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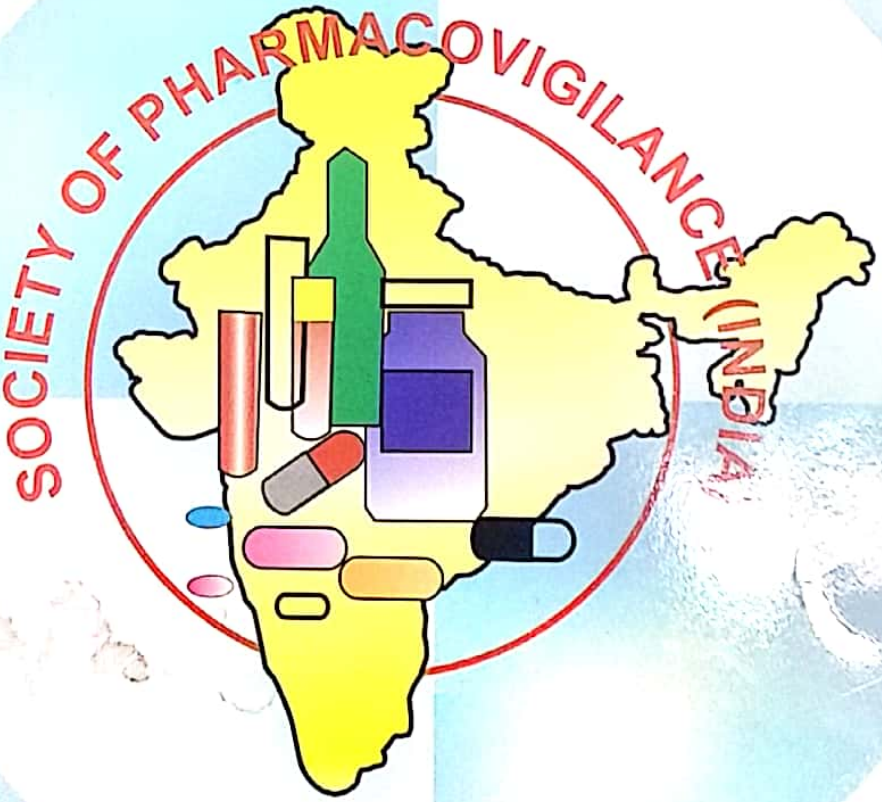

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Particulars

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FROM THE DESK OF EDITOR

Expecting the Unexpected — Adverse Drug Reactions (ADR)

When a new drug is first marketed, findings regarding its efficacy and safety are commonly based on the experience of several thousand people who have been treated in controlled clinical trials. Despite extensive testing, rare adverse events (those that occur in less than one patient per thousand) can easily escape detection, and unforeseen interactions with coexisting clinical conditions or other drug therapies may remain unexplored. As a result, the characterization of the full safety profile of a new drug relies heavily on clinicians careful observation of its effects in "real world" practice that is far removed from clinical-trial conditions.

An adverse drug reaction (ADR) is an expression that describes harm associated with the use of given medications at a normal dose. The meaning of this expression differs from the meaning of "side effect", as this last expression might also imply that the effects can be beneficial.
Spontaneous reporting is the core data-generating system of international pharmacovigilance, relying on healthcare professionals (and in some places consumers) to identify and report any suspected ADR to their national pharmacovigilance center or to the manufacturer. Spontaneous reports are almost always submitted voluntarily. One of this system's major weaknesses is under-reporting, though the figures vary greatly between countries and in relation to minor and serious ADRs. Another problem is that overworked medical personnel do not always see reporting as a priority. If the symptoms are not serious, they may not notice them at all. And even if the symptoms are serious, they may not be recognized as the effect of a particular drug.

Even so, spontaneous reports are a crucial element in the worldwide enterprise of pharmacovigilance and form the core of the WHO Database, which includes around 4.6 million reports (January 2009), growing annually by about 250,000. Some countries legally oblige spontaneous reporting by physicians. In most countries, manufacturers are required to submit through its Qualified Person for Pharmacovigilance (QPPV), all the reports they receive from healthcare providers to the national authority. Others have intensive, focused programmes concentrating on new drugs, or on controversial drugs, or on the prescribing habits of groups of doctors, or involving pharmacists in reporting. Pharmacovigilance is gaining importance for doctors and scientists as the number of stories in the mass media of drug recalls increases. The challenge of maximizing drug safety and maintaining public confidence has become increasingly complex. Pharmaceutical and biotechnology companies must not only monitor, but also proactively assess and manage drug risk.

The consequences of ineffective adverse drug event reporting and pharmacovigilance processes, procedures and plans could include brand damage, class action suits and exorbitant fines, among others. For rectifying the adverse drug reactions in future we should develop procedures for the identification, reporting and follow-up of adverse drug events, assess the current technology used in the drug safety process and assist with implementation of new systems.

Dr. Anurag Tomar
MBBS, MD (Pediatrics)
Editor in Chief
sopijaipur@gmail.com

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REVIEW ARTICLE

Pharmacovigilance and Unani Drugs - Present Scenario

FARKHUNDA JABIN

Department of Hifzane Sehat Wa Samaji Tibb (Social and Preventive Medicine)
Unani Medicine, A.M.U. Aligarh - 202 002

ABSTRACT

According to WHO, "Pharmacovigilance activities are done to monitor detection, assessment, understanding and prevention of any obnoxious adverse reactions to drugs at therapeutic concentration that is used or is intended to be used to modify or explore physiological system or pathological states for the benefit of recipient." These drugs may be any substance or product including herbs, minerals, etc. for animals and human beings and can even be that prescribed by practitioners of Unani or Ayurvedic system of medicine[1]. Unani system of medicine is an ancient traditional system of medicine. Drugs used in this system are time–tested and for centuries they are used for treatment. Reports of Adverse Drug Reaction (ADR) implicating Unani drugs are also negligible. Does it means Pharmacovigilance is not applicable to these drugs? With the passage of time, as the world is going under change there are various factors which make these time tested drugs vulnerable to emergence of adverse events. With safety as their prime concern ancient physicians were always rational in the use of their drugs while treating their patients. But present scenario has made them to be subjected to rules of Pharmacovigilance like any other contemporary medicines.

Introduction of Unani

Greeko-Arabic medicine, which is popularly known in India as Unani Tibb is one of the oldest systems of medicine in the world[2]. Tibb has journeyed through many teachers, philosophers and countries with principle that can be traced back to Egyptian, Greek, Arabic, Indian and Western medicine. It initially began with Imhotep, the renowned Egyptian and was later embraced by Greeks like Hippocrates and Galen and finally refined, over many centuries, by Arab physicians like Ibne Sina (980-1037)[3]. Unani medicine was introduced in India around 1351 AD by Arabs and flourished under the patronage of Mughal Emperors among the masses and spread all over the country[4]. It suffered a setback during the British rule but soon regained its momentum by endless efforts of Nizam of Hyderabad, Azizi family of Lucknow and Sharifi family of Delhi. At present Unani system of medicine has now been regarded and recognized as one of the Indian Systems of Medicine and forms an integral part of national health care delivery system[5].

Concept of Adverse Drug Reaction (ADR) in Unani

Unani is committed to using natural methods of treatment; it includes use of drugs of herbal, mineral and animal origin. Alqanoon fil Tibb (a classical text book of Unani Tibb) gives rather detailed pharmacological and pharmacotherapeutic characteristics of 811 drugs, among which those of vegetable kingdom constitute 594 (73.7%), of animal kingdom 118 (14.5%), and of mineral 99 (12.2%)[6].

But the first ethical rule in Unani Tibb is primum non nocere (first do no harm), meaning the anticipated benefit from any therapeutic modality must be balanced by potential risks and physician should at least bring no harm to the patient, if he can't bring any good to him. There is a popular misconception that Unani drugs are devoid of adverse reactions. However, Unani physicians were well aware of the adverse drug reactions associated with drug therapy. They were vigilant enough and took all possible steps to minimize the emergence of ADR. It is showed in the following facts that the drug therapy was adopted as the last therapeutic module when Ilaj bil Tadbeer (Regimental therapy) and Diet therapy failed to give relief. The Al-Qanoon fil Tibb describes possible (muzir asrat) harmful effects which are associated with different drug and (musleh) corrective drug is clearly mentioned. 'Parhez' meaning what to eat and what not to eat along with medication during treatment were also communicated to the patient. This system does not diagnose and prescribe, but identifies the pattern of illness based on specific temperaments and chooses the herbs and treatment strategies according to that[7]. Likewise, drugs are classified into four degrees (I, II, III, IV) according to their temperament, potency and actions, higher the degree higher the adverse drug reaction III and IV degree drugs are advised to be given with extreme caution. Mineral drugs were diligently processed and purified (muddabar)

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before use. A separate branch of Unani pharmacology called Saidla deals with preparation and detoxification of Unani drugs. Ancient Unani physicians use to write ADR's in their personal notebooks (bayaz) to communicate it further[8]. While choosing a herb, its constitutional nature (temperament), time of collection, part to be used, methodology of preparation, route of administration. As well as certain factors regarding the patient like body's humoral constitution (temperament), sex, age ,habit and season were taken into account and drug was individualised according to the patient not the vice versa. And, the drugs were administered after careful calculation by the physician as to which medicine will be suitable at which stage of an illness. All these factors were responsible for minimizing the emergence of ADR to Unani Drugs at lowest level. To summarize, Charaka said, "that even a strong poison can become an excellent medicine if administered properly. On the other hand even the most useful drug can act like a poison if handled carelessly"[9] was equally believed and practically applied by Unani physicians also.

Pharmacovigilance and Unani System of Medicine

In ancient times, the Unani physicians prepared medicines for their patients themselves. Today, only a handful of practitioners follow this practice and production and sale of Unani drugs has become formalized into a thriving industry. Manufacture and marketing of Unani drugs is covered by the Drugs and Cosmetics Act, 1940.[10] As on January 1999, the estimated number of Registered Unani practitioners in India was 40748 and total domestic market of Unani is about 100 crore (2.3% of total ISM drugs).[11] With influx of drugs into the market from, whether proprieteal or informal sector , has brought forth many challenges about Safe and rational use of Unani drugs, bringing into focus the need for formal ADR monitoring programs in the field. After promotion of safe and rational use of drugs by WHO and establishment of ADR monitoring centre Uppsala monitoring centre(UMC) reports of ADR associated with herbal drugs implicating Unani drugs have also come up. By the end of June 2004, the UMC had received more than 11,500 reports of adverse reactions from countries like UK, Germany, France, U.S.A, Spain etc, involving one or more herbal ingredients.[12] In a recent clinical trial of Unani herbal compound formulation in the patients of Bronchial asthma , 20% patients reported Adverse effect of different types ranging from mild to moderate and severe it included arrhythmia, sweating, insomnia, palpitation, blisters, redness, tremors, rhinitis, nausea, vomiting, headache, pruritis, myalgia, diarrhoea etc [13]. Henna, (lawsonia innermis linn) is reported to have caused dermatitis, further in persons of G_6P-D deficiency application of henna can cause haemolysis. Ginko biloba has shown to cause serious Adverse effects like increased blood pressure and bleeding disorders. And yet, the number of adverse reactions to Unani drugs reported or recorded in the National Pharmacovigilance Program in India is negligible.

Challenges in Introducing Pharmacovigilance to Unani System of Medicine

The strong belief that Unani medicine are natural hence safe, contributes to this problem to a large extent and the lack of knowledge about the concept and importance of Pharmacovigilance in Unani among its practitioners.

Same drug is prescribed for variety of ailments where as for one disease different types drugs can be prescribed.

Drugs are not used strictly according to the ancient text. They are used outside their original, clinical, cultural or pharmaceutical context or in combination with allopathic medicines. Concept of individualisation of drug according to patient is totally ignored leading to increased chances of emergence of ADR.

Dose-related responses are rarely measured and reported.

For drug therapy herbal compound formulation are used. The number of ingredients may range from more than 2 to 20 or sometimes even more.

Drug regulation governing the manufacture and sale of Unani medicines are not well defined at both national and the international level. Further, drug dispensing by private doctors and informal sector also make quality assurance and ADR monitoring very difficult.

Over the counter drugs are available for various conditions like improving vitality, memory which are never tested for their toxicity, efficacy and false claims. Self medications with these drugs are quite common.

Misidentification of drugs deliberately or by chance is sometimes also responsible for adverse events, for e;g Ruta Graveolens linn(suddab) was accidently replaced by Euphorbia drancunculoids, a toxic herb[14].

Collection and storage of raw plant drugs is not properly managed resulting in contamination with dust fungus, rat droppings etc.

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Use of counterfeit and spurious drugs is a major problem.

Using of raw plant material which are equally devastated by environmental pollution by use of pesticides and fertilizers.

The manufacturing units for Unani system of medicine are not well organized. The main institutions involved in the manufacturing process are Central Government controlled units, State Unani Pharmacies run by state government and some private pharmacies[11].

Manufacturing units not necessarily abide by pharmacopeal standards laid down by the Indian Govt. as there is no stringent policy to check finished products available in the market.

There is possibility of drug- drug interaction as it is commonly consumed along with drugs of narrow therapeutic margin and other systems of medicine.

Use of Drug substitutes in place of any ingredient is common practice[15].

Most of the pharmaceutical companies proclaim their drugs as 100% safe.

One of the most challenging aspects is the lack of expertise in performing causality analysis with Unani drugs. A person trained in Pharmacovigilance rarely understands Unani while an expert in Unani is not trained in the science of Pharmacovigilance. Physicians do not know what to report and where.

