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RESEARCH PAPER

PREVALENCE OF ADVERSE REACTION ALLIED WITH THE USE OF AYURVEDIC MEDICINES FOR DIABETES IN HUMAN POPULATION

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Abstract: Ayurvedic medicine is a system of traditional medicine native to India and a form of alternative medicine. As these drugs are of natural origin, the medical professionals earn a greater financial profit by publicly saying that such drugs are the safest with no adverse effects. But this is not true. As compared to allopathic medicines, ASU (Ayurvedic Siddha Unani) drugs are safe but still these have some potential of causing ADRs. This study was aimed to determine very rare ADRs as a result of ayurvedic treatment and also positive side effects if any, giving the contribution to Pharmacovigilance of ASU drugs in India. In this study, fifty patients suffering of diabetes were enrolled after a specific inclusion and exclusion criteria. The fifty diabetic patients enrolled were given the same combination treatment of dried Gurmar, Jamun seed powder, Kala Zeera and aloe juice in a final dosage form. The regimen as usual helped the patients in controlling their elevated blood glucose levels but it was not totally free of ADRs. In our study it was observed that a total of 148 non serious ADRs had occurred which were metallic taste (20.5%), nausea (19.8%), constipation (8.9%), flatulence (8.2%), dry mouth (7.5%), loss of libido (7.5%), loose stools (6.8%), bitter taste (5.5%), vomiting (4.1%), phlegm formation (2.7%), throat itching (2.7%), irritable bowel (1.4%) and taste disturbance (1.4%). From causality assessment it was found that Gurmar (66%), Jamun seed (14%), Kala Zeera (12%) and Aloe (8%) were responsible for causing all the above ADRs. Reported ADRs were evaluated for patient demographics, reaction and drug characteristics, causality, severity, and outcome.

***Keywords*:** ASU drugs, Non-Serious ADRs, Causality Assessment

INTRODUCTION

Traditionally, herbs and herbal products have been considered to be non-toxic and have been used by the general public and traditional medicinal doctors worldwide to treat a range of ailments. Ayurvedic medicine is a system of traditional medicine native to India and a form of alternative medicine.[1, 2].The active ingredients of plant extracts used in ayurveda are chemicals that are similar to those in purified medications, and they have the same potential to cause serious adverse effects. It is widely held myth that modern drugs are dangerous foreign chemicals with side effects, while herbals are natural, gentle and safe. The truth is that some herbs can be dangerous and can bring about serious diseases and even lead to death. Unlike conventional drugs, herbal products are not regulated for purity and potency and this could cause adverse effects and can even lead to drug interactions [3,4]. For example, veno-occlusive disease due to ingestion of plant containing pyrrolizidine alkaloids, which can be life threatening or fatal [5].

Worldwide movement for the improvement of patient safety is gaining momentum. In India, National Pharmacovigilance Programme (NPP) under the control of Central Drug Standards Control Organization (CDSCO) has already been started since 2003. WHO has emphasized that it should include traditional medicines in pharmacovigilance system and has published guidelines on safety monitoring of herbal medicines in pharmacovigilance systems in 2004 [6].To promote pharmacovigilance of ASU drugs in proper place in India, a National Pharmacovigilance Centre for ASU Drugs (NPC-ASU) was formed, under the control of Department of AYUSH, Ministry of Health & Family Welfare, Govt. of India, and New Delhi to monitor the programme centrally. This programme aims to provide adverse drug reaction data related to various drugs of

herbal, mineral, metallic, animal and other origin available in the country. A reporting form for suspected adverse reactions to ASU drugs has been developed under this programme and distributed among faculty members, research scholars and physicians.

Diabetes

Diabetes mellitus (DM), termed `Madhumeha' in Ayurveda is a syndrome of chronic disorder of carbohydrate, fat, and protein metabolism in which hyperglycemia occurs due to relative insulin deficiency, resistance, or both. Diabetes is usually irreversible and, although patients can have a reasonably normal lifestyle, its late complications result in reduced life expectancy and major health costs [7].

Classification

Type1 Diabetes *(insulin-dependent diabetes mellitus)*

Type1 Diabetes (insulin-dependent diabetes mellitus) results from the body's failure to produce insulin, and presently requires the person to inject insulin.

Type 2 Diabetes *(non-insulin-dependent diabetes mellitus)*

Type 2 Diabetes (non-insulin-dependent diabetes mellitus) results from insulin resistance, a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency.

