Open Access
Full Length Article

ORIGINAL ARTICLE

Single Blind, Placebo Control Phase III Study of Insty Granules to Evaluate its Efficacy and Safety

Muhammad Daniyal[1,] *, Syed Rashid Ali Jaffary[2], Syed Faisal Zaidi[5], Syed Waseemuddin Ahmed[2], Muhammad Khalid Adhia[3], Faheem Akhtar[4], Muhammad Ibrar Shinwari[6], Khan Usmanghani[4]

[1]Department of Medical Affairs and Training, Herbion Pharmaceutical (Pvt.) Limited, Karachi, Pakistan
[2]Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi, Karachi, Pakistan
[3]Hamdard University Hospital, Taj Medical Complex, Karachi, Pakistan
[4]Department of Research and Development, Herbion Pharmaceutical (Pvt.) Limited, Karachi, Pakistan
[5]Department of Basic Medical Sciences, College of Medicine, King Saud bin Abdul Aziz University of Health Sciences, Jeddah, Saudi Arabia
[6]Department of Environmental Sciences, Faculty of Basic & Applied Sciences, International Islamic University, H-10, Islamabad, Pakistan

Keywords: *Insty granules, Herbal treatment, common cold, upper-respiratory tract infection, controlled single-blind phase III study.*

Author`s Contribution
All the authors contributed significantly to the research that resulted in the submitted manuscript.

Article info.
Received: April 19, 2017
Accepted: August 01, 2017

Funding Source: *Nil*
Conflict of Interest: *Nil*

Cite this article: *Daniyal M, Jaffary SRA, Zaidi SF, Ahmed SW, Adhia KM, Faheem A, Shinwari IM, Usmanghani K, Single blind, Placebo control phase III study of Insty granules to evaluate its efficacy and safety. RADS J. Pharm. Pharm. Sci. 2017;5(3):2-10.*

****Address of Correspondence Author:***
daniyaldani151@yahoo.com

ABSTRACT

Aims and Objectives: Cold symptoms are well recognized as sore throat, nasal congestion and clogging, sneezing, coughing, headache and fatigue. This clinical trial was conducted to evaluate the efficacy and safety of Insty granules, at Taj Medical Complex Hamdard Hospital.

Introduction: Up to 499.99 million incidents of acute upper respiratory tract infection (i.e. the common cold) are estimated in the United States each year, with a cost associated with 39.99 billion dollars yearly. The common cold is one of the leading causes of work or school absenteeism and is responsible for an estimated 110 million doctor visits and 6 million emergency visits each year in the United States.

Method: This was a single blind, placebo control phase III clinical trial. Total 662 patients were enrolled in the study, in which 331 receive the Insty granules and 331 receive the placebo. The age range of patients was 19 years to above 50 years. The sample paired t-test was applied to evaluate the significant level.

Results: Insty granules was very effective in the treatment of cold and flu symptoms.

Conclusion: The Insty granules was safe and well tolerated in all patients and none of the patient reported any side effect.

INTRODUCTION

It is generally accepted that antibiotics are over prescribed for many types of infections in general and for those who accompanying common cold, in particular [1]. On the other hand, there is also a consensus that there is no rapid cure for this type of infection; In fact, even symptomatic treatment with antihistamines, decongestants, menthol, etc., has a capped

value. There is a recommendation for medical care to reduce the use of antibiotics to a minimum to reduce the increase in bacterial resistance. This situation has raised the need to search for new types of agents that can decrease: (1) The symptoms of colds and flu-like illnesses and their duration. (2) The frequency and intensity of secondary infections, such as sinusitis, otitis and bronchitis.

It is estimated that up to 499.99 million episodes of acute viral infection of the upper respiratory tract (i.e. the common cold) in the United States each year, costing an estimated $ 39.99 million per year [2]. Furthermore, the common cold is a major cause of work or school absenteeism [3]. and is responsible for an estimated 110 million visits and 6 million emergency visits each year in the United States [2]. Well recognized symptoms of the common cold are sore throat, nasal congestion and obstacles, sneezing, cough, headache and fatigue [3]. According to the National Institute of Allergy and Infectious Diseases, maximum people recuperate from colds within 10 days but the duration can be as short as 2 days or up to 2 weeks [3]. Approximately 30% of colds are accompanied by cough [4]. Cough is one of the 10 most common diagnoses that were made during visits to the outpatient department of the hospital [5]. The duration of the cough may be higher than that of the other symptoms of the cold illness with acute cough (acute bronchitis) was estimated at about 18 days [6].