Steps to Prevent Emergence of ADR in Unani

It is being increasingly recognised that ADR's are preventable thus early detection and prevention can help making the drug therapy a lot safer and cheaper. Although, therapeutic approach of allopathic and Unani medicine is different but Pharmacovigilance is equally applicable to the drugs of both the systems. Pharmacovigilance in Unani medicine is perhaps a new concept as but one should not wait for "Unani thalidomide" disaster to wake the community to the need of the hour. And the following steps should be taken to prevent the emergence of ADR at its nubile stage.

Awareness about the monitoring of adverse drug reactions should be created among the consumers and prescribers, with one of the most important task of dispelling the notion of 'natural means safe'.

Communication between the practitioners and policy makers of Unani medicine should be improved. Unani physicians and consumers should be made aware of the need to report and where to report.

Unbiased drug information about Unani drugs including both classical and proprietary formulations should be made available easily.

Students and physicians should be sensitized to the concept of Pharmacovigilance at both under-graduate and post-graduate levels.

Pharmaceutical industry should be motivated to generate safety data - either before or after marketing of the formulation.

Unani experts should be trained in the science of Pharmacovigilance and included in detection of signals, assessment and reporting of ADR.

Scales to assess the causality of the reported reactions to Unani medicines should be developed and validated.

Conclusion

It is evident that ancient Unani physicians were well aware of the associated adverse events with their drugs that is why they were extremely cautious while prescribing the drugs .But according to changing demands and need of the health care sector Unani drugs have also undergone some changes and modifications. So, need of the hour is that ADR monitoring for drugs of Unani System of Medicine should be made mandatory.

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REVIEW ARTICLE

Stevia rebaudiana: An Update

JITENDRA SINGH[1], PARUL GROVER[1], DHARAM PAL PATHAK[2]

[1]*Lord Shiva College of Pharmacy, Sirsa - 125 055*
[2]*Delhi Institute of Pharmaceutical Sciences and Research, Delhi*

ABSTRACT

Stevia rebaudiana (Bertoni) belonging to family Compositae is a natural, non-caloric and sweet tasting plant. The sweet taste of stevia lies in a complex molecule called stevioside. The history of the culture of stevia mainly stems from South America. Originally, stevia only grew in the northern regions of South America but its cultivation has become popular worldwide. Stevia is often referred to as the "sweetest plant of the world". Stevia can grow in places where the climatic conditions are favourable and the maximum day temperature is not exceeding 35°C with the night temperature not falling below 12°C. In India, it is cultivated from Rajasthan to Mizoram and from Punjab to Kerala. Its applications include its use in weight management, as a sweetener, for tooth care, diabetic care, hypertension, general tonic, dietary supplement and in skin care. It could be expected that in year 2015 stevioside will gain a market share of about 10-15%. The sales volume in real tons would be 1.800-2.700 tons in EU.

Keywords: Hypertension, Antioxidants, Acne, Hypoglycemia

Introduction

There have been few botanical discoveries quite as dramatic in nature as the realization that the leaves of a species of stevia plants, *Stevia rebaudiana* Bertoni (Compositae), are intensely sweet. Stevia is a natural, non-caloric, sweet-tasting plant used around the world for its pleasant taste, as well as for its increasingly researched potential for inhibiting fat absorption & lowering blood pressure.

Stevia is an herb that has been used as a sweetener in South America for hundreds of years. It is calorie-free, and the powdered concentrate is 300 times sweeter than sugar. Because they are commercially unprofitable, relatively few highly sweet plant components have been developed as sugar substitutes. However, due to the interest in natural food ingredients, the discovery that this stevia plant has naturally occurring sweetness has attracted great interest.

The sweet taste of Stevia lies in a complex molecule called stevioside which is a glycoside composed of glucose, saphorose & steviol. It is this complex molecule & a number of other related compounds that account for *Stevia rebaudiana's* extraordinary sweetness. The Stevia herb in its natural form is approximately 10-15 times sweeter than common table sugar. Stevia and stevioside, an extract of stevia, have a methanol-like, bitter aftertaste that limits their usefulness.

The technique of stevia culture originated from South America. Originally, stevia only grew in the northern regions of South America but its cultivation has become popular worldwide. The plant has been known for centuries by the native Guaranay-Indians for the sweet taste of its leaves. They use it, amongst other things, to make "mate" herbal tea. Stevia is often referred to as the "sweetest plant of the world".

History

For decades, people in South America have used a sweet leaf to sweeten bitter herbal teas including Yerba mate. For nearly 20 years, Japanese consumers by the millions have used extracts of the same plant as a safe, natural, non-caloric sweetener. Stevia is a fairly unassuming perennial shrub of the compositae family, native to the northern regions of South America. Stevia and its extracts have captured over 40% of the Japanese market. Major multinational food companies like Coca Cola & Beatrice foods, convinced of its safety, use stevia extracts to sweeten foods for sale in Japan, & other countries where it is approved.

The saga of American interest in stevia began around the turn of the 20th century when researchers in South America started hearing about "a plant with leaves so sweet that a part of one would sweeten a whole gourd full of mate".

In the 1970s, the Japanese government approved the plant and food manufacturers began using stevia extracts to sweeten everything from sweet soy sauce & prickles to diet coke. Researchers found the extract interesting, resulting in dozens of well-designed studies of its safety, chemistry & stability for use in different food products. In addition to Japan, other governments have approved stevia &

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stevioside, including those of South America, China & South Korea.

In 1991, stevia was totally banned by the FDA because "toxicological information on stevia is inadequate to demonstrate its safety." This ruling was very controversial. In 1995, the FDA revised its ban against stevia and allowed it for sale as a dietary supplement. The FDA has refused to allow stevia to be sold as a sweetener because several animal studies have linked the use of stevia to potential health problems. Although the studies are few, there are enough for the FDA to not allow it to be sold as a sweetener. According to some researchers, if stevia is used sparingly, once or twice a day, the risks are low. If stevia was marketed widely and used in diet sodas, it could be a potential health threat. Currently, Australia and Canada also have approved stevia as a dietary supplement. Stevia proponents point out that stevia has been used by millions of consumers in countries such as Japan for 30 years, with no reported or known harmful effects on humans. Stevia does not promote dental cavities, does not raise blood glucose levels and is safe for persons with phenylketonuria (an inability to breakdown the essential amino acid, phenylalanine).

Cultivation Process of Stevia

Money doesn't grow on trees, runs the maxim. While many of us believe in it, a perennial shrub – stevia – has been proving this statement wrong. Heralded as the 'sweetener of the future', the plant has been taking the farming community by storm worldover (both for its medicinal values and commercial prospects). This, however, is not the case in India, despite it being a fertile ground for the cultivation of the 'money plant'.

The land sites are plowed and are cultivated twice to prepare a fairly smooth, firm-planting surface. Transplants from cuttings would be superior, however cost makes it prohibitive. Therefore, stevia must be propagated from seed in plug trays placed in a greenhouse for a period of 7-8 weeks. Depending on different climate conditions Stevia is cultivable throughout the year except for times when it is extremely hot or cold. The plant appears to have low nutrient requirements. Stevia plant normally requires frequent, shallow irrigation. Harvesting of the leaves is done by plucking the leaves, if required in a small quantity. The entire plant with the side branches is cut leaving 10-15 cm from the base. The harvested branches are shade dried and the dried leaves are stripped off from the branches.

Stevia can grow in places where the climatic conditions are favourable and the maximum day temperature is not exceeding 35 °C with the night temperature not falling below 12°C. In India, stevia cultivation is spread from Rajasthan to Mizoram and from Punjab to Kerala in more than 500 acres with success rate more than 90%.

Comparison Chart of Stevia and Some Other Sugars

Per 2 teaspoons sugars	Stevia Plus	Sugar	Splenda®	Equal®	Sweet 'N Low®
Calories	0	32	0	0	0
Net carbohydrates	0g	8g	1g	1g	1g
Dietary Fiber	1g	0g	0g	0g	0g
Glycemic Index	0	70	80	80	80

Applications of Stevia

1. Stevia as a Sweetener

Stevia is the sweetener of the future. Because the human body does not metabolize the sweet glycosides (they pass right through the normal elimination channels) from the leaf or any of its processed forms, the body obtains no calories from Stevia. Processed forms of pure Stevia can be 70-400 times sweeter than sugar. Whether these products are called Stevia, Stevioside, Rebaudioside, Stevia Extract, or Stevia Concentrate, if they are in their pure unadulterated form they do not adversely affect blood glucose levels and may be used freely by both diabetics and hypoglycemics. For people with blood sugar, blood pressure or weight problems Stevia is the most desirable sweetener.

In all of its current forms Stevia has a taste unique to itself. Along with its sweetness there is also a bitter component. The poorer the quality of the leaf the more bitterness is evident in the taste. In good consumer products, however, this bitter flavor disappears as does the slight licorice taste of whole-leaf products when appropriately diluted for

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consumption. Unlike artificial sweeteners, the sweet glycosides do not break down in heat which makes Stevia an excellent sweetener for cooking and baking.

2. Stevia & Weight Management

Stevia users have long insisted that the leaves & concentrate reduced their appetite & their craving for sweets & fatty foods, thus being a very effective aid in weight loss.

Research now underway suggests that natural stevia may be beneficial for people who are overweight. It is believed that a defect exists between the stomach and the hypothalamus in many people who are overweight, which fails to "turn off" hunger sensations when the person is actually full. It appears, from the initial research, that stevia may correct this defect & actually rest the hunger mechanism, thus "turning off" hunger sensations when satiation has occurred.

3. Stevia for Tooth Care

It is well known that most of the dental formulations in powder, herbal or paste form use large quantities of sugar for imparting sweet taste. Since the sweetness is so much an integral part of our daily life it is very difficult to imagine a teeth cleaning preparation without customary sweet taste. In most of the cases sugar is most preferred sweetening agent. But many times some important aspects are neglected such as-

Sugar actually contributes to the teeth decay!

In highly concentrated from it reduced the activity of other herbal ingredients.

Stevia whole leaf powder offers an ideal alternative to replace sugar in the dental powders and pastes. Not only stevia eliminates the requirement of sugar but its anti bacterial activity actually enhances the productive and curative properties of dental preparations.

4. Stevia for Diabetic Care

Derived from a South American shrub, Stevia is recommended for anyone with diabetes, as well as those looking for natural, low-carb, low-calorie sweetener solutions.

- Improve the existing formulation targeted at controlling diabetes.
- To develop new formulations to tackle this severe problem of type 1 and 2 diabetes in the Asian population world wide.

The anti-diabetic properties of stevia can also help to reduce blood pressure & control blood sugar levels, as well as improve muscle tone & the health of the heart.

5. Stevia for Hypertension

We are all aware of the fact that most of the diabetics do suffer from hyper tension at some stage of their life. The earliest clinical studies have amply demonstrated that Stevia leaves have potent action in reducing chronic hypertension. Stevia leaves if consumed regularly have excellent scope to be used as a single medicine for the control of Diabetes as wall as hypertension.

6. Stevia as a General Tonic

Dried stevia leaves contain many vitamins and trace elements such as selenium, cobalt, chromium etc. We all know that these elements are potent antioxidants. Hence it has been proven that stevia can be used in herbal tonic formulation with promising results.

7. Stevia as a Dietary Supplement

The vast majority of reported health benefits, both from the research laboratory and consumer experience, come from daily use of a water based whole leaf Stevia concentrate. Scientific research has indicated that Stevia effectively regulates blood sugar and brings it toward a normal balance. It is sold in some South American countries as an aid to people with diabetes and hypoglycemia. Since its introduction into the US, numerous people have reported that taking 20-30 drops with each meal brought their blood glucose levels to normal or near normal within a short time period. Obviously each individual's condition is different and such experimentation should be done under the supervision of a qualified physician. An important benefit for hypo-glycemics is Stevia's tonic action which enhances increased energy levels and mental acuity.

Studies have also indicated that Stevia tends to lower elevated blood pressure but does not seem to affect normal blood pressure. It also inhibits the growth and reproduction of some bacteria and other infectious organisms, including the bacteria that cause tooth decay and gum disease. This may help explain why users of Stevia enhanced products report a lower incidence of colds and flu and why it has such exceptional qualities when used as a mouthwash or added to toothpaste. Many people report significant improvement in oral health after adding Stevia concentrate to their toothpaste and using it, diluted in water, as a daily mouthwash.

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ORIGINAL ARTICLE

Concept of Pratinidhi Dravyas (Substitution of Drugs) in Ayurveda System of Medicine

K.C. SINGHAL AND RABINARAYAN ACHARYA[1]

NIMS UNIVERSITY Rajasthan, Jaipur - 303 121 India
[1]Gujrat Ayurved University, Jamnagar - 361 008, Gujrat, India[1]

Introduction

The use of plants and animals as a source of food and medicine is as old as humanity. As the dictum "necessity is the mother of invention", goes, one finds the searching minds be it in a rural setup or a primitive society, looking for therapeutically useful drugs from the natural resources around them. The plants used by them for a variety of purposes may not always be most suited, but they are the best available locally; it is by compulsions, rather than choice, particular drug becomes a drug of choice. In the olden days plants were considered sacred and the collection was made with veneration prayer to the drug. The drug was picked up only in a particular season with due respect to factors like *Kala (time), Graha (planets), Nakshatra,* etc. All these are ignored now a day, and the drug collection is being over exploited with commercial interest uppermost in the minds. This has led to depletion of number of important commonly used herbs. This in turn has led to search of alternate source of drugs, foods and other life supporting plant drugs. This back to nature approach has led to seek guidance from folk and other tribal communities living closer to nature. Apart from this, therapeutic hints from remote mists of time hold key of the treasures of medical knowledge. From the large array hints, claim, principles and practices handed over from generation to generation, the investigator of today has to promulgate best and beneficial and recant the one not useful.

