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Original Research Article

A prospective, post-marketing surveillance (PMS) study to monitor the safety of fixed dose combination of Triprolidine Hydrochloride IP 2.5 mg and Phenylephrine Hydrochloride IP 5 mg [Recofast Tablets] for the symptomatic relief in patients with upper respiratory tract infections

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ABSTRACT

Background: Upper Respiratory Tract Infection (URTI) is the most frequent illness in humans. The vast majority of acute upper respiratory tract infections are caused by viruses. These cause a variety of patient diseases including acute bronchitis, common cold, influenza, and respiratory distress syndromes.
Aim & Objective: The study was conducted in patients with upper respiratory tract infections to see if the medication provides symptomatic relief in these conditions. Other conditions like allergic rhinitis and influenza were also included in the study for symptomatic relief.
Materials and Methods: This is an open label, multicentric, active Post Marketing Surveillance (PMS) study with an objective to assess safety of fixed dose combination regarding Recofast tablets (Triprolidine Hydrochloride IP 2.5 mg and Phenylephrine Hydrochloride IP 5 mg) which was evaluated in 150 participants from different geographical regions. And then results were documented.
Finding: A total of 19 (13%) patients recorded minor adverse event from these regions. Out of 150 patients 95 were male & 55 were female. All the patients were in the range of 18-80 years.
Results & Conclusion: No significant adverse events were observed during the course of the study, only 13% patients recorded minor adverse events from all regions. Thus this formulation is completely safe and effective in the management of Upper Respiratory Tract Infections and allergies.

1. Introduction

Upper Respiratory Tract Infection (URTI) is the most repeated illness in humans which results into common cold. The frequent usage of proprietary formulations of this kind reflects the commonly held belief that concurrent therapy with an antihistamine and a decongestant provides some symptom alleviation.[1] Most individuals who have a common cold treat themselves with over-the-counter (OTC) cold drugs. There are several cough and cold medications that may be bought and sold without a prescription.[2] There is a global issue with the inappropriate and unnecessary use of antibiotics to treat respiratory tract infections. Polypharmacy results from the addition of additional medicines to symptomatic treatment. This issue may be solved by educating medical professionals and patients on the fundamentals of sensible drug usages.[3] Viral infections are the main cause of acute upper respiratory tract infections. Rhinitis, pharyngitis, acute bronchitis, tonsillitis, laryngitis, the common cold, influenza, and respiratory distress syndromes are just a few of the disorders that are brought on by this.[4] Identification of the disease is

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difficult in most of these patients because the presentations associated with upper respiratory tract infections (URTIs) often overlap and have similar etiologies. The main symptoms of URTI are nasal stuffiness, sneezing, a scratchy or sore throat, cough, excess mucus, nasal congestion, hyposmia, or a loss of the sense of smell and sometimes headache.[5] Low-grade fever is a fluctuating condition that affects children more frequently than adults. Most of the time, common colds are caused by viruses, and antibiotics are not usually necessary until they are made worse by acute otitis media with effusion, tonsillitis, sinusitis, and lower respiratory tract infection.[6] Upper respiratory tract infections are characterised by self-limiting irritation and inflammation of the upper airways along with a cough. There must be no evidence of pneumonia, no other illness to explain the patient's symptoms, and no prior history of COPD, emphysema, or chronic bronchitis.[7] Infections of the upper respiratory tract affect the nose, sinuses, larynx, pharynx, and major airways. Despite the fact that the condition is not life-threatening, URTIs place a major financial burden on sufferers due to the cost of drugs, trips to doctors and other healthcare professionals, and absenteeism. Adults experience 4-6 URTIs annually, whereas young children often experience 6-8 URTIs.

2. Epidemiology

Colds occur throughout the year, although less frequently in the summer. A greater incidence of rhinovirus infections often occurs in the fall, typically in August or September, marking the start of the respiratory virus season. The rise in sickness during this period is the result of several, relatively isolated outbreaks of various viral infections. Although transmission through big particle aerosols has also been recorded, experimental investigations on rhinovirus colds in human volunteers show that direct contact is the most effective approach to spread this virus. No matter how an infection spreads, nasal mucosa contact with the rhinovirus seems to be crucial for the development of an illness. Persistent infection is impacted by very little viral inoculation administered to the nasal cavity. In contrast, introducing a virus into the mouth is an ineffective method of spreading it. It was determined that 0.3 tissue culture infectious doses (TCIDs0) by nasal and 2260 TCIDs0 by oral inoculation were needed to achieve a 50% infection rate. As the virus is transferred directly into the nasal cavity through the nasal tube, conjunctival injection with the virus is also a reliable method of transmission.[8]

Acute respiratory infections occur in 20-40% of outpatients and 12-35% of inpatients in common hospitals. Upper respiratory tract infections including nasopharyngitis, pharyngitis, tonsillitis and otitis media accounting for 87.5% of all respiratory tract infections.[6] Adults' primary motive for seeking outpatient care during the first few weeks of sickness is the relief of symptoms, and the majority of these visits result in doctors prescribing antibiotics or H-1 receptor antagonists.

