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PHARMACOVIGILANCE OF HERBAL DRUGS IN POLY ARTHRITIC PATIENTS

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ABSTRACT: AUS - Ayurveda, Unani and Siddha is the traditional system of medicines in India more than 3000 years old and still practiced extensively in India and neighbouring countries. Assurance of the safety margin, potency of medicinal plants that make the herbal products has now become a key issue in industrialized with developed countries. Pharmacological studies is a science relating to the screening, assessment, interaction and prevention of adverse effects particularly long term and short term side effect of medicines. The present work was carried out at National Institute of Siddha, Sanatorium, Tambaram, Chennai, and Tamil Nadu. By keeping this idea the present vigilance on Siddha formulation was conducted in poly arthritic patients. In the clinical study totally 50 arthritic patients are included in which 25 male and 25 female patients. These patients were prescribed with Cap. RGM, Tab. KVC, Tab. KUKIL and PAIN BALM. The Siddha formulation which is prescribed for the treatment was found to be 60% of efficacious which is directly observed from the patient's feedback form. In contrast, 16% of male, 12% of female patients are not responded with the formulation. However the efficacy has to be properly determined in terms of pharmacokinetic and pharmacodynamic parameters in patient's plasma.


INTRODUCTION: Pharmacovigilance is gaining importance advantage technique to help the doctors and scientist as the member of stories in the mass media of drug recalls increases^{1,2}. Because clinical trials involve several thousand patient's at most, less common side effects and ADR or often unknown at the time a drug enters the market^{3,4}. There is a need to monitor the Quality of drugs pre and post medication for it's successfully tested and launched in the market. Pharmacovigilance mainly involves monitoring and assessing the quality of drugs detection and preventing its adverse effects of drugs.

It mainly involves evaluating the information provided by primary health care providers, pharmaceutical companies, and clinical reports and in patient's order to understand the risks and benefits involved with the medicated drugs though for centuries ASU drugs are considered as safe and innocuous drugs⁵.

Methodology:

Study Design and Period: This was a prospective study conducted for over a period of 7 months. The work was carried out at National Institute of Siddha, Sanatorium, Tambaram, Chennai, and Tamil Nadu. Under the guidance of Dean and HOD Dr. M. Murugesan M.D(S), Department of Toxicology⁶.

Study Site: The study was conducted in hospitalized patients and outpatients who have visited the National institute of Siddha, Sanatorium, Tambaram, Chennai, Tamil Nadu. On an average

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of 180 out-patients are treated per day and 10 in-patients are admitted and particularly in the standard format for Reporting Adverse drug events for ASU drugs has been in the department of Pharmacovigilance controlled by the Head Dr. M. Murugesan M.D(S), Technical committee member, National Pharmacovigilance program in AYUSH ⁷.

Study Criteria: ⁸

Inclusion Criteria:

- Patients admitted in Pharmacology, toxicology, general medicines, special medicines, pathology, male, female medical wards and pediatric wards of National Institute of Siddha, Tambaram, and Chennai.
- Patients, who have visited the out-patient department.

Exclusion Criteria:

- Patients with intentional & accidental poisoning (Overdose).
- Patients with drug abuse.

Various forms were designed for this study they are⁹:

- **Form No.1:** Adverse Drug Event Reporting Form
- **Form No.2:** Documentation Form
- **Form No.3:** Modified Hartwig and Siegel scale.
- **Form No.4:** Wills and Brown classification form.
- **Form No.5:** Assessment form.

Form No. 1: Adverse Drug Event Reporting

Form: This is the reporting form obtained from National Pharmacovigilance Resource Centre for ASU drugs, I.P.G.T & R.A., G.A.U., Jamnagar, and Gujarat ^{9,10}.

The reporting form contains details such as,

- ❖ Patient information
- ❖ Date of event starting
- ❖ Date of event stopping
- ❖ Description of event or problem
- ❖ Details about suspected medication- name of the drug (brand or generic name), dose frequency, route used, and duration of the therapy and diagnosis for use.

- ❖ Whether event abated after use, stopped or dose reduced, or event reappeared after re-introduction. A brief description of the adverse reaction was to be
 - Patients with intentional and accidental poisoning (Overdose).
 - Patients with drug abuse.
 - Mentioned by doctor, along with the name of reporting doctor, nurse, specialty, and ward along with the signature of the practitioner.

Form No. 2: Documentation Form: This form was designed for obtaining the demographic characters of the patient and also includes details like patient diagnosis, suspected drugs with dose and frequency, duration of the event and brief description of the reaction ¹².