Many species of medicinal plants have become extinct. It means the species is not survived by any living member of its own throughout the world. Sometimes the species may disappear from an area but still be available in other areas (locally extinct species), on the other hand when number of individuals of a species in a community in diminished so much so that it is not able to exert any considerable impact on its associates, it is called ecologically extinct species. Besides there are species in a state of decrease in their population size and therefore, may go under extinction in the near future.

The decrease in biodiversity adversely affect and eliminate many species from their natural habitat. The important causes thought to be responsible include –

a) Destruction of habitat due to increase in human population

b) Vast areas of land under cover of trees, herbaceous vegetation and wild herbivores have been cleared and put under cultivation of crops, construction of living units, industries, dams and other purposes.

Overexploitation of Natural Resources

A large number of vegetation products are used as timber, fruits and other eatables besides for medicine. Medicinal plants are being extensively harvested thereby causing their depletion. This has resulted in significant reduction in their density and even survival of many is threatened.

Environmental Pollution

Pollution of soil water and air has not only affected man and animals but has also resulted in elimination of many plant species including those of Medicinal value. Sewage water containing organic or heavy metals such as iron, copper, zinc, mercury, lead, nickel etc. are dumped in to sewage pounds, reach river and other water bodies where from they get entry in to plants. When present in toxic concentrations, these become lethal for many plant species and these may get extinct or their availability declines.

Shifting cultivation (Jhum) is prevalent in many parts of the world. In India it is more common in hilly areas, which are rich in wild vegetation. The farmers create a ground for cultivation by felling trees and burning vegetation by putting fire. The land is used for growing crops for few years till it gets depleted of its nutrients. The farmer moves to new areas often turning the fertile land to waste land. The "Jhum" cultivation practice is responsible for destruction of wild flora and fauna. Many rare species may become extinct or endangered.

Indian systems of Medicine suffers from a big drawback of lack of availability of many herbs, mentioned in various texts. For these substitutive herbs or Pratinidhi Dravya are used. Meaning representative form of the original drug.

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The original drug's efficacy is altered by the use of substitute but for the extinct group there is no way at all.

Safety Issues: Several problems are associated with the monitoring of herbal drugs. These include a. identification, collection, and storage of plants b. processing or preparation of drugs including mixing, powdering, triturating, making decoction, fermentation, contamination, substitution, use of preservatives, changes of ingredients but still keeping the same brand name and many others. It is recommended that strict mandatory regulations for the control of manufacturing, formulation, dispensing be enforced. Lack of enforcement of drug regulations for drugs of Indian Systems of Medicine has offered a casual approach in the manufacture and distribution of these drugs and has led to poor quality control system and loose distribution channels like sale over internet and via mail address. Contamination of traditional medicines with toxic and potentially dangerous substances including heavy metals e.g. mercury, lead, arsenic and steroids has been reported and this has adversely affected the export of drugs of ISM to European countries and U.S.A. Care must be excercised while prescribing herbal drug with drugs of allopathic system. Concomitant use of traditional medicine with other drugs can result in unwanted drug interactions

Pharmacovigilance methodology is similar for drugs of traditional system and allopathic system of medicine. However due to disorganized nature of the field of traditional medicines some modifications have to be made in the pharmacovigilance system established for allopathic system. The names of medicinal plants need rationalization. One plant is known by several names even in the botanical nomenclature. Adverse reaction terminology except for Ayurvedic drugs (recently made available by the translation in Hindi by Prof. K. C. Singhal) is not available, while the prescribers of ISM understand their terminology than the allopathic one. An initiation has been made by Department of AYUSH, Government of India and has formulated a core committee for the monitoring of drugs of ISM. The headquarter is located at Gujrat Ayurvedic University, Jamnagar and several regional and peripheral centers have been established. Besides, training is provided to participants of the programme at several centers in the country through regulars short courses.

Substitution in herbal drug therapy has become its essential and necessary component. Reasons could be many including nonavailability of herbs in a particular season, in a particular geographical region, destruction of herbs by natural calamities or by animals or over-usage. Another factor related to scarcity could be related to market shift causing increase in the cost. All these and many other factors appear to have compelled the Ayurvedic Physicians of yester years to find suitable alternatives. The concept of Mukhya (main) and Pratinidhi (representative) drugs does not appear in Charak Samhita[1] and in Sushruta Samhita[2]. It seems to be a later development and mentioned for the first time in Astanga Hridaya[3].

History of Pratinidhi Dravyas (Alternate Drug's)

In ancient literature like Charaka[1] and Sushruta Samhita[2] there is no direct reference or listing of Pratinidhi dravyas. Acharya Vagbhata, the author of Astanga Hridaya[3], has stated in his work that, In case of non-availability of any particular drug in the preparation of a compound one should try to get another similarly potent drug having similar ***Rasa (Physical Properties), Guna (Pharmacological actions), Virya (Potency)*** **and** ***Vipaka (Effect of digestion and interaction)***

त्र्यस्त्रिंशदिति प्रोक्ता वर्गास्तेषु त्वलाभतः।

युञ्ज्यात्तद्वेधम यञ्च द्रव्यं जह्यादयौगिकम्।। अ ह्र सू १५

Detail description regarding Pratinidhi dravyas can be traced from other texts of Ayurveda related with compilation of formulations and their indications such as in Bhavaprakasha[4], Yogaratnakara[5] and Bhaishajya Ratnavali[6].

Basis of Selection of Pratinidhi Dravya:

Explaining the basis of selecting Pratinidhi Dravya, Bhavamisra, the author of Bhabaprakash mentioned that, if any drug is not available then any other drug which is similar to it in Rasa, Guna, Virya, Vipaka, should be selected by the physician[7].

अत्र प्रोक्तानि वस्तूनि यानि तेषु च तेषु च।
योज्यमेकतराभावे परं वैद्येन जानता।।
रसवीर्यविपाकाद्यै समं द्रवय विचिन्त्य च।।
युञ्यात्त द्विधमन्यच्च द्रव्याणां तु रसादिवत्।

The author of Yogaratnakara also states the same concept regarding selection of the Pratinidhi dravyas[5]

अलाभे सति तदद्रव्यं प्रत्यामनायेन योजयेत।
तदभावे तु दरदं योजयेत्तत्र बुद्धिमान्।। ४४
रसवीर्यविपाकाद्यै समं द्रव्यं विचिन्त्य च।
युञ्जात्तद्विधमन्थच्च द्रव्याणां च रसादिकम्।। (Abhava Varga)

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The author of Bhaishajya Ratnavali also stated the similar concept for the selection of the Pratinidhi dravya[6].

कदाचिद् द्रव्यमेकं वा योगे यत्र न लभ्यते।
तत्तद्गुणयुतं द्रव्यं परिवर्तेन गृह्यते॥५७॥ (Paribhasha Prakarana)

The author of Bhaishajya Ratnavali has specifically mentioned that the main drug in any formulation should not be substituted however other drugs in the formulation can be substituted by appropriate Pratinidhi drug having the same properties[6].

रसवीर्यविपाकाद्यै समं द्रव्य विचिन्त्य च।।
युञ्जयात्तद्विधमन्याच्च द्रव्याणा तु रसादिकम्॥६२॥
अलाभे यच्च तद् द्रव्य प्रत्याम्नायेन योजयेत्॥६६॥
योगे यदप्रधानं स्यात्तस्य प्रतिनिधिर्मतः।
यत प्रधानं तस्यापि सद्गुणं नैव गृह्यते॥१००॥(Paribhasha prakarana)
व्याधेरयुक्तं यद् द्रव्यं गणोक्तमपि तत्यजेत।।
अनुक्तमपि युक्तं यत्योजयत्तदसादिवित्।।

Bhavaprakasha[7], Yogratnakara[8] and Bhaishajya[6] Ratnavali these are three Nighantus (Materia Medica) that have provided a list of 108 drugs with their alternatives. The alternatives are sometimes more than one and also may differ from one text to another. Another list of sixteen alternatives have been mentioned in Ayurvedic Formulary of India as offical substitutes[4]. Still another list of 108 substitutes has been listed in Ayurveda Samgraha[9]. However, substitution of one drug with anothert in single drug preparation is not permissible in Ayurveda.The substitution is permissible in multicomponent formulation and that too for adjuvant vehicle and excipient. Substitution is not recommended for ingredients with desirable pharmacological activities.

Substitutions of drugs (Al-Abdal) has also been in practice of Unani system of medicine for which too principles have been laid down. However, the difference still exist and these can be traced into

1. Type of Drug to be substituted
2. Principal of Substitutions

The Principle on the basis of which a substitute is selected for Ayurvedic drugs depends upon Rasa (Physical Properties), Guna (Pharmacological properties), Virya (Potency) and Vipaka (Effect of digestion and interaction) of the drug, whereas, in Unani system of medicine, it depends upon the Mijaz (Temperament) of the drug which could be a combination of Hot, Cold, Dry and Moist. No literature is available to suggest or deny that selection of substitutes has anything to do and is commensurate with the present day knowledge of the concept of medicine. The grey and baren area is required to be studied in detail considering and comparing the pharmacological actions and clinical response of the Mukhya (main) and Prathinidhi (alternativ) drugs.

Ayurveda does not recommened substitutions for the Mukya dravya (Main/Principle/Active ingradient) whereas in Unani system of medicine there is no such distinction, while recommending substitutions.

The Principal on the basis of which a substitute is selected for Ayurvedic drugs depends upon Rasa (Physical Properties), Guna (Pharmacological actions), Virya (Potency) and Vipaka (Effect of digestion and interation) of the drug, whereas, in Unani system of Medicine it depends upon the mijaz of the drug which could be a combination of Hot, Cold, Dry and Moist. No literature is available to suggest or deny that selection of substitute has anything common in these two system of Medicine. This has to be studied in detail considering and comparing the Pharmacological actions and clinical response.

Table-1

List of Pratinidhi dravyas as reported in three important text of Ayurveda i.e Bhavaprakasha, Bhaishajyaratnavali and yogaratnakara

Sr. No.	Mukhya Dravya	Pratinidhi Dravya		
		Bhavaprakasha	Yogaratnakara	Bhaishajya Ratnavali
1.	Ahimsra Anamirta Coceulus(Linn.) Wight & Arn.	Manakanda Alocasia indica (Roxb.) Schoott		
2.	Amlavetasa (Garcinia pedunculata Roxb.)	Chukra, Rumex acetosella Linn.,		

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3.	Anara (Punica granatum Linn.)	--	--	Vrikshamla Garcinia indica Choisy
4.	Milky exudates of Arka (Calotropis procera R.Br.)	Leave juice of Calotropic procera		
5.	Ativisha (Aconitum heterophylum Wall.)	Nagaramotha (Cyperus rotundus Linn.)	Haritaki (shiva) (Terminalia chebula Retz.)	Nagarmotha (Cyperus rotundus Linn.)
6.	Badi Haritaki (Terminalia chebula Retz.)	Choti Haritaki : Small variety of Terminalia chebula Retz.	--	--
7.	Bakuchi (Psoralea corylifolia Linn.)	Chakramarda (Cassia tora Linn.)	--	--
8.	Bakula (Mimusops elengi Linn.)	Utpala (Nymphea stellata Wild.)		Nila Utpala (Nymphea stellata Wild.), Rakta Utpala (Nymphea rubra Roxb. Ex Salish),
		Kamala (Nelumbo nucifera Gaertn.	Pankaja (Nelumbo nucifera Gaertn.), or Bank of Mimusops elengi Linn.	
9.	Bhallataka (Semicarpus anacardium Linn.)	Root of Chitraka (Plumbago zelynica Linn.)		
		Raktachandana, (Pterocarpus santalinus Linn.f.;	Nadibhallataka,	Rakta chandana (Pterocarpus santalinus Linn.f
10.	Bharangi (Clerodendrum serratum (Linn.) Moon	--	Talispatra, (Abies webbina Lindl.); Root of kantakari (Solanum xanthocarpum S.W.)	
11.	Bhringaraja (Eclipta alba (linn) Hassk)	Talisapatra (Abies webbina Lindl.) Kantakari (Solanum Xanthocarpum S.M.)	--	--
12.	Chavya (Piper chaba Hunter.)	Pipplamoola (Root of Piper longum Linn.)		Maushlika moola
13.	Chitraka (Plumbago zelynica Linn.)	Danti mula (Root of Baliospermu montanum Muell. – Arg.); Apamarga / Shikhirija kshara (Alkali extract of Achyranthes aspera Linn.)		
14.	Chukra (Rumex acetosella Linn.,	--	Jambiri nimbu rasa (Expressed fruit Juice of Citrus limon (Linn.) Burm.f.	--
15.	Daruharidra (Berberis aristata D.C.)	Haridra (Curcuma longa Linn.)		
16.	Dhamasa / Dhanvayasa (Fagonia cretica Linn.)	Yavasa / Duralabha (Alhagi pseudalhagi (Bieb.) Desv.		
17.	Dhanyaka (Coriandrum sativum Linn.)	--	--	Shatapushpa (Anethum sowa Kurz.)
18.	Draksha (Vitis venifera Linn.)	Gambhari phala (Fruit of Gmelina arborea Roxb.)	Gambhari phala (Fruit of Gmelina arborea Roxb.); Madhuka pushpa (flower of Madhuca india J.F. Gmel.)	
19.	Dugdha (Milk)	Soup prepared out of Mudga (Phaseolus radiates Linn., non Roxb. & auct.) or Masura (Lens culinaris Medic.)		