Gestational Diabetes

Gestational diabetes is when pregnant women, who have never had diabetes before, have a high blood glucose level during pregnancy which may improve or disappear after delivery. It may precede development of type 2 DM [8].

Diagnosis

Laboratory Findings

Blood Testing Procedures

Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following: [9]

- Fasting plasma glucose level at or above 7.0 mmol/L (126 mg/dL).
- Plasma glucose at or above 11.1 mmol/L (200 mg/dL) two hours after a 75 g oral glucose load as in a glucose tolerance test.
- Symptoms of hyperglycemia and casual plasma glucose at or above 11.1 mmol/L (200 mg/dL).

Patients with fasting glucose levels from 100 to 125 mg/dL (5.6 to 6.9 mmol/L) are considered to have impaired fasting glucose. Patients with plasma glucose at or above 140 mg/dL (7.8 mmol/L), but not over 200 mg/dL (11.1 mmol/L), two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance. These two conditions are considered to be pre-diabetic stage which is a major risk factor for the progression of the disease into diabetes [9].

In Ayurveda, the dried leaves of the climber ‘Gurmar’ (meaning “destroyer of sugar” in Hindi), Gymnema sylvestre (family Asclepiadaceae) has been used in India for management of diabetes for about 2000 years. Today in India it is being used to treat primarily type II diabetes and type I as well. The herb has shown to reduce blood sugar, glycosylated haemoglobin and glycosylated plasma proteins when used for 18-20 months [10]. The active components responsible for lowering glucose are the gymnemic acids. Gymnemic acids are antisweet principles and exhibit inhibitory effect on levels of plasma glucose.

Syzygium cumini (Linn.), a member of family Myrtaceae commonly known as Jamun in Hindi and Black Plum or Black Berry in English, is a large size evergreen tree. Out of a large number of herbal drugs stated to possess anti-diabetic activity in the Ayurvedic system of medicine.

MATERIALS & METHODS

Study Design & Population

The study was being conducted in a total number of 50 patients of either sex in the age group of 18-60 years, the study of Diabetes. Diabetic patients were treated with the oral combination of Gurmar (1gm), Jamun seed powder (1gm), Kala Zeera (500mg) and Aloe (250mg) in the dried, powdered and purified form as daily dose. Moreover, the study was a purely an open labeled type. During dechallenge, the suspected drug component was not mixed in the combination while during rechallenge, again the same combination was administered as was given for the first time.

Study Period

The study was being conducted from January 2010 to June 2010 in which all the enrolled patients in the study were monitored for adverse effects.

Inclusion Criteria

- Patients, who had filled, completed and undersigned the informed consent form.

- Patients who had completed their allopathic medicines a month back before starting the ayurvedic therapy and stopped the same treatment.

Exclusion Criteria

- Patients below 18 years and above 60 years age-group.
- Patients who were concomitantly suffering from chronic diseases or systemic infections (e.g. carcinoma, renal diseases, liver diseases, etc.)
- Patients who were concomitantly taking allopathic medicines.
- Patients who had recently undergone surgery.
- Patients who had failed in maintaining the follow-ups.
- Female patients who were either pregnant or lactating mothers.

Data Collection & Analysis

Questionnaire

This form included essential medical enquiries such as patient demographics, signs & symptoms, past medical history, laboratory findings and investigations, diagnosis, treatment, details of Adverse Reaction/Event, Suspected drug, dechallenge & rechallenge outcomes, causality assessment & score using Naranjo's Algorithm and the narrative. The questionnaire forms were filled and completed by the patient as well as the investigator.

After diagnosis was made, each Diabetic patient was provided with the oral ayurvedic combination of powdered Gurmar, Jamun seed, Kala Zeera and dried Aloe Vera for the duration of either 15 days or a month and was counseled for F/U on scheduled date with the information of ADR/AEs that had occurred. All the above crude drugs were obtained in the powdered form, in sealed packets as usual from the stockiest free of contamination or adulteration and of authentic quality. Each patient was under f/u for a period of 2 months. In few cases, the patient could not physically present himself/herself on scheduled date, thus they were telephonically contacted for the information of ADR/AEs. Dechallenge and Rechallenge was being carried out by the investigator on scheduled F/U visit to determine the suspected drug and its association with ADR/AEs. Finally with the help of 10 questionarre Naranjo's Algorithm, causality assessment was carried out for the suspected drug and scores were noted to classify an event in the causality categories(certain, probable/likely, possible, unlikely, conditional/unclassified, unassessable/unclassifiable).