Children experience 6 to 8 colds annually on average, compared to 4 to 6 for adults. The total disease burden brought on by these diseases is larger than that brought on by seasonal flu since cold weather occurs year-round. The United States has the highest number of cases with 35,283,729 and more than 626,668 deaths, followed by India with 31,341,507 cases and more than 420,196 deaths as on July 24, 2021.[9]

3. Materials and Methods

This post marketing surveillance was conducted in accordance with Good Post-marketing Study Practices, or the Standard for Conducting Post-marketing Surveillance and trials of Drug and Testing Practices regulated under the ICHGCP guidelines of India. This surveillance was conducted on Recofast tablets (Triprolidine Hydrochloride IP 2.5 mg and Phenylephrine Hydrochloride IP 5 mg). This surveillance requires informed consent from patients who are participating in it.

3.1. Patients

150 subjects were analysed for safety of Recofast tablets. To account for possible loss to follow up of 10%, a maximum of 165 patients were recruited from different regions. The study subjects were volunteers, with symptoms of common cold of less than 3 days. Patients with allergic rhinitis and influenza were also recruited, to see if the medication provides symptomatic relief in these conditions as well. Actual numbers of patients enrolled were 150.

3.2. Design

This is an open label; multicentric, randomized, active Post Marketing Surveillance (PMS) study with an objective to access safety of fixed dose combination of Recofast tablets (Triprolidine Hydrochloride IP 2.5 mg and Phenylephrine Hydrochloride IP 5 mg). Tablet Recofast was taken orally. Randomization is not applicable because it is an open label study. The study was conducted in 150 patients suffering from common cold from different regions of India. We collected data from New Delhi, Patna, Mumbai Metropolitan Region and Thane District.

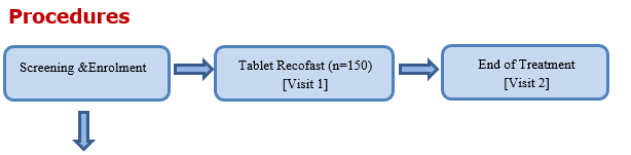
Primary objective of this PMS is safety evaluation of Recofast Tablets. Safety analysed by the number of reported adverse events associated with the use of Recofast / number of patients.

When a patient with common cold came to a clinic (i.e. Visit 1), he/she was considered to be a potential participant for this study and prior to any study procedures, the nature of the study had to be explained to him/her by the study investigator or designee and the potential participant was asked to give written informed consent. Informed consent

must be obtained prior to any study procedures. If found eligible and participant agrees to participate, he/she was enrolled into the study.

During Visit 1 (Day 0), the physician recorded all the details, symptoms and history as enumerated in the CRF for each subject. CRF was filled noting down the symptoms and the scores of each symptom. The dosage of the study medication was explained to the subject. Each subject was given a strip of 10 tablets of the FDC Recofast, to be taken three times daily for 3 days, as a treatment.

The Visit 2 occurred on the 3rd/4th day after starting the medication. The subject should have taken 9 doses of the medication for completion of the study period and to be considered for final analysis for safety. The details for this follow up and final visit were recorded in the CRF for further evaluation. The remaining strip of the medication was taken back to monitor compliance.



Study Visits	1	2
Days	0	3/4
Interval (Days)	0	3/4
Medical history	*	
History of prior medications	*	
Physical examination	*	*
Inclusion/ Exclusion criteria	*	
Informed consent	*	
Safety assessment		*

Fig. 1: Trial process

3.3. Visit 1

All patients with common cold were evaluated for entry criteria when the patient seeks medical treatment at hospital. They can be suffering from any of the symptoms of common cold such as sneezing, runny nose, blocked nose, sore throat, cough, and headache. However, to be enrolled in the trial, patients were required to have runny nose or at least one other cold symptom. Eligible candidates were included in the study, only after taking an informed consent from them. During Visit 1 all physical parameters and symptoms in CRF or protocol were recorded.