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20.	Gajapippli (Scindapsus officinalis Schout.	Pippalimoola (Root of Piper longum Linn.)		--
21.	Gambhari phala (Fruit of Gmelina arborea Roxb.)	--		Madhuka pushpa/Bandhuka kusuma (flower of Madhuca indica. J.F. Gmel.)
22.	Guduhi satva (Starch extract of Tinospora cordifolia (Wild) Miers.)	--	Guduchi rasa (Expressed juice from stem of Tinospora cordifolia (Wild) Miers.)	--
23.	Haritaki (Terminalila chebula Retz.)	--	Karkata shringi (Pistacia integerrima Stew. Ex. Brandis.)	Amalaki (Emblica officinalis Gaertn)
24.	Rishabhaka microstylis muscifera	--	--	Vanshalochana (Bambusa bambos Druce)
25.	Ikshu (Saccharum officinarum Linn.)	Nala (Phragmites karka Trin. Ex. Steud.)		
26.	Javitri (Myristica fragrance Houtt.)	Lavanga (Syzygium aromaticum (Linn.) Merr. & Perry)		
			Jatiphala (Fruit of Myristica fragrance Houtt.)	
27.	Jiraka (Cuminum cyminum Linn.)	--	--	Dhanyaka (Coridandrum sativum Linn.)
28.	Jivaka (Microsylis musifera Ridley)	--	--	Guduchi (Tinospora cordifolia (Wild) Miers.)
29.	Jivaka, Rishabhaka (Microstyllis mucifera Ridley).	Vidarikanda (Pueraria tuberosa DC)		--
30.	Kokoli, Kshirakakoli (Lilium polyphyllum D.Don.)	Asvagandha (Withania somnifera Dunal.)		Shatavari (Asparagus racemosus Willd.)
31.	Kamala (Nelumbo nucifera Gaertn.)	--	Kamalasha (Seeds of Nelumbo nucifera Gaertn.)	--
32.	Kamola (Piper cubeba Linn.f)	Javitri (Myristica fragrance houtt.)	Jati/Malati pushpa (Jasmine officinale)	
33.	Karkatashringi (Pistacia integerrima Stew. Ex.Brandis.)	--	--	Mayambu phala
34.	Karpura (Cinnamomum camphora (linn.) Nees & Eferm.)	Sugandhi mustaka (Cyperus rotendus Linn.) Raktachandana (Pterocarpus santalinus Linn. F.)		
			Granthiparna (Leonotis nepetaefolia R.Br.)	
			--	Nava ushira (Vetiveria zizaniodes (Linn.) Nash

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35.	Keshara (Corcus sativus Linn.)	Kusumbha pushpa (Flower of Carthamus tinctorius linn.)		Haridra (Curcuma longa Linn.)
36.	Kokilaksha (Asteracantha longifolia Nees.)	--	--	Gokshura bija (Seed of Tribulus terrestris Linn.)
37.	Kumkuma (Coorcus sativus Linn.)	--	--	Kusumbha kusuma (Flower of Carthamus tinctorius linn.)
38.	Kusha (Desmostachya bipinata stapl.)	--	Kasha (Sacharum spontaneum Linn.)	--
39.	Kustumbaru (Nepali dhaniya) (Zanthoxylum alatumRoxb.)	--	--	Dhanyaka (Coriandrum sativum Linn.)
40.	Kutaja (Holarrhend antidysenterica (Linn Wall)	--	--	Maushilika moola
41.	Kutherika (Cedrela toona Roxb.)	--	Tulsi (Ocimum sanctum Linn.)	--
42.	Lakshmana Ipomoea obseura	Mayurashikha / Nilakanthashikha (Elephantopus scaber Linn.)		
43.	Langali (Gloriosa superb Linn.)	--	--	Kushtha (Saussurea lappa C.B. Clarke)
44.	Madhuyashti (Glyeyrrhiza glabra Linn.)	Dhataki pushpa (Flower of woodfordia fruticosa Kurz)		
45.	Mahameda (Polygonatum cirrhifolium Royle.)	--	--	Anantamoola (Hemidesmus indicus R.Br.)
46.	Meda (Polygonatum cirrhifolium Royle.)	--	--	Ashwagandha (Withania somnifera Dunal.)
47.	Meda, Mahameda (Polygonatum cirrhifolium Royle.)	Shatavari (asparagus racemosus Willd.)		--
48.	Murva (Marsdenia tenacissima W& A)	Jinginai twak (Bark of Odina woodier Roxb.)		Manjishtha twaka (Bark of Rubia cordifolia Linn. Sensu Hook.F.)
49.	Mustaka (Cyperus rotendus Linn.)	--	Haritaki (Terminalia chebula Retz.	--
50.	Nagakeshara (Mesua ferra Linn.)	Padmakeshara (Nelumbo nucifera Gaertn.)		
51.	Nakha (Achatina fulica Fer.)	Lavanga kusuma (syzygium aromaticum (Linn.) Merr. & Perry)		
52.	Nata/ Tagara (Valeriana wallichii DC.)	Kushta (Saussurea lappa C.B. Clarke)		Sihali moola (root of Bauhinia vahlii W.& A.)
53.	Nilotpala / Nilakamala (Nymphea stellata Wild.)	Kumudini (Nelumbo nucifera Gaertn.)		--
54.	Nirgundi (vitex negundo Linn.)	--	Tulxsi (Ocimum sanctum Linn.)	--

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55.	Prishnipami (Uraria picta Desv.)	--	--	Haridra (Curcuma longa Linn.)
56.	Punarnava (Boerhavia diffusa Linn.)	--	Rakta punarnava (Red variety of punarnava)	--
57.	Pushkara moola (Innula recemosa Hook.f.)	Kushtha (Saussurea lappa C.B. Clarke)		
			Eranda jada (Root of Ricinus cumunis Linn.	
58.	Raktachandana(Pterocarpus santalinus Linn.f.	Khasa (Vetiveria zizanioides (Linn.)		--
59.	Rasanjana	Daruharidra (Berberis aristata D.C)		--
60.	Rasna (Pluchea lanceolata C.B. Clarke.)	--	Kulinjana (Alpinia galangal Willd.	Vandaka (Vanda roxburghii R.Br.)
61.	Riddhi (Herbinaria intermedia)	--	--	Bala (Sida cordifolia Linn.)
62.	Riddhi – Vriddhi	Varahikanda (Discorea bulbifera Linn.)		--
63.	Shali (Oryza sativa Linn.)	--	--	Shashtika (other variety Oryza sativa Linn.)
64.	Shrikhanda Chandana / shweta chandana (santalum album Linn.)	Karpura (Cinnamomum camphora (linn.) Nees & Eferm.)		
			Nava Ushira (newly collected Vetiveria zizanioides (Linn.) Nash	
65.	Somaraji (Psoralea Corylifolia Linn.)	--	Prapunnataphala (Fruit of Cassia tora Linn.)	--
66.	Sthauneyaka (Taxus baccata Linn.)	--	Kushtha (Saussurea lappa C.B. Clarke)	
67.	Talisapatra (Abies webbiana Lindl.)	Svarnatalisa (Taxus baccaata Linn.)		
68.	Tulasi (Ocimum sanctum Linn.)	--	Nirgundi (Vitex negundo Linn.)	--
69.	Varahianda (Diascorea bulbufera Linn.)	Charmakar aluka (Diascorea bulbufera Linn.)		
70.	Vriddhi	--	--	Mahabala (Sida rhombifolia Linn.)
71.	Yashtimadhu (Gvevrrhiza glabra Linn.)	--	--	Chavya (Piper chaba Hunter,non Blume)
72.	Yunjataka	--	--	Talamastaka (Katusurana) amorphophallus campanulatus Blume.
73.	Khanda	--	Sita (sugar)	--
74.	Pushpa (flower)	--	--	Amaphala (unripe fruit)

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75.	Purana guda (old jagery)	--	--	Fresh jagery kept in direct sunlight for 4 hours
76.	Shukta	--	--	Kanji
77.	Mishri (Crystal sugar)	Khanda	--	Khanda
78.	Matsyapindaka	Saphead shakkar	--	--
79.	Matsyanda (rava)	--	Khanda	Mishri
80.	Madya (Alchohal)	--	--	Shindaki
Other than Plant Products				
81.	Godugdha (Cow milk)	--	Ajadugha (Goat's milk)	--
82.	Goghrita (cow's ghee)	--	Ajaghrita (goat's ghee)	--
83.	Kant aloha	Tikshna loha		--
84.	Kasturi (Deer musk)	Kamkola (Piper cubeba Linn.f.)		
			Malati puspa (flower of Myristica fragrance Houtt.)	Gandhashati (hedychium spicatum Ham. Ex. Smith
85.	Mukta (Pearl)	Muktashukti	Muktashukti	--
86.	Mukta bhasma (Calcium oxide)	--	--	Sukti bhasma
87.	Vaidurya	--	Muktadi Bhasma	--
88.	Parad bhasma (Calcinated mercury)	--	Rasasindura	--
89.	Rajata (Silver)	Raupya Makshika	--	Rajata makshika
90.	Rasasindura	--	Shuddha Hingula	--
91.	Rajata Bhasma	Kantaloha Bhasma	--	Loha bhasma
92.	Madhu (Honey)	Purana Guda	Purana Guda	Purana guda
93.	Raupyamashika	--	Suvarna gairika	Suvarna gairika
94.	Ruchaka lavana	Pansu Lavana	Pansu lavana	--
95.	Saindhava	--	--	Samudra, vida
96.	Lavana	--	Saindhava	--
97.	Suvarna	Suvarna makshika	Suvarna makshika	Makshika
98.	Suvarna Bhasma (gold oxide)	Kantaloha Bhasma	Loha bhasma	loha bhasma
99.	Suvarna makshika	Suvarna Gairika	Raupya makshika	Suvarna gairika
100.	Loha	--	--	Mandura

Substitution of Other Plant: Yogaratnakara has cited certain examples and reported that some plant can be used,as useful plant,in case of non availability of the main plant[5].It is categorically reported that Dashmoola(a group of roots of ten plants)if not available then one can use another drug which is having similar Rasa, Virya, Vipaka to that particular drug[5].

वरी विदारी मुसली जीरकं च निषाद्वयम्। दीप्यकं देवदारुच्श्राभावे त्वेकं प्रयोजयेत्।।
कण्टकारीयुगं चैव धावनीयुगमेव च। षतपुश्पाद्वयं चेव उषीरयुगलं तथा।।
मुद्रपर्णीषमाापर्णीयुग्मं चेव ततो भवेत्। तर्कारीयुगलं चेव सर्वत्रति विनिश्च्य।। (Y.R.)
एतेषां दषमूलामेकमूलं प्रयोजयेत्। अभावे तद् गुण मूलं योज्यं वैद्यविषारदः।।

(Yogaratnakar)

In the Ayurveda pharmacopeia of India[4] some official substitutes are mentioned.

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Official Substitutes given in API

Ajmoda,Ajwain (*Aquilaria agallocha*)	Sath Agwain Trachyspermum roxburghianum (DC.) Craib
Shringataka (*Trapa natans* Linn.)	Arrow root*Maranta arundinacea* Linn.
Dugdhika –(*Euphorbia prostrata* W. Ait.)	*Choti Dudhi Euphorbia. Thymifolia Linn.*
Renuka – (*Vitex agnus-castus* Linn.,)	*Nirgundi Vitex nigundo Linn.*
Vidarikanda - *Pueraria tuberosa* DC.	*Giant ootato Ipomoea digitata Linn.*
Agnimantha (*Clerodendron phlomidis linn.f.)*	*Bakar Premna mucrnaata Roxb*
Meda Polygononatum cirrtifolium Royle	*Asparagus racemosus wild Shatawar*
Mahameda *Polygonatum cirricifolium* Royle	*Asparagus racemosus wild shatavar*
Kakoli *Linum polyphyphyhllum D.Don*	*Ashwagandha Withania somnifera*
Kshirakakoli (*Lilium polyphyllum D. Don*)	*Ashwagandha Withania somnifera*
Vasuka (*Calotropis gigantea linn*)	*Calotropis procera R.B Alarku*
Rasna (*Pluchea lanceolata*)	*Alpinia galangal wild Kulanjan*
Jivaka Microstylis musciferas	*Pueraria tuberose Vidari kand*
Rrishabhaka microstyils wallichi	*Pueraria tuberose DC. Vidari kand*
Laxmana Ipomoea pbscura	*Solanum xanthocarpum S.&W.*

Some Other Pratinidhi Dravyas Accordig To Ayurveda Sara Samgraha[14]

Sr. No.	Mukya Dravya	Pratinidhi Dravya
1.	Agara (*Gelidium amansii KUTZ*)	Dalachini, *(Cinnamon zayeanicum Blume Syn)* lavang *(Luvunga scandens)* Kewar (Pandanusodoratissimus Linn)
2.	Ajamoda (*Carum roxburghianum*)	Ajavain (*Trachyspermumammi sprague*)
3.	Akarakara (*Spilanthes acemell Linn*)	Murr, Maharashtri *(Spilanthes oleracea)*
4.	Akashavela Amaravalli (*Cuscuta reflexa*)	Nishotha, Pittapapada Trivrit (Operculina turpethum)
5.	Akhrot Akshoda (*Juglans regia*)	Buchanania lanzan spreng Chironji *(Buchanania latifolia Roxb)*
6.	Alubukhara (*Prunus armeriaca* Linn)	Imli – pakwa Chincha (*Tamarindus indica*)