RESULTS & DISCUSSION

ADRs were recorded during the patients' follow-ups from a total of 50 diabetic patients enrolled in the study. All the diabetic patients were given the same combination of Gurmar, Jamun Seed, Black Caraway and Aloe in the final dosage form as the treatment. Out of 50 patients enrolled, 31 patients were males (62%) and 19 patients were females (38%). At the end of the study it was observed that a total of 148 non-serious events had occurred either singly or in association in all the 50 diabetic patients. None of the patients under study died/required hospitalization/had any life threatening or serious event. More number of ADRs reports was recorded in males with 90 reports (60.8%) as compared to 58 reports (39.2%) in females. The highest number of ADRs that had occurred irrespective of gender was in the age group 51-55 accounting for 52 reports (35%) and in the age group 56-60 with 37 reports (25%) with least number of ADRs in the age group 36-40 consisting of 10 reports (6.8%).The maximum number of ADRs reported (figure 1&2) was of metallic taste with 30 reports (20.6%) and of nausea with 29 reports (19.9%). Also, 11 reports (35%) indicating loss of libido in males were obtained out of total 31 male patients exposed as shown below in the figure. No positive side effect was seen in any of the patient under study.

Dechallenge and Rechallenge was done in 42 patients out of 50 patients to have a causality assessment. From this assessment, it was found that out of 148 events, 18 (12.2%) were Definite ADRs, 95 (64.2%) were Probable ADRs, 11 (7.4%) were Possible ADRs and 24 ADRs (16.2%) were Unassessable.

Gurmar was a suspected drug for causing metallic taste, bitter taste and taste disturbance. In Naranjo's Algorithm of assessment for metallic taste (30 reports) 6 were definite ADRs, 20 were probable ADRs, and 1 was a possible ADR while 3 events were Unassessable. For Bitter taste (8 reports), 2 were definite ADRs, 4 were probable ADRs while 2 were unassessable. There were 2 cases of taste disturbance in which 1 event was definite ADR while 1 event was a probable one. Apart from this, in loss of libido (11 reports) which had a causal relationship with Gurmar had 9 events as Probable ADRs while in 2 patients it was unassessable. In case of nausea (29 reports), 7 were Definite ADR, 20 were Probable ADR while 2 were unassessable. For vomiting (6 reports), 1 was a Definite ADR, 3 were Probable, 1 was Possible while 1 was unassessable. For dry mouth (11 reports), 10 were Probable while 1 was unassessable. Jamun seed powder was found to be suspected for causing constipation (13 reports) in which 7 reports were Probable ADRs, 4 were Possible ADR while in 2 cases it was unassessable. Also it had a causal relationship with

throat itching and phlegm formation with 4 reports of each in which 4 were Probable ADRs, 1 was Possible ADR while in 3 cases it was unassessable. Black caraway was found to be suspected for causing flatulence (12 reports) and associated abdomen tenderness (6 reports). For flatulence, 7 were Probable ADRs, 2 were Possible ADRs while 3 were unassessable. In case of associated abdomen tenderness (6 reports), 5 were Probable ADRs while 1 was Possible ADR.Aloe was suspected for causing loose stools (10 reports) in which 1 was a Definite ADR, 6 were Probable,1 was a Possible ADR while 2 were unassessable and for irritable bowel (2 reports) in which 1 was Probable ADR while was a Possible ADR.Distribution of ADRs according to System Organ Class (SOC) in diabetic patients is shown in figure 3.

CONCLUSION

Herbs and Ayurvedic drugs are considered to be 100% safe and free of adverse effects. But in the above study it is clear that the ayurvedic preparations have the potential to cause ADRs to some extent although not serious. The reason may be either under reporting or lack of interest of such reporting. Therefore further studies in larger population are required on a wide therapeutic class as well as the crude drugs. From this study it was observed that every diabetic patient enrolled reported some kind of ADR which were tolerable and non serious. From causality assessment it became clear that most of them were probable.