Form No. 3: Modified Hartwig and Siegel Scale

Form: This scale is used for severity assessment. Depending upon the severity of the suspected reaction, this scale is divided into two categories. They are mild, and severe. The mild type reaction requires no change in the treatment with the suspected drug. For moderate reactions the suspected drug should be discontinued or otherwise changed, and /or an antidote or other treatment is required. There is no need to increase in length of hospital stay for these patients. In severe type of reactions, intensive medical attention is required ¹³.

Form No. 4: Brown Wills and Classification

Form: This classification is based on the type of origin of the suspected ADRs. According to this ADRs are classified as follows ¹⁴,

1. Type A (Augmented)
2. Type B (Bugs)
3. Type C (Chemical)
4. Type D (Delivery)
5. Type E (Exit)
6. Type F (Familial)
7. Type G (Gonado-toxicity)
8. Type H (Hypersensitivity)
9. Type U (Unclassified)

Form No. 6: Assessment Form: This form basically analyses the outcome, severity, causality, and type of suspected ADRs and also covers other sections that sought information about outcome of

the reaction such as fatal, recovered, continuing and unknown¹⁵.

Study Procedure: The patients admitted in the different medical wards with poly arthritis were grouped into male and female and were assessed for the adverse effects and patient's specific information was collected at the bed side. The suspected or identified ADRs were noticed to the physician verbally or through telephone¹⁸. Assessment of severity by Modified Hertwig and Siegel scale was followed by the conformation the reactions. Using Wills and Brown method of classification the suspected reactions were classified to understand the origin of the reaction. Clinical pharmacist participated in the management of ADRs by providing information of drug withdrawal or dose reduction based on severity^{16, 17}. The suspected ADRs were also reported by nursing staffs and doctors at different wards by using reporting forms¹⁹.

Finally the suspected reactions were informed to the regional Pharmacovigilance center Gujarat as adverse events. The initial stage of bringing the healthcare professionals to co. operate in this study was done by putting up posters in the wards with name for easy accessibility or communication²⁰. ADR Reporting form was kept in the hospital in the Department of Toxicology only to impart a continuous message and create awareness about reporting of ADRs. The doctors were also encouraged to report any suspected cases in which ADRs could have probably occurred during their practice in the hospital²¹.

The particulars are observed from the patients like suspected drug used for the treatment, date of drug started and description of adverse drug reactions and all the observations are recorded in Form 2. (Annexure - 2) and duly signed by the pharmacist. To know the exert of severity of ADR severity assessment scale was used (Annexure-3). Wills and Brown classification method was used to classify the type of ADR Reactions. (Annexure-4), and finally assessment forms (Annexure-5) were filled up as mentioned by Arthritis patient which basically analyze the Outcome, Severity, Causality and types of suspected ADRs, and also it includes the reaction such as Fatal, Recovered or Unknown^{23, 24}.

RESULTS: The adverse drug reporting effect (Pharmacovigilance) has been conducted in patients treated with Siddha drugs like Cap. RGM, Tab. Kvc, Tab. Kukil and Pain balm for poly arthritis^{25, 26}. The arthritic patients are divided into two groups like Male and Female. Each group contains 25 patients. The details were collected from the patients on the following aspects.

- Age of the patients.
- Efficacy of patients.
- Adverse reactions of patients.
- Recovery of the patients.

The results were shown in **Fig. 1 - 8**.