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7.	Am haldi (*Curcumaamada Roxb*)	Bakuchi (*Psoralea corylifolia*)
8.	Amlavetasa (*Solina amplexicaulis [Lam]*)	Kokam (Garcinia india), chana patra Chanaka *(Cicer arietinum L)*
9.	Anar Dadima (*Punica granatum*)	Vrikshamla (*Garcinia Indica*), Imli Chincha (*Tamarandus indica*)
10.	An nanas (*Annanasa sativa comosa*)	Sev *(Malus domestica)*
11.	Aphim Ahiphena (*Papaver somni ferun*)	(Trachyspermum copticum), Kuchsla (Strychnos nuxvomica)Linn
12.	Arahar Adhaki (*Cajanus cajan L milsp*)	Masura (*Lens culinoris*)
13.	Adrak (*Zingiber officinale*)	Saunth Shunthi (Zingiber officinale (dried)
14.	Ashwagandha (*Withenia somnifera*) Dunal	Kutha Kushta *(Saussurea lappa CB clarke)*
15.	Badam taila (*Prunus amygdalus Batsch-oil*)	Khas – khas taila (*Vetiveria zizaniodes oil*)
16.	Bakuchi (*Psoralea corylifolia*)	Kalijiri,Krishna Jeeraka (Carum carvi), Pavada bija (Emblica officinalis seeds)
17.	Bakul pushpa (flower *of Mimusops elengi*)	Nilofarve (*Nymphaea stellata*)
18.	Bakul twaka (mimusops elangi Linn)	Babul twaka (Acaia arabica)
19.	Banapsa (*Ageratum veronica*)	Nilakamala (*Nympaea stellata*)
20.	Bharangi moola (*Clerodendrum serratum*)	Kantakari mul (Solanum xanthocarpum), talisapatra (Abies webbiana)
21.	Bibhitaka (*Terminalia belerica*)	Haritaki chhoti (Terminalia chebula)
22.	Bijora rasa (*Citrus medica*)	Narangi rasa (Citrus auranitium), Jambiri rasa (Citrus lemon)
23.	Bramhadandi (*Tricholepis glaberrina*)	Karela (Momordica charantia Linn)
24.	Bramhi (*Bacopa monnieri*)	Mandukaparni (*Clastrus Celastrus paniculatus*)
25.	Brihati (*Solanum indicm anguivi*)	Kantakari (*Solanum xanthocarpum scdhrad*)
26.	Chameli patra (*Jasminum irandiflorum*)	Lavanga (*Luvanga scandens*)
27.	Chaval (*Oryza sativa*)	Juvar (*Tamarix dioica*) Sarghum bicpler
28.	Chitrak moola (*Plumbago zeylanica*)	Dantimoola (*Baliospermum montanum*)
29.	Choka	Chobchini (*Smilax china*)
30.	Dhataki pushpa (*Woodfordia fruticosa*)	Madhuka pushpa (*Mallotus phillippensis*)
31.	Ela – chhoti (Elettaria cardamomum Caton)	Elaichi – Badi (Amomum subulatum Rox), shitala mirch (piper cubeba)
32.	Elua	Nshotha
33.	Esabagol (*Plantago ovata*)	Bedana (Cydonia vulgaris PERS.)
34.	Gokshura (*Tribulus terrestris*)	Kakdi bija (*Cucumis sativusseed)*
35.	Gopichandana (Silicate of alumina)	Phitakari (Ammonium chloride)
36.	Guduchi satva (Extract of *Tinospora coraifolia*)	Guduchi ras (Juice of Tinospora cordifolia)

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37.	riddhi, vriddhi, Habinaria edgeworth ill Hook.f.	Varahikanda (Dioscorea bulbifera), Bala (Sida cordifolia), Mahabala (Sida rhombifolia)
38.	Indrajava (*Holarrhena antidysentrica*)	Jayaphal Jatiphala (Myristica fragrans)
39.	Indrayana phala (*Trichosanthes tricuspidata*)	Kaladana, Usare revenda (Ipomoea hederacea.Jaeg)
40.	Javasa (*Linum usitatissimum*)	Dhamasa Dhanvayasa (*Fagonia arabica cretica*)
41.	Jetuna taila (*Olea europea Linn oil*)	Eranda taila (*Ricinus communis oil*)
42.	Jira (*Cuminum cyminum*)	Dhaniya Dhanyaka (*Coriandrum sativum*)
43.	Kabila (*Abies webbiana*)	Vidanga (*Embelia ribes*)
44.	Kachura (*Curcuma calsia*)	Adarak (Zingiber officinale), Anjira (Ficus carica), Kapurakachari (Headychium spicatum)
45.	Kadira sara (*Acacia catehu wild*)	Katha (*Acacia chundra roxb*)
46.	Kakoli (*Fritillaria royle*)	Madhuyasti (*Glycerrhiza glabra L*)
47.	Kala namak (Black salt)	Sambhara namak (lake salt)
48.	Kaladana (*Ipomoea nil Roth*)	Indrayanamoola Indravaruni mula(*Citrulus colosynthis*)
49.	Kali mirch (*Terminalia chebula*)	Lavanga (*Luvunga scandens*)
50.	Kali musli (*Curculigo orchioides Gaetrth*)	Sweta musli (*Chlorophytum borivillanum*)
51.	Kalihari (*Citrullus lanatus*)	Kutja (kadva) (*Holarrhena pubescens {Buch ham }*)
52.	Kalonji (*Nigella sativa*)	Syah jira (*Bunium persicum Baiss*)
53.	Kamalgatta (*Nelumbo nucifera seeds*)	Amalki bija (*Emblica officinalisseeds* .)
54.	Kamalkeshara (*baussurea gossypiphora*)	Nagkeshar (*Mesua ferrea L*)
55.	Koranji Karanja (*Pongamia pinnata Pierre*)	Nimbu rasa (*Citrus limon*)
56.	Kantakari (*Solanum xanthocarpum*)	Brihati, Kutha (*Solanum anguivi Lam.*)
57.	Kantaloha	Pholada
58.	Katahal – pakwa Ripe (*Artocarpus heterophyllus*)	Pakwa (Ripe) kela (*Musa parddisiaca*)
59.	Kateli moola (*Solanum xanthocarpum* Schrad root)	Neem panchang (*Azadirachta indica*)
60.	Katira (*Sterculia urens*)	Babul gond (*Acacia nilotica [L] wild*)
61.	Kattha,Khadir (*Acacia catechu [wild]*)	Khrasara, Geru (*Mimosa catechu*)
62.	Kaunch bija Kapikacchu (seed of *Mucuna pruriens*)	Utingana bija (seeds of *Blepharis edulis*)
63.	Kevada Ketaki (*Pandanus odoratissimus Linn*)	Raktachandana (*Pterocarpus santalinus*)
64.	Khadir twaka (*Acacia catechu [wild]*)	Neem twaka, Kattha (*Acacia catechu [wild] Azadirachta indica*)
65.	Kinva	Madhuka pushpa(*Madhuca indica*)

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66.	Krishna anantamul (*Hemidesmus indicus*) R.Br.	Sweta anantamul
67.	Kulattha (*Dolichos biflorus*)	Alasi (*Linum usitatissimum Linn*)
68.	Kulinjan (*Alpinia galanga*)	Shitalamirch (*Piper cubeba*), Dalachini (*cinnamomum cassia Blume*)
69.	Kustha (*Saussurea lappa*)	Akarakara (Spilanthes acemella Linn), Pushkar moola (Inula royleana)
70.	Lavang (*Syzygium aromaticum*)	Marich (*Piper nigrum*)
71.	Lodhra (*Symplocos recemosa*)	Kattha Khadira (*Acacia catechu [wild]*)
72.	Madya	Asava – Arista
73.	Manikya bhasm	Rajat bhasm
74.	Masura (*Lens esculenta*)	Urad Masha (*Vigna rediata*)
75.	Mayurashikha (*Adiantum caudatum*)	Harade Haritaki (*Terminalia chebula*)
76.	Mooli (*Raphanus sativus*)	Shalgam (*Brassica rapa rapa*)
77.	Murva (*Chonemorpha fragrans*)	Dalchini (*Cinnamomum zeylanicum Blumesyn)* , Yastimadhu (*glycerrhiza glabra*), Pippli moola (*piper longam*)
78.	Netrabala (*Myristica fragrance*)	Nagaramotha (*Cyperus rotundus*)
79.	Nilakamala (*Nymphaea stellta*)	Kumudini (*Nymphoides hydrophyla*)
80.	Nimburasa (*Cyprus aurentifolia*)	Chuka (*Rumex vasicarius*) rasa, anara (*Punica granatum*) rasa, kanji (*Pongamia pinnata L. Pierre*)
81.	Patha (*Cissapelos pareira*)	Padhala Patala (*Stereospermum colais*)
82.	Pippali (*Piper longum*)	Kali Mirch Maricha (*Piper nigrum*)
83.	Pipplimoola (*Piper longum*)	Chitrakamoola(*Plumbago indica*), Jatamansi (*Nardostachys jatamansi D.C.*)
84.	Pista (*Pistacia chinensis*)	Badam (*Prunus amygdalus*)
85.	Pitta papad(*Fumaria indica*)	Sanaya Markandika (*Cassia senna, cassia angustifolia*)
86.	Raktachandana (*Acacia concina*)	Netrabala (*Pavonia odorata wild*)
87.	Satyanashi mula (*Argemone maxicana*)	Kuth Kushta (*Saussurea lappa*)
88.	Shilajit (*Asphaltum[mineral pitch*])	Kalmi shora
89.	Shyonaka (*Oroxylum indicum*)	Krishna nimba (*Bergera koenigii*)
90.	Swetachandan (*Santolum album*)	Raktachandana (*Pterocarpus santalinus.*)
91.	Syaha jira (*Bunium persicum*)	Sweta jiraka (*Cuminum cyminum*)
92.	Tila (*Sesamum indicum*)	Alsi Atasi (*Linum usitatissimumLinn*)
93.	Tulsi rasa (*Ocimum sanctum*)	Vanatulsirasa (*Ocimum canum Sines Sym*)
94.	Unnab (*Zizyphus sativa Gaetn*)	Lisoda (*Cordiawallichii G Don*), Munnaka (*Vitis vinefera*) Linn
95.	Vacha (*Acorus calamus*)	Murvam (*Sansevieria roxburghiana*), Kulinjan (*Alpinia galanga*), Kuth (*Saussurea lappa*)
96.	Varahikanda (*Dioseorea bulbifera Linn*)	Vidarikand (*Pueraria tuberosa*) DC
97.	Vidhara (*Argyreia nervosa*)	Nishoth(*Operculina turpethum*) Dantimoola (*Baliospermum montanum [wild]*)

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Other Than Plant Products		
98.	Abhraka bhasma	Loha bhasma
99.	Aja dugdha	Godugdha (cow milk)
100.	Aja mutra	Gomutra (cow urine)
101.	Dadhi (curd)	Mattha (whey)
102.	Nilam bhasma	Suvarn bhasm
103.	Panch lavan	Saindhava lavan
104.	Panchakshara	Apamarga kshara
105.	Panna bhasma	Pravala bhasma
106.	Pokharaja bhasma	Abhraka bhasma
107.	Samudra namak sea water salt	Saindhava namak Rock salts
108.	Vaidurya bhasma	Yashada bhasma, Sukti bhasma, Giloya satva

The substitution though not desirable as another plant or plant part is unlikely to match with the other entirely in its constituents and more so in Pharmacological actions; but is permissible because of non-availability or at times high cost of the originally recommended drug. The situation is further complicated by the fact that a plant is known by several names not only in the same country but in different regions of the same country. The reason can be sought in differences in languages spoken, for example in India atleast 14 languages are in vogue in different parts of the country. It is, therefore, likely that one plant may be known by 14 different names.

There is need to adopt most commonly used bionomial names (including their bionomial synonyms) for medicinal plants to eliminate the confusion by common names. The exact scientific name of the plant, the plant part used, herbal ATC classification system adopted by Uppsala Monitoring Centre (UMC) may remove some of the ambiguity about the plant/part of plant used for the manufacture of medicine.

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ORIGINAL ARTICLE

Pharmacovigilance in Ayurveda

YOGESH KUMAR GOYAL, KAVITA GOYAL[1], GOVIND MOHAN[2], KAMLESH KUMAR SHARMA[1].

Department of Pharmacology, M.G. Medical College, Jaipur, [1]Ayurved Chikitsa Kendra, Agra,
[2]Department of Pharmacology, Institute of pharmaceutical research, GLA University, Mathura, [1]National Institute of Ayurveda, Jaipur

ABSTRACT

It is generally believed that ayurvedic drugs are safe and do not produce any side effects. This notion is not very true because we have studied the adverse effects of many ayurvedic drugs and formulations available in our country. The symptoms varied according to the drugs and formulations which include weight gain, skin eruptions, hypotension, dryness of skin, diarrhoea, abdominal pain / cramps, constipation, hyperacidity etc.

Object

In Ayurveda – Charaka in his treatise Charak Sanhita has stated that a strong poison can prove to be a very effective drug with judicious use, whereas an effective drug can prove to be a fatal poison if used injudiciously. In depth knowledge about the characteristics of the drug in relation to pathology of the disease with the knowledge of pharmacodynamics and pharmacokinetics of the drug may reduce such untoward side effects. Unfortunately some of the ayurveda physicians lack such knowledge eg. milk on one side is nutritious for kapha (not cough) and shukra dhatu, but it has depleting action on vaayu. Therefore this study has been under taken to see the side effects of various ayurvedic drugs and formulations.

Methods-The Prescriptions collected between January 2007 to December 2009 were analyzed and side effects observed with the possible drug, were recorded. The drug was withdrawn (Dechallenge) to confirm the observed ADR and was rechallenged to verify the observed ADR with the same drug / formulation.