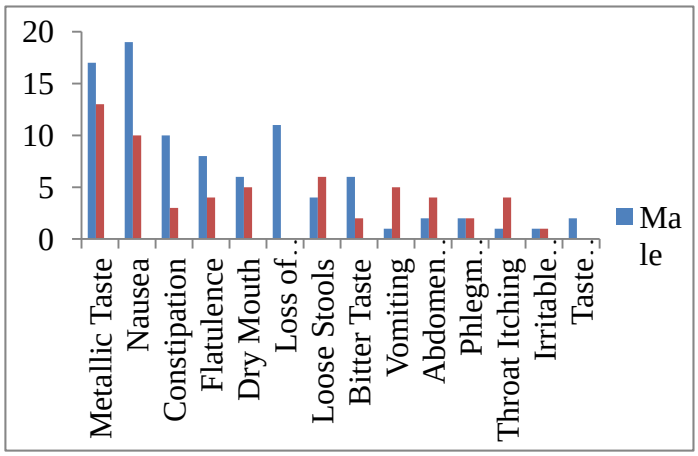

Fig.1: Bar graph representing various ADRs (x-axis) versus no. of reports (y-axis) in diabetic males and females

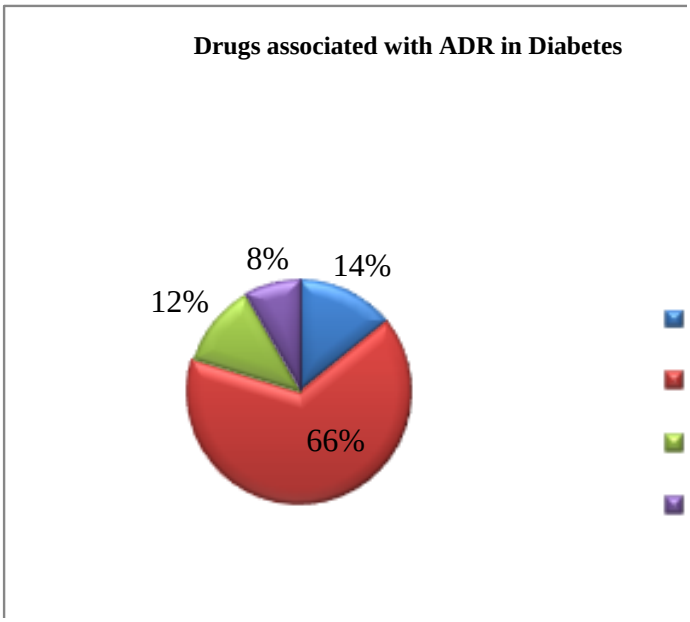

Fig. 2: Distribution of ADR according to the drugs in diabetic patients

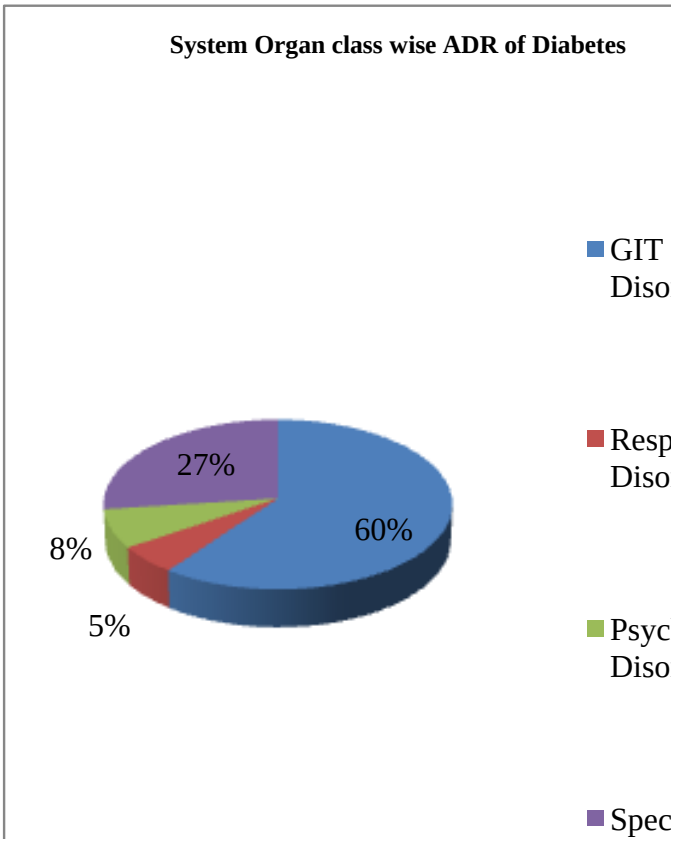

Fig. 3: Distribution of ADRs according to system organ class (SOC) in diabetic patients

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