But it may also be advantageous if the drugs create an unfavorable environment for the growth of microorganisms and / or possessing a general anti-inflammatory effect [7]. Recent research has shown that the creation of an anti-inflammatory and antiviral environment in the respiratory tract and particularly in or near the nasopharynx, is significant to accomplish a beneficial effect in the treatment of the common cold [8]. Hence, a drug with either direct anti-microbial effect or creating an environment not suitable for bacterial/viral survival might be beneficial in treating diseases like common cold and flu. This study is therefore conducted to validate the efficacy and safety of Insty granules (Table **1**) in the treatment of upper respiratory tract infections particularly cold and flu.

METHODOLOGY

The monitoring of the study was executed in line with the Guidelines for Good Clinical Practice and incompliance with the revised declaration of Helsinki. The protocols of the study were reviewed and approved by the Ethical Review Committee of the Herbion Pharmaceutical (Pvt.) Limited Pakistan. This clinical trial was a single blind, placebo controlled and randomized study conducted at the Taj Medical Complex Hamdard Hospital. Patients were unaware of the treatment assigned to them. The evaluation was based on the patient's self-evaluation questionnaire. The patients were recruited according to criteria given below, after having received written and verbal information about the study.

Patient Inclusion Criteria

1) Patient aged 19 years to above 50 years, of both genders.
2) Patients with a diagnosis of uncomplicated upper-respiratory tract infection and with onset of symptoms within the last 36 hours. Symptoms includes common cold, flu, acute respiratory viral infection (ARVI) associated cough, rhinitis, headache, running nose, muscle soreness, sneezing, and post nasal drip.
3) All patients were informed about the study verbally and written consent was requested.

Patient Exclusion Criteria

Known hypersensitivity to any component of the study formulation; Aspirin-induced asthma; Diabetes mellitus; Concomitant use of anti-tussive and drugs that reduce the formation of phlegm; use of anticoagulants and acetylsalicylic acid; any current acute disease or uncontrolled exacerbation of chronic disease; clinical

evidence of immunosuppression; vaccination against influenza upto 1 week before inclusion; need for antiviral therapy to treat influenza A or B infection; need for antibacterial therapy to treat acute respiratory infection; use of medication to treat conditions acquired before inclusion for a time shorter than two time intervals of administration of these drugs; and participation in another clinical trial less than 1 year before.

Study Procedure

At the first visit of randomization, a detailed clinical history with particular emphasis on the history of cold and flu symptoms was obtained from all patients. The severity of cold and flu symptoms was evaluated by a questionnaire. All patients were randomly assigned to Insty granules groups (n=331) or placebo group (n=331). Each patient received either Insty granules or placebo. The result of each group was measured by associating the cold and flu symptoms before treatment and after treatment.

Statistical Analysis

Statistical analysis was performed using the SPSS version 22 program. The analysis included all subjects randomized in the groups to which they were assigned. The change in the various parameters for the statistical analysis between group's analysis at the entry and at the end of the study was evaluated. The paired t-test was used to assess the extent of significant proportions. The minimum significance was set at 95% confidence, and the p value <0.05 was considered significant.

Ethical Committee Approval

This clinical trial is approved by the ethical committee of Herbion Pharmaceutical (Pvt.) Limited, Karachi, Pakistan.

Table 1. Composition of Insty granules.

Insty granules contains the following ingredients
1. Salix alba (bark)
2. Adhatodavasica (leaves)
3. Glycyrrhiza glabra (roots)
4. Thea sinensis (leaves)
5. Viola odorata (leaves)
6. Valeriana officinalis (roots)
7. Foeniculum vulgare (fruits)
8. Emblica officinalis (fruits)

RESULT

A total of 662 male and female outpatients (n = 331 Insty granules) group; n = 331 placebo group) were included into the study. None of patient stated any adverse or side effect of the study drug. Cold and flu was considered positive by clinical sign and symptoms of flu, acute respiratory viral infection, fever, rhinitis, headache, sneezing, muscle soreness, running nose and post nasal drip. Patient's age distribution; sex distribution and frequency distribution of Insty granules group and placebo group are shown in Figure **1** and Figure **2** respectively.