Observations and Results

Case – 1: A 65 years male came with diagnosis of Hepatitis B. He was non diabetic, non hypertensive, non alcoholic or non tobacco user. He was prescribed Arogya vardhani vati 250 mg twice a day after meal for one month, which contains kutki 22part as a chief ingredient, other ingredients being kajjali (pure mercury) 1 part, shodhit gandhak (pure sulphur) 1 part, loha bhasm (iron) 1 part, abhrak bhasm (mika) 1 part, tamra bhasm (copper) 1 part, triphala 2 part, pure shilajit 3 part, pure guggulu 4 part, chitrak root bark 4 part. He noticed abdominal cramps and loose motion after 15 days of treatment. The patient was not satisfied with the treatment and reached to our centre. Arogya vardhani vati was withdrawn and he was given Kutki powder alone being the chief ingredient in the dose of 500 mg BD as a rechallenge. Patient reported with the same complaints within 4 days. It was therefore concluded that kutki, a herbal drug was responsible for causing creating abdominal cramps and diarrhoea.

Case – 2: A 15 year old patient came with the complaint of white patches on the skin of both knees for past 1 year. She was non diabetic, non hypertensive, non alcoholic and non tobacco user. She was taking some Ayurvedic medicine from a hospital of near by town in the form of dry powder / mixture of unnamed nature for last 2 months. She came to us for further treatment of her problem of white spot on both knees. She was given Ras manikya 65mg, Gandhak Rasayan 250mg along with honey and Vakuchi powder 1gm with water Arogyavardhini Vati 250mg and Khadirarishtha 15ml, all twice a day and tolenorm oil (JRK Siddha) for local application. After 2 months of treatment the size of patches reduced to 25% of the original one but another white patch appeared over her right cheek. After appearance of a new white patch the oral medication was discontinued.

Case – 3: A 45 year old nondiabetic, non hypertensive, non alcoholic and non tobacco user female came with complaints of joint pain with swelling for last 6 months. She was advised to take Triyodashang guggulu 1gm, Maha vatvidhwansan Ras 125mg, Shunthi powder 500mg, with luke warm water after meals twice a day and Triphala powder 3gm at night. After taking these medicines for one month she complained of dryness of mouth and skin and rashes on skin. These symptoms disappeared after discontinuing all medicines after seven days.

Case – 4: An obese female of 30 years and the weight of 90kg reported with the history of scanty menstruation. She was non diabetic, non hypertensive, non alcoholic or non tobacco user. She was given Triphala Guggulu 1.5gm twice a day. After 2 months of treatment menstruation

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became normal. She reduced 5kg weight and complained the dryness of mouth and skin and hyperacidity which disappeared within 7 days of stopping the drug which she was taking.

Case – 5: A 50 years female came with the complaint of sleeplessness. Her weight was 60kg and the blood pressure 130/84 mmHg. She was non diabetic, non alcoholic or non tobacco user. She was taking alprazolam 0.25mg daily and wanted to switch over to Ayurvedic medicine. She was given Brahmi vati 125mg twice a day for 10 days. After 10 days she complained of giddiness. When her BP was measured, it was 90/60mmHg. She was advised to stop the treatment for 7 days, after that her BP was recorded as 120/78mm of Hg. She was again asked to start Brahmi vati in reduced dose i.e. 65mg BD with the advice to take Makardwaj Ras 125mg in case of fall in blood pressure. She could continue treatment uneventfully there after.

Case – 6: A 38 years old female came with complaints of dark patches on face for past more than six months. She was non diabetic, non hypertensive, non alcoholic or non tobacco user. Her haemoglobin was 13.5 gm%. She was treated with Ras Manikya (which is a preparation of an ore known as Hartal, with chemical composition of arsenic trisulphide [As_2S_3].) 125 mg, Gandhak Rasayan (a compound of Sulphur) 500 mg along with honey and Khadirarishta (a liquid preparation of bark of khair tree known as khadir.) 20ml with equal amount of water after meals, all twice in a day. She noticed improvement in her dark patches over face after 1 month and the patches became still was feeling lighter after about after 3 months. She was satisfied with the treatment but after another 1 month, she noticed white patches behind her right ear, thighs and abdomen which persisted. She was advised to stop the medication which she was taking. After stopping the drug no white patches and there was no increase in its size.

Discussion

According to Charak Samhita

एतावदेव हि भेशजप्रयोगे फलमिष्टं च स्वस्थवृत्तनुश्ठाने
च यावद् धातूनां साम्यं स्यात।
–*१ च.शा. ६/७

एवमेव सर्वधातुगुणानां सामान्य योगाद् वृद्धिः विपर्यय।द् – हासः।
–*१ च.शा. ६/१०

This particular reference from Charak samhita is a direct indication of effects and side effects of the drug. This also refutes the popular claim of some Ayurvedic Physicians that Ayurvedic drugs do not have side effects. It is well acclaimed fact that there is no such thing in the universe and ayurvedic drugs can not be an exception to it. Under the circumstances a physician will always have to weigh the beneficial effects and adverse reactions side effects of the drug while treating a patient. Water, Ghee, Milk and cooked rice are exclusively wholesome to human body. Drug which are exclusively wholesome are always health promoting, whereas exclusively unwholesome drug act against the health of an individual. Another example of exclusively unwholesome drug is plumbago zeylanica (Chitrak). It is useful in hemorrhoids but proves to be destructive for health.

Hence unwholesome drugs are scarcely used in healthy conditions. Such drugs can be used in some of the diseased conditions e.g. Dashmool, although unwholesome drug can also be effectively used in some of the disease conditions. These are some example to clarify, that ayurvedic drugs are not very safe as is the notion of most of the ayurvedic practitioners and public at large and Ayurvedic drugs need monitoring too. Efforts in this direction have been initiated in an organized manner.

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ORIGINAL ARTICLE

To Investigate the Effect of Enalapril & Losartan On Pain Threshould in Healthy Population

SHOBHA KULSHRESHTHA, UMA ADVANI, AMIT MANHAS[1], AMIT SHARMA[1], MANINDER PAL SINGH[1]

Department of Pharmacology, NIMS Medical College & Hospital, Shobha Nagar, Jaipur - 303 121
[1]NIMS Institute of Pharmacy, NIMS UNIVERSITY Rajasthan, Shobha Nagar, Jaipur - 303 121

ABSTRACT

Modulation of pain perception has been reported with both enalapril & losartan in animals & human beings. This study was conducted to investigate whether enalapril & losartan have any effect on pain perception. 150 healthy male volunteers, divided in 3 groups of 50 each: Group 1: Enalapril 5mg. Group 2: Losartan 50 mg. Group 3: Placebo (Multivitamin). Pain was produced by using method of cola cap & hand cuff of sphygmomanometer. Two parameters were taken: (A) Pain perception threshold reading.(B) Maximum pain threshold reading. Readings were taken at baseline (0 hrs), at 2 & 4 hrs of single dose administration.

Both the group 1 & 2 showed significant reduction in both parameters A & B at the end of 2 & 4 hrs of single dose treatment when compared with baseline reading. Our study reveals that both enalapril & losartan have acute algesic effect.

Keywords: Enalapril, Losartan, Pain threshold.

Introduction

Complex mechanism and numerous pathways underlines in pathophysiology of pain perception.The renin angiotensin system participate significantly in the pathophysiology of hypertension, congestive heart failure, myocardial infarction (MI) etc[1]. Angiotensin converting enzyme (ACE) inhibitors inhibit the enzyme dipeptidyl-carboxypeptidase which is involved in conversion of angiotensin I to angiotensin II & in degradation of kinin & other peptides[2]. The ACE inhibitors thus increase the level of pain producing peptides like bradykinin & substance P[3]. Angiotensin receptor blockers (ARBs) block activation of AT_1 receptors & it is suggested that AT_2 receptors increases bradykinin activity. Recent studies have shown that ACE inhibitors & ARBs play role in modifying pain perception[4]. AT_2 receptor has pro-nociceptive activity & has anti-opioid activity. Pre-clinical studies have reported that both ACE inhibitors & losartan acted similarly on pain threshold, the pain sensitivity being increased[5]. A clinical study has also shown variable modulation in pain perception & maximum pain threshold with ACE inhibitors & losartan with single dose administration in healthy volunteers[6]. These results on pain encourage us to investigate the effects of enalapril & losartan on pain threshold in healthy population.

Aim & objective

1. To study effect of single dose of enalapril on pain perception in healthy population.
2. To study the effect of single dose of losartan on pain perception in healthy population.

Methods

The study was conducted with the objective to know the effect of enalapril & losartan on modulation of pain perception & maximum pain threshold.

Inclusion Criteria:

1. Healthy normotensive males aged between 20-40 years and having average weight ranging from 50-70kg.
2. No history of hypertension, renal disease and use of analgesics for last 7 days were selected for study.

Exclusion Criteria:

1. Obese individuals, those with gouty arthritis & intake of alcohol.
2. Hypersensitivity to any of drug used.
3. Those who do not turn up for next reading.

The study protocol was submitted to Institutional Ethical Committee (IEC). After the permission of IEC, the study

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was conducted in the department of pharmacology, in National Institute of Medical Sciences (NIMS), Medical College & Hospital, Jaipur. The study period was from Aug 2009- Dec 2009. The study type was double blind randomized placebo control trial done in a 150 healthy male volunteers based on above inclusion and exclusion criteria. All volunteers were first asked to fill the written informed consent. Both the investigators & volunteers were unaware of name of the drug. Code list of randomization of three groups was kept sealed till the end of study.

Group 1: (n=50) received enalapril (5mg) tablet (single dose).

Group 2: (n=50) received losartan (50 mg) tablet (single dose).

Group 3: (n=50) received placebo (single dose).

Pain perception threshold was accessed by method of using sphygmomanometer & cola cap (metallic serrated margin) i.e. pain was produced by using ischaemic pain method. A cola cap with smooth serrated margin was placed on the ventral aspect of the right forearm and the blood pressure cuff was wrapped around it & bulb was inflated with gradual rise of 10mmHg each time, volunteers were not allowed to see reading on the apparatus. Two parameters of pain were taken as:

(A) Pain perception threshold reading i.e. the point at which an individual first perceived the pain, that pressure reading in sphygmomanometer was noted in terms of mmHg.

(B) Maximum (tolerance) pain threshold reading i.e. the point at which volunteer tolerated maximum pain & told to remove the cuff, that pressure reading in sphygmomanometer was noted in terms of mmHg.

The pain perception threshold reading and maximum pain threshold readings were recorded for each individual at 0 hrs (baseline reading) after that volunteers were asked to pick up the packet and tell the code number allotted to him, their respective codes were noted, and whatever tablet was present in the packet was given with glassful of water, they were called for next reading at end of 2 & 4 hrs respectively. Each time three readings were taken and corresponding readings were tabulated against their code at 0, 2 & 4 hrs. Though each individual acted as its own control at 0 hrs i.e. before the administration of tablet, but in order to exclude the placebo effect of consuming a tablet on pain perception over a period of time, we included the placebo group who received the multivitamin tablet (placebo) & it acted as a positive control.

Statistical Analysis: All the data were expressed as mean± S.E & were analyzed by using paired 't' test within each group. P values < 0.05 were considered significant.

Results

At the end of study decoding was done and case report forms of group 1, 2 & 3 were separated. Numbers of healthy volunteers were 47 in group 1, 48 in group 2 & 47 in group 3, as 8 volunteers were withdrawn as they did not turn up for further readings. Mean reading of two parameters were entered in the master chart. Statistical test was applied within each group & readings at the end of 2 and 4 hrs of drug administration were compared with the baseline readings. There was significant reduction in pain perception threshold reading in group 1 & 2, while no any significant change was observed in group 3, as shown in table I.

Similarly there was significant reduction in maximum pain threshold reading without any significant change in group 3 as shown in table II.

Table-I

Showing the effect of single dose of enalapril and losartan in comparison on pair perception threshold at 0, 2 and 4 hours.

Time → / Group ↓	0 hrs.	2 hrs.	4 hrs.
GROUP1 ENALAPRIL (N=47)	122±6*	98±4 (p<0.05)	88±2 (p<0.05)
GROUP2 LOSARTAN (N=48)	124±8	100±5 (p<0.05)	90±7 (p<0.05)
GROUP3 PLACEDO (N=47)	121±10	126±3 (p>0.05)	124±6 (p>0.05)

Results are expressed in mean ± S.E.M.

Table-II

Showing the effect of single dose of enalapril and losartan in comparison with placed on Maximum (Toleramen) pain threshold at 0, 2 & 4 hours.

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Time → / Group ↓	0 hrs.	2 hrs.	4 hrs.
GROUP1 ENALAPRIL (N=47)	250±4#	210±6 (p<0.05)	192±4 (p<0.05)
GROUP2 LOSARTAN (N=48)	244±10	221±8 (p<0.05)	197±5 (p<0.05)
GROUP3 PLACEDO (N=47)	248±6	254±3 (p>0.05)	247±8 (p>0.05)

Results are expressed in mean ± S.E.M.

Discussion

Role of renin angiotensin system in pain perception has been reported in earlier studies[1]. However pain perception is in itself a complex phenomenon which has central and peripheral component and both have been historically found to be linked differently in their sensitivity to pain in response to renin & renin substrate[8]. In our study, the single dose of enalapril and losartan both increased pain perception threshold and maximum (tolerance) pain threshold reading in healthy population. Regarding the effect of ACE inhibitiors on pain sensitivity, controversial results have been found in animal study[5,5,9]. Bradykinin may be the cause for algesic effect. Other actions have reported intra-cerbroventricular angiotensin receptor blocker produced analgesic effect that could be blocked by naloxone[10]. Experimental study found that increased renal bradykinin concentration following AT_1 receptor blockade, due to unopposed action of angiotensin II on AT_2 receptor[5,10]. Common side effect of ACE inhibitiors is a chronic nonproductive cough that dissipates when the drug is stopped. The finding that angiotensin AT_1 receptor subtype antagonist do not cause cough provides presumptive evidence for the role of bradykinin in this effect , but the mechanism & receptor subtype involved have not been clearly defined. Preliminary data suggest that bradykinin also may contribute to the effects of the AT_1 receptor antagonist. With AT_1 receptor blockade, angiotensin II concetration increase & AT_2 receptor heteromerizes with bradykinin[10]. The production of algesia in an early phase of treatment can be rather beneficial in angina or cardiovascular risk, where warning signs of an impending MI may save patients life by converting a painless silent MI into painful one[5], but this algesic effect will be rather harmful in patients of arthritis or any other painful disorder who are on these medication.

