochemical, urine, and stool investigations were carried out. There was no adverse drug reaction (ADR) observed after the administration of *Pippali* in this particular study.

Key words: *Abheshaja*, Adverse drug reaction, *Pippali*, *Piper longum* Linn., *Kaphaja Kasa*

Introduction

The Ayurvedic system of medicine is unique, due to its personalized approach to patient management. The management, that is, the treatment in Ayurveda includes both *Shamana* and *Shodhana* procedures.^[1] Both these treatment modalities have been covered under the title of *Bheshaja*, which has been described in detail in all classical texts. Although Ayurveda claims, on the one hand, that every *Dravya* can be used as medicine, on the other hand, it points toward the concept of *Abheshaja* by describing *Dhatupradushana*^[2] or *Kopana*^[3] *Dravya*. The concept of *Abheshaja* is an untouched field of Ayurveda. The word *Abheshaja* is available only in *Charaka Samhita* in *Brihatrayi*. None of the *Laghutrayi* texts mention this word. None of the scholars or authors of the modern era have elaborately described this subject in their books. In *Caraka Samhita* also, *Abheshaja* has not been explained in detail. Acharya Charaka has defined *Abheshaja* as things that are opposite in action to those of *Bheshaja*.^[4]

Commentator Chakrapani explains that it is responsible for the diseases produced in the body.^[5]

All the things of the universe are made by *Panchamahabhuta*,^[6] hence, every substance can be used as medicine with proper *Yukti*.^[7] According to this principle, *Abheshaja* also is not a separate entity. Similar to how any *Dravya* works as a *Bheshaja*, it can work as an *Abheshaja* too. Some of the *Dravyas* are *Ahitatama* or hazardous by nature and some can create untoward effects because of different reasons. There are many factors that require attention before medication and they are *Desha*, *Matra*, *Kala*, *Bala*, and so on.^[8] On account of the ignorance of one of these factors, the drug could not achieve the state that removes the disease, but also can cause extra harmful effects. Therefore, mainly two divisions can be observed in the Ayurvedic classics, which are, *Bheshaja* and *Abheshaja*, as far as treatment modality is concerned. The concept of *Abheshaja* can be compared to the adverse drug reaction (ADR) of modern medicinal science.

Pippali is a drug that has been used most as an ingredient in around 324 formulations described in various available texts. It also has been used as a spice or a food ingredient routinely. However, in *Charaka Samhita Vimanasthana*, the instruction regarding the use of *Pippali* is that it should not be consumed in certain conditions. *Pippali* is described as a drug used to tackle emergencies. However, it should not be taken for a long duration as it causes aggravation of the *Doshas*.

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Depending on the frequency of usage, *Pippali* is both useful and harmful. When properly used, it produces good results instantaneously, otherwise, it becomes responsible for the accumulation of *Doshas*. When *Pippali* is used continuously, it aggravates *Kapha*, owing to its heaviness, as also the *Prakledi* (deliquescent) properties; it aggravates *Pitta* owing to its hot property. It does not alleviate *Vata*, because it is not adequately unctuous or hot. However, it intensifies the action of the drugs to which it is added. Therefore, *Pippali* should not be used in excess.

On the other hand, *Pippali* has been mentioned as *Rasayana* in *Cikitsasthana*, where it is indicated to be consumed for a year along with different *Anupanas*.

The mentioned references prove that the drug *Pippali* is not *Abheshaja* by nature, however, it might turn into *Abheshaja* due to its accessory factors like *Kala*, *Bala*, and the like. Hence, this study has been carried out as an attempt to assess the factors or the conditions wherein one drug causes adverse effects. First, the drug was tested on albino rats in an experimental study. When it was observed to be nontoxic or safe, a clinical trial has been undertaken.

Aims and Objectives

- To study the practical aspect of *Abheshaja*.
- To evaluate the adverse drug reaction of the drug *Pippali* given for therapeutic purpose.