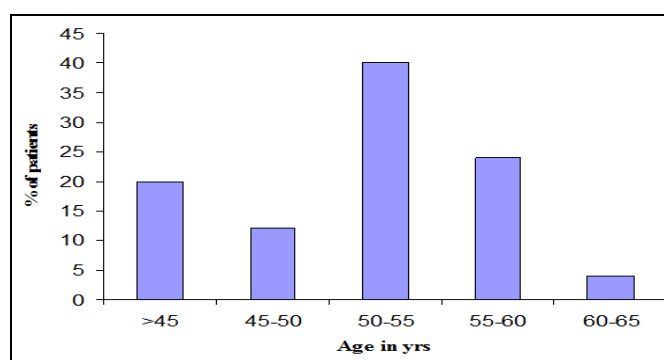


FIG. 1: AGE OF THE PATIENTS

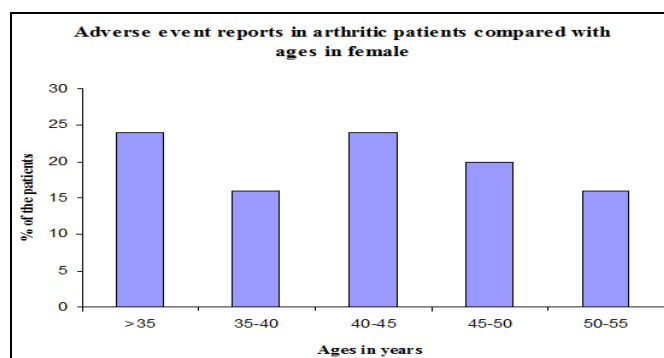


FIG. 2: AGE DISTRIBUTION TABLE AMONG FEMALE PATIENTS

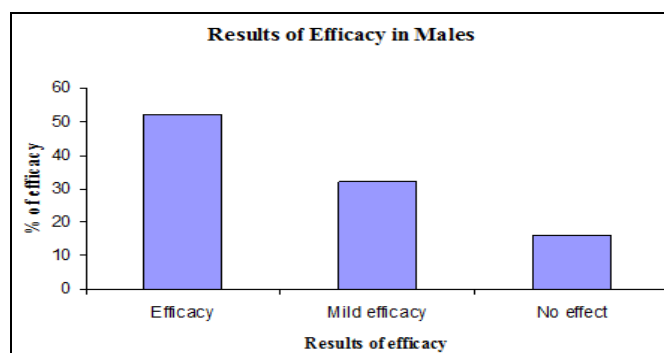


FIG. 3: RESULTS OF EFFICACY OF THE PATIENTS IN MALE

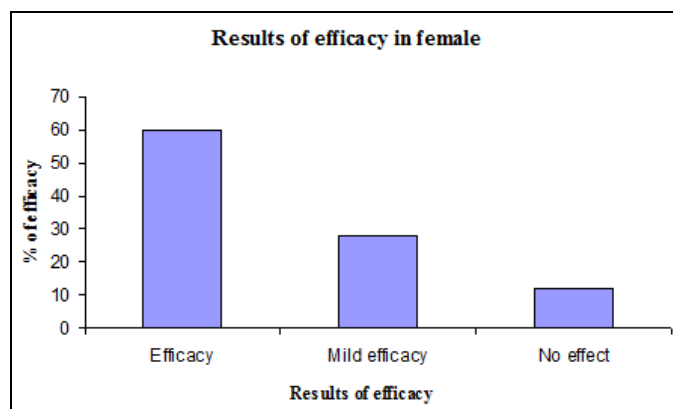


FIG. 4: RESULTS OF EFFICACY OF THE PATIENTS IN FEMALE

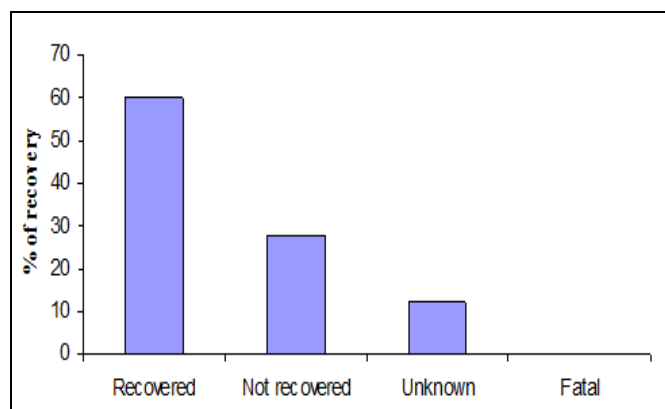


FIG. 8: RESULTS OF RECOVERY IN FEMALE PATIENTS

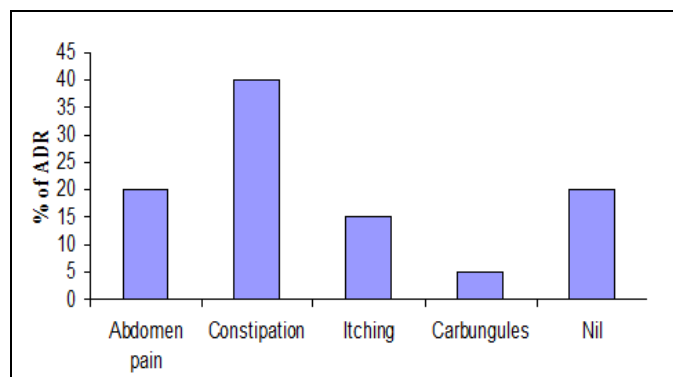


FIG. 5: ADVERSE DRUG REACTIONS IN MALE PATIENT

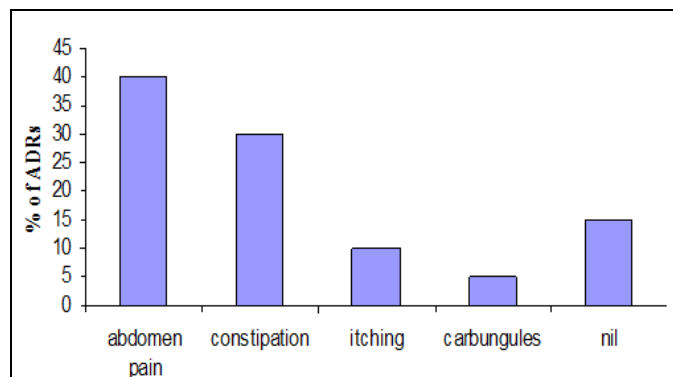


FIG. 6: ADVERSE DRUG REACTIONS IN FEMALE PATIENTS

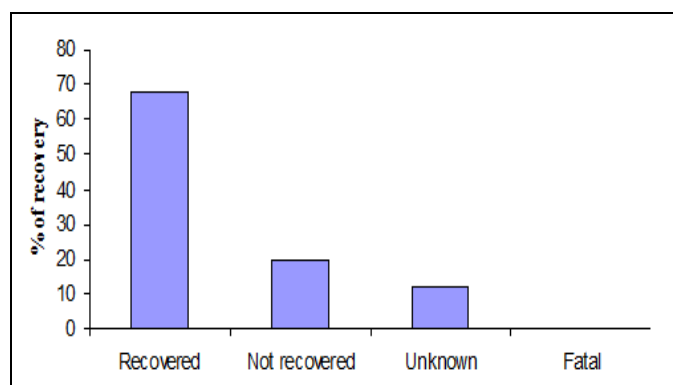


FIG. 7: PERCENTAGE OF RECOVERY IN MALE PATIENTS

DISCUSSION: The present study highlights the pharmacovigilance study of Siddha formulations used for the anti arthritic purpose²⁷. The basic idea of conducting this pharmacovigilance survey is that more number of patients are turn to Siddha preparation because conventional allopathic drugs like non steroidal anti-inflammatory drugs (NSAIDs) or Disease Modifying anti-rheumatic drugs (DMARD's) are known for server side effects like urinary and water retention, gastric ulceration and some time chronic use may lead to chronic renal failure^{28, 29}. However the pharmacovigilance study on efficacy and side effect of the Siddha formulation has not been properly conducted in some Siddha formulation which are claimed to be 100 percent efficacious and devoid of adverse effects^{30, 31}.