Conclusion

Both enalapril & losartan increased the pain perception threshold and maximum pain threshold at the end of 2 & 4 hrs, of single dose administration in healthy population. It reveals that both enalapril and losartan have immediate algesic effect with single dose administration. Further studies are needed and should be done for correlating acute effect in healthy population as well as chronic effect on pain threshold in hypertensive patients & others who are on these medications.

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ORIGINAL ARTICLE

Role of Early Therapy of Gabapentin in Treating Nocturnal Pain of Herpes Zoster and Post Herpetic Neuralgia

SANJAY KUMAR KANODIA, S.R. SHUKLA, PRAMOD BHARDWAJ[1]

Department of Darmatology, Venereology & Leprosy, NIMS Medical College & Hospital, Jaipur - 303 121
[1]Department of Psychiatry, NIMS Medical College & Hospital, Jaipur - 303 121

ABSTRACT

Herpes zoster and Postherpetic neuralgia (PHN) are often intractable painful conditions that eludes effective treatment in many patients. This study was aimed to determine the efficacy and safety of the anticonvulsant drug gabapentin in reducing nocturnal pain of herpes zoster and post herpetic neuralgia. In this randomized placebo-controlled 12 week trial conducted from August 2008 through January 2010 in total of 22 subjects, eleven patients received gabapentin in the dosage of 300 mg/day, and 11 received placebo at the start of herpes zoster or later at night time before sleep. Subjects receiving gabapentin had a statistically significant reduction in VAS(visual analog scale) score and sleep disturbance from 8.5 to 5.0 points than in placebo, expressing the efficacy of Gabapentin in the treatment of pain and sleep interference associated with herpes zoster and PHN.

Key words: Herpes Zoster, Postherpetic Neuralgia(PHN), Gabapentin

Introduction

HERPES ZOSTER (shingles) is accompanied in the majority of patients by intense pain that is variously described as "burning," "deeply aching," "tearing," "electric shocklike," and "lancinating." Abnormalities of sensation in affected dermatomes are common, including hyperpathia or allodynia[1]. The nocturnal pain in Zoster and Postherpetic neuralgia is usually refractory to simple analgesic therapies, and treatment most often is pharmacologic, including a wide variety of drugs and routes of delivery[2,3]. The most commonly used agents are oral analgesics and opioids in the initial part of disease and for PHN is with various tricyclic antidepressants (TCAs) (amitriptyline, desipramine, and clomipramine) either as monotherapy[4-6] or in combination with other medications, such as carbamazepine or opioids[7,8]. Unfortunately, only about 50% of patients treated with TCAs for PHN in clinical trials experience pain relief in the absence of intolerable adverse effects[9].

Gabapentin has been reported anecdotally to relieve pain in patients with intractable neuropathic pain[10] in spontaneous pain and tactile allodynia in patients with peripheral or central pain[11]. We report here the results of placebo-controlled trial of gabapentin for the nocturnal pain associated with herpes zoster and in post herpetic neuralgia.

Methods

The study was done from August 2008 to January 2010 at department of Dermatology, National Institute of Medical science and Research, NIMS University (Jaipur). This study was a randomized controlled trial to assess the efficacy and safety of gabapentin 300 mg versus placebo, given daily at night for 12 weeks in the treatment of patients with uncomplicated acute herpes zoster infection having zoster associated nocturnal pain as early as in active disease state or patients with post herpetic neuralgia. Subjects were seen for a minimum of 6 scheduled visits: an initial enrollment visit and 5 subsequent visits at 2, 4, 6, 8 and 12 weeks of study treatment.

Inclusion criteria included the following: patient above 18 years of age; pain present at night during or after herpes zoster (rating 6 or above at baseline) with sleep disturbance. Exclusion criteria included the following: pain present at night during or after herpes zoster rating less than 6 at baseline or without sleep disturbance; prior treatment with gabapentin or history of hypersensitivity to the drug or its ingredients; immunocompromised state; significant hepatic or renal insufficiency; significant hematological disease; severe pain other than that caused by PHN.

Eligible subjects who gave informed written consent underwent physical examination and blood samples were

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Table-I Demographic and disease characteristic of the patients

		Oral Gabapentin 300 mg n=11	Placebo n=10	P value
Sex	Male	7	7	N.S.*
	Female	4	3	N.S.
Age (years)	Mean	54.5	53.5	N.S.
	Average	32-64	29-67	N.S.
Localization	Trigeminal	0	0	-
	Cervical	1	1	N.S.
	Thoracic	7	8	N.S.
	Lumbar	3	2	N.S.
	Sacral	0	0	-
Median time since zoster		18 days	22 days	N.S.
Number of herpes zoster cases having post herpetic neuralgia		6	4	N.S.
Mean Base line VAS score (pain/ sleep disturbance at night)		8.6	8.3	N.S.

N.S.: *- Non Significant

Table-II Comparison of pain score following Gabapentin treatment with placebo in patients of herpes zoster and PHN

	Baseline	2nd week	4th week	6th week	8th week	10th week	12th week	P value
VAS Gabapentin	8.6	7.6	7.4	6.7	6.5	6.4	5	<0.01
VAS Placebo	8.3	8.1	8.4	8.2	7.5	8.1	8	N.S.*

N.S.: *- Non Significant

taken for routine hematology and chemistry. Medical histories and demographics were obtained. Neurological examination was done by psychiatrist. Study participants at baseline (week 0) were randomly assigned to receive gabapentin with a dose of 300 mg/d or placebo at night time. At each visit (weeks0, 2, 4, 6, 8 and 12), subjects were asked about pain and sleep disturbance on 10-cm Visual analog scale (VAS score), and adverse events assessed.

Results

A total of 21 patients were enrolled in the study, 11 patients in the gabapentin group and 10 patients in the placebo group. Both the groups were statistically equally distributed in terms of age group and male female ratio. The mean age of the patients in gabapentin group was 54.5 while in placebo group was 53.5 with a range of 32-64 years and 29-67 years respectively. The median time since zoster lesion was 18 days in gabpentin group and 22 days in placebo group (Table-I). Acute Pain Assessment in patients showed change in baseline VAS score fortnightly, from 8.6 to 5 in gabpentin group($p<0.01$) while in placebo group there was no significant change from baseline to 12th week of the therapy (Table-2).

Safety

Measures of frequency, nature, and severity of adverse events were derived from a total 11 subjects who had received gabapentin. Overall, the most frequently reported adverse effects among the gabapentin group, which occurred at higher incidences than those in the placebo group were somnolence (27.4%), dizziness (23.9%) and ataxia (7.1%).

Discussion

Gabapentin (1-[aminomethyl]-cyclohexaneacetic acid) is a structural analog of γ-aminobutyric acid (GABA) is antiepileptic drug which is lipophilic in nature and penetrates the blood-brain barrier. Its mechanism of action has not yet been fully elucidated, but appears not to involve binding to GABA receptors[12] and is distinct from that of

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TCAs. Introduced in the United States in 1994 as an anticonvulsant, gabapentin is used clinically to benefit patients with epilepsy by reducing seizure frequency when added to conventional antiepileptic drug regimens.[13] Gabapentin has been reported anecdotally to relieve pain in patients with intractable neuropathic pain and reflex sympathetic dystrophy, allowing the reduction or termination of other analgesic medications and relieving symptoms associated with painful disease manifestations[10,11]. It also reduced spontaneous pain and tactile allodynia in patients with peripheral or central pain[14].

Recent reviews and meta-analyses of 11 randomized, controlled clinical trials for PHN concluded that TCAs appeared to be the only agents that provided reliable pain relief[12-14]. Tricyclic antidepressants, however, can also have significant adverse effects, such as arrhythmias, postural hypotension, sedation, dry mouth, constipation, confusion, and urinary retention[8]. Their use is not appropriate in many patients with cardiovascular disease, which makes the use of these agents problematic in the 60 years and older age group, in which PHN is most prevalent[9]. A single nonopioid agent that provides both substantial relief and a good safety profile is thus needed.

We report here the results of a placebo-controlled trial of gabapentin for the pain of PHN. The results of our study clearly show that gabapentin reduces nocturnal pain in herpes zoster and postherpetic pain compared with placebo. Significant improvement was evident during the initial phase (at the 2-week time period) and continued to accrue over the course of 12 weeks of treatment. Adverse effects of gabapentin were minor and well tolerated, consisting primarily of somnolence and dizziness.

From the safety and efficacy evidence in our study, a strong case can be made for considering gabapentin as a first-line oral medication for management nocturnal pain herpes zoster and pain of PHN. Because of its relative lack of adverse drug interactions, multidrug regimens to control chronic neuropathic pain can include gabapentin if gabapentin monotherapy fails. In summary, based on the results of this 12 week study, gabapentin can be added to the list of first-line medications for treatment of chronic neuropathic pain syndromes such as PHN especially at night time.

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ORIGINAL ARTICLE

Relief of Pain in Planter Fascitis by Glucosamine: A Study

MUKESH TIWARI

Department of Orthopedics, NIMS Medical College & Hospital, NIMS UNIVERSITY Rajasthan, Jaipur - 303 121

ABSTRACT

Planter fasciitis is the most common cause of the planter heel pain. Its main features are pain, tenderness mostly on the medial aspect of the calcaneum near the sole of heel. There are many conservative methods for treatment of the planter fascitis which include rest, massage, night splints, orthoses, injections, casts, NSAID, shock wave therapy. The glucosamine is one of the nutritional product which has a good antiinflammatory properties and is already in use for arthritis knee. Depending on anti inflammatory analgesic property can also be used in planter fasciitis.In this study 17 patients were studied after giving fixed dose of 1200mg of glucosamine .The evaluation was done on linkert pain score. The p-value in studied group was <.00001 which shows a good effect of this compound on planter fasciitis.

Key words: Glucosamine, Planter Fascitis

Introduction

The planter fascitis is an inflammation of the thick band of the tissues which connects the heel bone to the toes. This band of tissue is meant to support the bony arch of foot. Planter fascitis can be a degenerative chronic tendopathy. The micro tears of the bone tendon union may be the root cause. Healing this union more efficiently may speed the recovery[1]. Persons with foot arch problems, obesity, repetitive loading on feet, long distance runners[2-5]sudden weight gain, tight tendo achillis and persons wearing poor arch support are most liable to suffer from this. It generally affect from the middle age to older age groups.

Patients with planter fascitis complain of the pain in heel specially at the first step in morning[6] and with walking. This pain aggravates with sudden weight gain. There may also be presence of stiffness in the feet. On clinical examination there is tenderness on the medial aspect of calcaneal tuberosity. There is specific test known as weight bearing Windlass test[7], where one may have pain on stretching of the toes due to stretching of the planter fascia during weight bearing.

Various treatments available for planter fascitis include pharmacological therapy by NSAID[8], exercise[9], myofascial release[10], ionotophoresis and local corticosteroid injections.

Glucosamine is one of the nutritional adjuvant which possess anti inflammatory action and is used in arthritis knee. Limited number of studies have been done to assess its effectives in planter fascitis. This study is planned out to know the pain relieving effect of glucosamine on planter fascitis.

Method

This study was conducted at the orthopedic department of NIMS University & attached hospital .The patients were randomly selected from the out patient department which are coming from near by areas. A total of 17 patients were studied for the effect of glucosamine for their pain due to planter fascitis. The pain intensity was evaluated before and after treatment according to Linkert scale[12]. The patients evaluated on verbal rating scale of Linkert starting from 0 for no pain to 5 for overwhelming pain.

The inclusion criteria for study were –

-Pain in heel area less then 2 months.

-Pain worse with first morning step

The pateient were excluded from this study depending upon following criteria-

-Prior use of glucosamine for any purposes.

-Traumatic injury.

-Pregnancy or lactation.

All subjects received 1200mg of glucosamine per day for at least 6 weeks or longer till they become pain free.

Results

Of the 17 patients 14 were male and 3 were female in the age group of 25 year to 60 year. The median age was 44.75 year. Out of 17 male patients the Linkert Pain Score Before Treatment (LPSBT) in ten patients was 4 and four patients had score 5. All the females had the LPSBT of 4.

Following treatment with glucosamine the Linkert Pain

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Score After Treatment (LPSAT) was two in twelve and one in two male patients. The LPSAT was two in two female patients and one female patient had no relief.

Glucosamine treatment caused significant relief in pain (94.11%) although the regression of noticeable amount of severity (LPSAT of 1) was only seen in only about 11.7% of patients. The LPSBT & LPSAT was same in 5.88% of patients.

Depending on these results the mean LPSBT 4.25 while the LPSAT was 2.On this basis the t –score was 11.86.The analysis shows that p value in this study in after treatment group is <.00001,This shows a significant change in pain status after treatment. (Table-I & II).

Table-I

N=17		LPSBT
M	10	4
	4	5
F	3	4

Table-II

N=17		LPSAT
M	12	2
	2	1
F	2	2
	1	4

Discussion

Glucosamine is marketed as a single agent or in combination as nutritional supplement in many countries. It is also used in to relieve musculoskeletal pain. Studies have shown its effectivity in arthritis comparable to NSAID.

Glucosamine is a constituent of nearly all human tissues and is present in high concentration in cartilage and other connective tissues of human body. Glucosamine is an aminoglycoside and is an intermediate substrate for the synthesis of glycosaminoglycan and proteoglycan compound of cartilage.