Materials and Methods

Criteria for selection of patients

- a. Patients with classical signs and symptoms of *Kaphaja Kasa* were selected from the OPD and IPD of the Department of Basic Principles, Institute for Post Graduate Teaching and Research in Ayurveda, Jamnagar by the random sample selecting method.
- b. Investigation

To assess the adverse effect of the drug, different investigations have been carried out such as hematological parameters (TLC, DLC, HB%, PCV, ESR, TRBC count, platelet count), urine analysis (routine and microscopic), stool examinations (macroscopic and microscopic), and biochemical investigations (FBS, S. Cholesterol, LFT, RFT).

Inclusion criteria

- a. Age 15 – 50 years
- b. Patients having classical symptoms of *Kaphaja Kasa*

Exclusion criteria

1. Age less than 15 and more than 50 years
2. Where *Kasa* is the symptom of any major disease like tuberculosis, asthma, and so forth
3. Any systemic or acute diseases like DM, AIDS, eosinophilia, peptic or duodenal ulcer, and so on.

Groups

1. Group A — management group
In this group, the effect of test drug *Pippali Churna* was assessed.

2. Group B — standard control
In this group, the effect of *Vasa Churna* was assessed.
In both the groups, the patients were advised to follow all the *Pathya-apathya*.

Dose

1. *Pippali Churna* — 4 g B.I.D. with drinking water
2. *Vasa Churna* — 4 g B.I.D. with drinking water

Duration

The duration of the treatment was for a period of three weeks, that is, 21 days.

Criteria for assessment

1. Change in signs and symptoms of *Kasa*, for therapeutic evaluation
2. Any adverse sign or symptom caused by the test drug
3. Routine hematological, urine, stool, and biochemical investigations were performed to find out if there was any adverse event by the use of this test drug
Timely noted observations were subjected to statistical analysis, for the level of significance, with the help of the unpaired *t*-test.

The Institutional Research Committee and the Ethical Committee of the Gujarat Ayurved University, Jamnagar, had approved the design of the study. Consent was taken from each patient willing to participate, before the start of trial study.

Observations and Results

A total of 39 patients were registered; among them 21 patients in Group A and 12 patients from Group B had completed the treatment.

The maximum number of patients (58.97%) were found in the age group of 40 to 50 years. The maximum number of patients (64.10%) were females. A majority of the patients (69.23%) were taking a *Madhura Rasa*-dominant diet. About 56.41% were taking a *Usna Guna*-dominant diet, with the *Ruksha Guna* dominance in the diet of 41.03%. The maximum number of patients were having *Vishamagni*, with a percentage of 76.92%. Using *Dashavidha Pariksha*, the total *Atura Bala* was assessed. *Atura Bala* was found to be *Madhyama* in 56.41% of the patients followed by *Pravara Atura Bala* in 43.59% of the patients. No patient was observed with having *Avara Bala*.

A maximum number of patients (56.41%) had given a history of *Atishita Annasevana* as *Aharaja Hetu*. A maximum number of patients (48.72%) had expelled sputum after much difficulty. About 66.66% patients had the disease, which was recurrent in nature, either frequently, twice or thrice a year, or once a year. *Madhyama Vyadhi Bala* was found in 48.72% of the patients, and 43.59% patients had *Pravara Vyadhi Bala*. With reference to *Rtu*, a maximum number of patients were registered as *Hemanta* (38.46%), followed by *Sishira* (30.77%), and *Vasanta Ritu* (20.51%).

A maximum number of patients (90.48%) had not developed any kind of adverse events or reactions during the therapy. None of the patients had shown any kind of statistically significant changes in vital parameters like temperature, blood pressure, and the like, or in laboratory investigations like LFT, RFT and so on.