After enrollment, all the study participants received a strip of Tablet Recofast, containing 10 tablets to be administered orally. All the tablets were to be taken by the patients at their home. The patients were instructed to take medicines three times daily for 3 days and return the used strip to PI at the end of treatment. The day of the treatment initiation was Study Day 0.

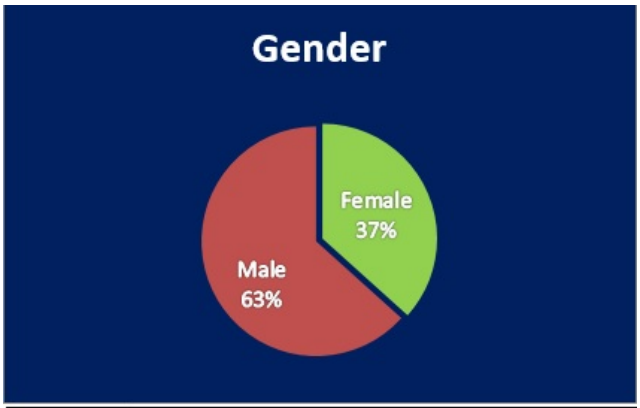
3.4. Visit 2

Each study participant returned for evaluation to the clinical study site on 3^{rd}or 4^{th} day.

The participants' results were documented in CRF forms.

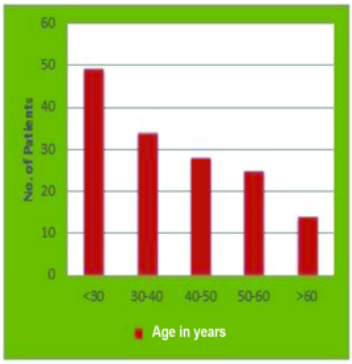
4. Statistical Consideration

The study was conducted for safety evaluation of Recofast tablet on 150 patients with URTI and out of that only 19 patients (13%) reported minor adverse events (majorly nausea, drowsiness, GI upset, sleepiness, dry mouth). There are some statistics based on data collected,



Gender	No. of patients use Recofast tablet
Female	55
Male	95

Fig. 2: Gender ratio



Age	No. of patients use Recofast tablets
<30	49
30-40	34
40-50	28
50-60	25
>60	14

Fig. 3: Age wise participation

5. Results and Conclusion

In this PMS study, we analysed the Safety of Triprolidine HCl IP 2.5 mg and Phenylephrine HCL IP 5 mg. Recofast tablets were taken orally by all patients three times daily on Day 0, 1, and 2. No significant adverse events were

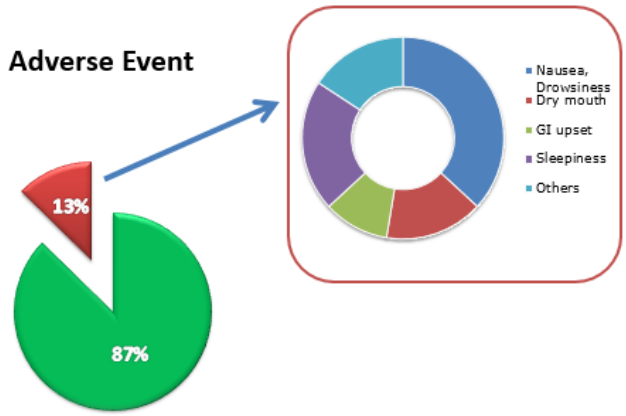


Fig. 4: Percentage of adverse events

observed during course of the study. Only 13% patients recorded minor adverse events from all regions which were mentioned above. Thus, this formulation is completely safe and there was no abrupt termination of the medication.

6. Limitations

Post-marketing monitoring can be conducted using a variety of techniques. Although spontaneous reporting of unpleasant occurrences is a rapid procedure, its drawbacks include under-reporting and non-representatively.

Rigorous search provides high-quality data but is expensive. Case-control studies can be consulted using medical data, but occasionally the diagnosis is wrong. Prospective studies are an informative way to obtain these results but it takes time.

The drawbacks of PMS are the cost and delayed appearance of the information. Finally, data on drug use is valuable because it provides an estimate of the size of the population using a given drug and indicates whether adverse event warnings affect prescribing patterns.

7. Disclosure

Employees of Shreya Life Sciences Pvt. Ltd. Mumbai, have no conflicts of interest in this study.

8. Source of Funding

None.

9. Conflict of Interest

None.

10. Acknowledgments

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