Glucosamine exerts its effect gradually. Animal studies have demonstrated its role in stabilizing the cell memebranes. It reduces the generation of oxygen free radicle by macrophages and inhibits lysosomal enzymes. It may also inhibit the neutrophil and there inhibitory effects.

In clinical trials Glucosamine has been found to be more effective than placebo in providing relief from pain and inflammation with efficacy equal or more in comparison with ibuprofen.

It has shown the beneficial effect on pain in comparison to celecoxib.[12] It has also shown antiulcerogenic effect. This effect is due to its ability to neutralize hydrochloric acid the stomach and its capability to strengthen mucosal barrier by increasing mucosal glycoprotein synthesis and its free radical scavenging property[13].

Glucosamine has shown the anti inflammatory activity in acute, subacent and chronic conditions as seen in experimental studies in rats[14,15].

The molecular mechanism behind the pain relieving & anti inflammatory effect of glucosamine is due to suppression of LPS induced nitrous oxide expression of Inos and COX-2 and by binding NF-Kappa b. It also do phosphorylation of P38 MAP KINASE[16].

Conclusion

Glucosamine has been shown to be effective in reducing intensity of pain and inflammation in served experimental as well as clinical studies. The present study shows its usefulness in the treatment of planter fascitis requiring treatment for about six weeks.

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SHORT COMMUNICATION

Role of Coaltar (1%) Lotion in Chronic Stable Plaque Psoriasis

VENKATESH PUROHIT

Department of Dermatology and Venereology, Government Medical College, Surat

ABSTRACT

Psoriasis is a chronic proliferative epidermal disease affecting 1% to 3% of world's population. Tars inhibit DNA synthesis, coal tar has long been regarded as first line treatment for chronic plaque psoriasis. To assess the efficacy and tolerability of coal tar (1%) lotion in chronic stable plaque psoriasis, patients were on treatment with coal tar (1%) lotion thrice daily for 12 weeks and after that 4 weekly follow up was done in surveillance phase for 8 weeks. Of the 50 patients completing the study, after 12 weeks treatment with coal tar (1%) lotion, psoriasis area severity index (PASI) decreased by 80.07% from the baseline. Coal tar (1%) lotion is highly efficacious and having increased cosmetic acceptability and tolerability.

Key Words: Coal tar (1%) lotion, Psoriasis Area Severity Index (PASI), Chronic Stable Plaque Psoriasis.

Introduction

Psoriasis is a common Papulosquamous skin disease which frequently present therapeutic challenge to physicians[1]. There are various oral and topical treatment options available for psoriasis but each is having its own side effects[2]. Coal tar is used from many decades in different concentrations and proved to be cheaper and effective option for psoriasis.

The primary objective of our study was to assess the evidence for the efficacy and tolerability of coal tar (1%) in chronic stable plaque psoriasis and secondary objectives was to identify side effects, if any due to it and also to see relative outcome of the study medication in the context of total time duration.

Methods

The clinical trial was conducted between January, 2007 to August, 2007 at the department of Dermatology and Venereology of Government Medical College, Surat, Gujarat. A total of 50 male patients (Age range 25-50 years) suffering from chronic stable plaque psoriasis with no prior treatment were primarily selected for the study, diagnosis was made by history and clinical features.

Baseline evaluation was made at the first visit which included the body surface area involvement, thickness, redness, scaliness of plaques. Photographs of each lesion was taken at every visit.

Present study was divided into 2 phases. in the 1st phase i.e. treatment phase coal tar (1%) lotion thrice daily was applied for 12 weeks. in the 2nd phase i.e. surveillance phase, no treatment was given to the patients and weekly follow up was done for 8 weeks.

Results

Change in Severity Parameters and Body Surface Area

There was 84.25% reduction in the redness of lesions, 72.44% decrease in thickness of lesions and 89.21% reduction in scaliness of the lesions and 72.96% decrease in body surface area.

After 12 weeks treatment with coal tar (1%) lotion, psoriasis area severity index (PASI) decreased by 80.07% from baseline.

In physician assessed global improvement score of coal tar (1%) lotion, 32% had complete clearance of the psoriatic lesion, 42% patients had >75% clearance, 12% had 50%-75% clearance, 4% had 25-50% clearance, 6% had <25% clearance.

Regarding the patient assessed cosmetic acceptability of 1% coal tar lotion, the cosmetic acceptability was highly favourable for 52% patients, markedly favourable for 34% patients, slightly favourable for 12% patients and slightly unfavourable for 2% patients. in post treatment surveillance 8% patients relapsed, 88% were on maintenance & 4% were resistant to treatment. Regarding patient global assessment of tolerability of coal tar (1%) lotion at the end of the study, 76% patients had good tolerance and 24% had fair tolerance.

Regarding the Adverse Effect of coal tar (1%) lotion, 6%

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patients developed folliculitis, irritation in 6%, pruritus in 6%, photo sensitivity in 2%, burning in 2% , burning in 2%, erythema in 2%.

Discussion

In the U.S. pharmacopeia XX (1980) Coal tar is defined as the tar obtained as a byproduct during the destructive distillation of bituminous coal[2]. It is a mixture of thousand of hydrocarbon compounds and has been used for a century to treat psoriasis. It seems to work by enzyme inhibition and antimiotic action[4]. In experimental studies it has shown to suppress DNA synthesis in mouse epidermis[5]. Most tar regimes were not standardized; preparations varied in content and therapeutic effectiveness according to their source[6].

In our study, there was 80.70% decrease in PASI after 12 weeks of treatment with coal tar (1%). In a study by Lowe NJ et al, crude coal tar at 2-5% in different bases was effective in treating psoriasis[7]. The 1% crude coal tar in yellow soft paraffin had a lower efficacy than 5%. In the study by Williams et al, there was no benefit from routinely increasing the concentration beyond 5% since the dose response curve reached a plateau between 1% and 5%.

Conclusion

A new formulation of coal tar which is 1% coal tar lotion containing esterfied fatty acids in liposomal base differing from conventional coal tar which is 5 to 20%. It has the base with essential fatty acids which maintains cell membrane integrity and also increases transdermal carriage of tar.

Advantages of coal tar (1%) lotion are:

- Highly efficacious
- Leads to long term remission of disease.
- Less relapse and resistance to treatment.
- Improves the quality of life of the patients.
- Very good cosmetic acceptability by patients.
- Increased tolerability of the drug to the patient.
- Less chances of discontinuation of treatment

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LETTER TO EDITOR

Medical Surveillance to Save Gentamycin by Antibiotic Cycling

RAJ KUMAR ARYA, DINESH K. JAIN

Department of Pharmacology, G.R. Medical College, Gwalior - 474 001

β-lactamase genes of gram negative bacteria could reach virtually any gram negative bacterium and become a major threat in the future. Faced with this gloomy picture, 21st Century clinicians must turn to compounds developed decades ago and previously abandoned because of toxicity or test every-thing they can think of and use whatever looks active.[1]

Excessive use, over-prescription and the emergence of antibiotic resistant infections means antibiotics being likened to a lit window in the night that flashes open for just a moment before it shuts again.[2]

The emergence of gentamycin resistant bacilli has been documented at a number of institution.[3]

Gentamycin is an important agent for the treatment of many serious gram negative bacillary infections. It is the aminoglycoside of first choice because of its low cost and reliable activity against all but the most resistant gram negative aerobes.[4]

Therefore, it is important to know sensitivity status of gentamycin to save it and to make beneficial antibiotic policy regarding gentamycin.

Retrospective study was conducted at G.R. Medical College, Gwalior MP in department of pharmacology and department of microbiology. Uropathogenic strains of bacteria from out patients and in patients were studied. The culture and sensitivity reports of urinary tract infection in 1994 and 2008 were compared. The samples were processed using standard procedures. The isolates were identified based on colony morphology and staining characters.

The antibiotic sensitivity testing was done using antibiotic sensitivity disc method. After 18 hours of incubation at 37°C, the diameter of the zone of inhibition was measured using a millimeter scale around each antimicrobial disc on the undersurface of the plate. The zone size around each antimicrobial disc was interpreted as sensitive or resistant.

The results of the present study are summarized in Table-I

Sensitivity Of Urinary With Gentamycin

Table-I

Urinary Pathogens	Year 1994			Year 2008		
	S*	R*	Total	S*	R*	Total
E.Coli	95	55	150	212	200	412
Klebsiella	21	07	28	14	07	21
Staphylococci	05	03	08	16	03	19
Streptococci	01	01	02	02	00	02
Proteus	01	01	02	0	0	0
Total	**123**	**67**	**190**	**244**	**210**	**454**

(S*=Sensitive) (R*= Resistant)

The incidence of resitance of E.coli to Gentamycin was 35.2% in 1994. This increased to 46.2% in 2008. the difference may be attributed to sample size which is twice as much in 2008 as compared to 1994, while at the same time real increase in the insensitivity of bacteria due to resistance can not be ruled out.

It is very alarming situation. Surveys have shown that as much as 50% of all antimicrobial use is inappropriate.[5] Therefore such system should be evolved which have the benefit of improving the effectiveness of antibiotic prescribing. To decrease resistance of antibiotics, antibiotic cycling is a potentially employable method. Antibiotic cycling is a process of planned antibiotic restriction introduced through the cycling of drug selection based on local surveillance, with a plan drawn up for the scheduled rotation of one class of antibiotics and the cycle repeated.[2] Essentially it is a structured way of introducing antibiotic heterogeneity in to prescribing practice, where mathematical modeling has demonstrated that heterogeneity ,as opposed to availability restriction, is the most likely way to reduce selection pressure leading to antibiotic resistance.[6]

"The idea at its simplest is that antibiotics are withdrawn from use for a period of time with the intention of limiting resistance to the cycled agent to be reintroduced later on.[7]

It is suggested to restrict use of gentamycin and use other antibiotic for which there is no resistance to save the gentamycin for future.

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LETTER TO EDITOR

Regulations of Medical Council of India and Future Research

DINESH K. JAIN, RAJ KUMAR ARYA

Department of Pharmacology, G.R. Medical College, Gwalior - 474001

Medical Council of India, According to MCI NO. 12(2)/2009-Med-22654[1], In exercise of the powers conferred by section 33 of the Indian Medical Council Act, 1956 (102 of 1956), the Medical Council of India makes following regulations regarding research publications to amend the "Minimum Qualifications for teachers in Medical Institutions Regulation 1998". These regulations may be called the "Minimum Qualifications for teachers in Medical Institutions (Amendments) Regulations 2009". In the amendment following modifications have been made to promote research activity in medical institutions. The teaching and research experience requirements in all the subjects of broad specialties shall be as under

(A) For Professor: (1) as Associate Professor in the subject concerned for three years in the recognized medical college. (2) Minimum of Four research publications in indexed/national journals.

(B) For Associate Professor : (1) As Assistant Professor in the concerned subject for four years in the recognized medical college. (2) Minimum of two research publications in indexed/national journals.

Before these amendments research publications were not compulsory. They were desirable only. Promotion was possible without any research publication. Before amendments, for the post of Professor, in the broad-specialties, teaching experience as Associate Professor was four years and for the post of Associate Professor in broad specialties, teaching experience as Assistant Professor was five years. In amendments, duration of teaching experience has been reduced by one year for the promotion with compulsory research publications.

According to Medical Council of India, MCI No. 712(2) 2009-Med.Misc/56925, amend notification[2] was made on 15th December 2009 regarding research publications. These research publications should be published or accepted for publications in the journals by the national associations/societies of the respective specialties as the first author.

Medical Council of India made these amendments with the intention to increase research activities in medical institutions. But it will be very difficult to improve research activities by these amendments because they have many anomalies. The main drawbacks of these amendments are :

(1) The credit for research work is given to first author only. Other authors will not get any advantage of their research work in their promotions.

(2) Research papers should be published in the journals by the national associations or societies of the respective specialties. If research paper is published in a medical journal other than his own specialty then credit will not be given to any author.

These two drawbacks will interfere research activities in the medical institutions. Purpose of Medical Council of India can not be fulfilled by these amendments. When credit of research publication will be given to first author only then who will cooperate and coordinate for research work. In medical field research is done by team work. One person can not do complete research work. He has to take help from other person. Active cooperation of another person is required for research activity. Credit of publication is not being given for second or third author. Then help from other people is not possible neither at intellectual level nor at practical level. Then nobody will disclose intellectual and creative ideas. There are limited numbers of research journals where limited numbers of research papers are published. Every research paper, sent for publication, is never published. More than 50% research papers are returned back. Only first author will get reward then there will be unnecessary competition and struggle among medical teachers. Mutual cooperation in research work will be the thing of past. There are limited numbers of post for promotion in medical colleges. It may create bitterness and fierce rivalry among medical teachers.

Usually for research activity, medical teacher of one specialty requires help from scientist of other medical specialty. If second person will not get any reward for research cooperation, then he will not help. Coordination between different specialty will be failed. If pharmacologist wants to work in medicine or in surgery department, they will not cooperate. Then actual research work, required for the welfare of the society, will not

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progress. Every medical teacher will restrict his work to his respective subject. Then research work will not be the priority. The priority will be the publication in the journal of his subject. Quality of research activities will be weakened.

After these amendments, if research paper of a medical teacher of one specialty as first author, is published in journal of other specialty then advantage of publication will not be given to his promotion. Then medical teacher of one specialty will neither work not send his research paper to journal of another medical specialty. Then cooperation among different specialties will be disturbed for research work and objectives of medical council of India to improve research atmosphere in medical institutions remain unfulfilled.

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1. Medical Council of India, Amendment Notification, New Delhi, the 21st July, 2009.
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