Table 1: Details of two patients who had developed Urodaha

Parameters	Patient 1	Patient 2
Age / sex	37 years / Female	17 years / Male
Weight	51 kg	48 kg
Height	5.3 ft.	5.5 ft.
Religion	Hindu	Hindu
Occupation	Housewife	Student
Desha	Sadharana	Sadharana
Type of diet	Vegetarian	Vegetarian
Frequency of diet	Thrice a day	Thrice a day
Type of Ashana	Adhyashana	Samashana
Dominant Rasa in Ahara	Madhura, Amla, and Katu	Katu
Dominant Guna in Ahara	Ushna, Snigdha	Ushna
Nidra (type of sleep)	Sound	Sound
Addiction / habit	Tea	No addiction
Mala Pravritti (bowel habits and consistency)	Regular – Baddha	Regular – Picchila
Mutra Pravritti	Normal	Normal
Menstrual cycle	Regular, but painful	-
Emotional makeup	Angry	Anxiety
Medicine given in (Kala)	Vashanta	Vashanta
Prakriti	Pittavata	Pittavata
Agni	Vishama	Vishama
Koshtha	Madhyama	Mridu
Atura Bala	Madhyama	Madhyama
Vyadhibala	Madhyama	Pravara
Reaction occurred	On the thirteenth day of administration	On the nineteenth day of administration
Severity	Mild	Mild
Reaction released	By dechallenge	By dechallenge
Apathya Sevana	Unlikely	Unlikely
Previous history of the symptom	Not found	Not found
Rechallenge	Positive result	Positive result
Changes in other objective parameters including laboratory investigations	Not found	Not found
Medicine obtained from pharmacy on	7 December, 2007	7 December, 2007

Two of the Pippali-treated group patients had developed Urodaha (chest burning) during the treatment. The symptom obtained during the treatment was mild in nature and not severe. The details of both of the patients have been postulated in Table 1. The results are shown in Figure 1.

Discussion

Probable mode of action of the Pippali in Kaphaja Kasa

According to the Samanya – Vishesa principle, Pippali with the opposite Gunas like Katu Rasa, Laghu, and Tikshna Guna, causes alleviation of Kapha Dosha, with opposite properties like Madhura, Guru, Manda, and so on, of Kapha Dosha. Pippali with Tikshna Guna causes Bhedana of Kapha, which is stuck to the Srotasa by Picchila and Sandra Guna. Once the Dosha is separated from the Srotasa, the Ushna Guna of the drug causes Vilayana of Kapha and generates easy expectoration. Kaphasthivana causes Srotoshuddhi, and hence, Vata Sanga and

Vimarga-gamana are corrected. That leads to Vyadhi Shamana.

Pippali in relation to adverse drug reaction

A maximum number of patients, that is, 90.48% had not developed any kind of adverse events or reactions during the therapy. None of the patients had shown any kind of statistically significant changes in vital parameters like temperature, blood pressure, and so on, or in laboratory investigations like Liver Function Tests, Renal Function Tests, and the like.

Many reasons can be thought of for the drug not causing any harmful effects, although the adverse effects are already mentioned in the classics.

- It has been mentioned in the classics that Pippali should not be used for long durations in continuous use. Here the drug has been used for 21 days, which might not be sufficient to consider it as long duration usage.
- Pippali has properties like Tikshna, and so on. It is mentioned as an Apatabhadrta, that is, an emergency medicine. Hence, Pippali can be taken as the Bhesaja