The Siddha formulation which is prescribed for the treatment was found to be 60% of efficacious which is directly observed from the patient's feedback form. In contrast, 16% of male, 12% of female patients are not responded with the formulation³². However the efficacy has to be properly determined in terms of pharmacokinetic and pharmacodynamic parameters in patient's plasma. These particulars are noted on the AYUSH approval format for reporting form for suspected adverse reactions of ASU drugs^{33, 34}. These reports were submitted to the Dean, technical committee member of pharmacovigilance in Siddha, National Institute of Siddha, Sanatorium, Tambaram, and Chennai³⁵. All the forms have been sent to National Pharmacovigilance Resource Centre for ASU (NTRC-ASU); IPGT and RA, Jamnagar, for the further evaluation³⁶.

CONCLUSION: The pharmacovigilance study on efficacy and side effect of the Siddha formulation has not been properly conducted in some Siddha formulation which are claimed to be 100 percent efficacious and devoid of adverse affects³⁷. By keeping this idea the present vigilance on Siddha formulation was conducted in poly arthritic patients³⁸. In the clinical study totally 50 arthritic patients are included in which 25 male and 25 female patients. These patients were prescribed with Cap. RGM, Tab. KVC, Tab. KUKIL and PAIN BALM. The Siddha formulation which is prescribed for the treatment was found to be 60% of efficacious which is directly observed from the patient's feedback form. In contrast, 16% of male, 12% of female patients are not responded with the formulation³⁹. However the efficacy has to be properly determined in terms of pharmacokinetic and pharmacodynamic parameters in patient's plasma.

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CONFLICT OF INTEREST: No.

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