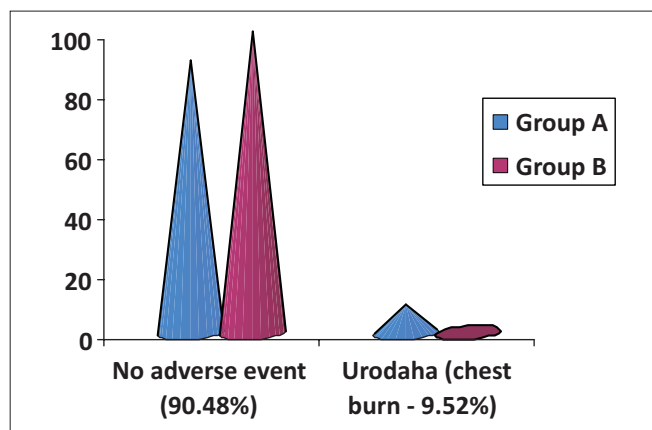


Figure 1: Distribution of patients showing occurrence of ADE in both groups

having *Tikshna Virya* or *Pravara Bala Bheshaja*. A maximum number of patients had *Madhyama Atura Bala* with *Madhyama* and *Pravara Vyadhi Bala*. Considering the *Madhyama Atura Bala*, *Madhyama* or *Pravara Vyadhibala* and *Pravara Bheshaja Bala*, it can be said that ratio of three *Bala* was maintained. Hence, there are minimum chances of ADRs. On the other hand, patients with *Madhyama Vyadhi Bala* and *Madhyama Atura Bala* have also not shown adverse effects, although the *Bheshaja Bala* must be *Madhyama*. The reason behind the drug not being able to attain the stage that causes a reaction may be because of accessory factors like:

- 1) *Bheshaja Kala*: The administration period of the drug was after meals. Hence, the *Tikshnata* of the *Bheshaja* might be less as compared to the *Bheshaja* given on an empty stomach.
- 2) *Dosha*: The chief *Dosha* on which *Pippali* was administered was *Kapha*, which has almost the opposite properties of *Pippali*. Opposite properties of the drug and *Kapha Dosha* might create favorable circumstances of a balanced state and relieve the disease rather than cause any vitiation of the *Dosha*.
- 3) *Ahara Guna*: A maximum number of patients were taking *Ushna* and *Ruksha Guna*-dominant *Ahara*. *Ruksha Guna* again might be able to balance the *Kleda* of the *Pippali*, if produced.
- 4) *Kala Prabhava*: A maximum number of patients were given medication in either *Kapha Sanchayavastha* or in *Prakopavastha* of *Kapha*, that is, in *Sishira* and *Vasanta Rtu*. A good percentage of patients were given medication in *Hemanta Ritu*. In all these seasons, the substances in *Katu Rasa*, *Tikshna*, and *Laghu Guna* with *Ushnata* are accepted as *Pathya*. Hence, there are less chances of occurrence of any abnormality with these types of substances.

Adverse events observed in two patients in Group A: Two of the *Pippali*-treated group patients had developed *Urodaha* (chest burning) during the treatment. The symptom obtained

during the treatment was mild in nature and not severe. The details of the patients are given in the clinical observations. By dechallenge and rechallenge, the causality of the reaction due to the drug had turned positive. Both the patients had *Pittavata Prakritti*. Both the patients were taking *Katu Rasa*- and *Ushna Guna*-dominant *Ahara*. All these factors were significant in evolving dominance over *Pitta Dosha* in both the patients. Therefore, they might not be able to tolerate the drugs that were *Agneya* by nature. Although the drug was administered in *Kaphaja Kasa* in the *Vasanta Ritu*, that is, *Kapha Prakopa Kala*, the drug was able to produce only a mild reaction apart from alleviating the *Kapha Dosha*.

Both the patients had the habit of *Adhyashana* and *Vishamashana*, which was suggestive of the chance of some sort of *Agnidusti* in the patients. On the other hand, both the patients had *Vishmaggni*, which again was suggestive of improper *Pachana* of the drug.

Conclusions

As all the *Dravyas* found on the earth are *Panachabhautika*, *Abheshaja* is not a separate entity, but there are multiple factors that are responsible for converting *Bheshaja* into *Abheshaja*. To prevent the effects from *Abheshaja*, *Yukti* is the single most required quality of the physician.

It is very difficult to decide an adverse drug reaction for an Ayurvedic drug, as there are multiple factors like *Prakriti*, *Desha*, *Kala*, *Satmya*, and so on, which should be considered before drug administration.

In clinical trials, an adverse event* of *Pippali* that was used for therapeutic purpose, was observed in two out of 21 patients, which is very common according to the classification of adverse drug reactions in modern medicinal science. However, to prove that the drug is *Abheshaja* or causes an adverse drug reaction, more data is needed from different regions.

(*An adverse event does not mean an adverse drug reaction. In an adverse drug reaction, the causal relationship between the drug and the reaction is been already proven. However, in an adverse event, the causal relationship between the drug and the reaction is still doubtful; in an adverse event, other factors except the drug might be involved).

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