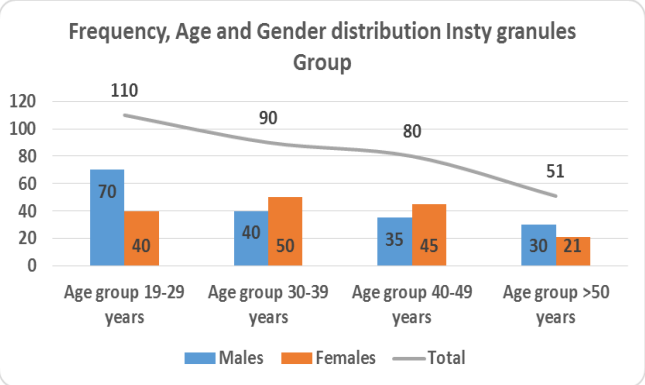

Figure 1. Frequency, age and gender distribution Insty granules group.

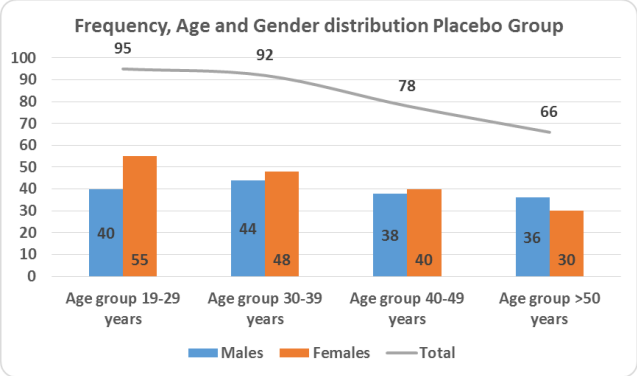

Figure 2. Frequency, age and gender distribution placebo group.

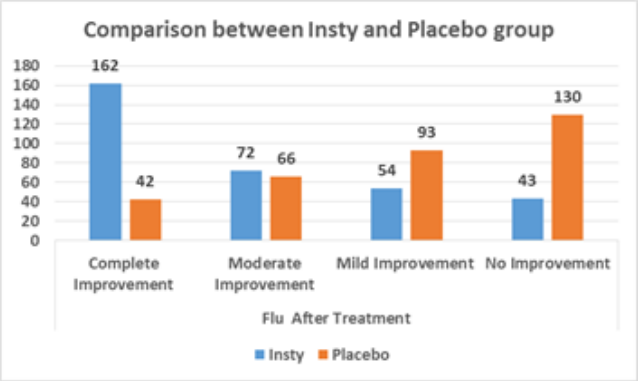

Figure 3. Comparison of flu after treatment in Insty granules group and placebo group.

FLU

Flu symptom has been recorded in patients. Patients presenting with symptom of flu observed after treatment in both groups. In Insty granules group 49.9% patients show complete improvement, 21.8% show moderate improvement, 16.3% show mild improvement and 13% show no improvement. In placebo group 12.7% patients show complete improvement, 19.9% show moderate improvement, 28.1% show mild improvement and 39.3% show no improvement. The overall effects of Insty granules and placebo on flu after treatment is shown in Table **2** and Figure **3**.

Acute Respiratory Viral Infection (ARVI) Associated with Cough

Acute respiratory viral infection associated with cough symptom has been recorded in patients. Patients presenting with symptom of ARVI associated with cough observed after treatment in both groups. In Insty granules group 36.3% patients show complete improvement, 28.1% show moderate improvement, 21.8% show mild improvement and 13.9% show no improvement. In placebo group 18.1% patients show complete improvement, 19.9% show moderate improvement, 29.9% show mild improvement and 32% show no improvement. The overall effects of Insty granules and placebo on acute respiratory viral infection after treatment is shown in Table **3** and Figure **4.**

Table 2. Comparison of flu after treatment in Insty granules group and placebo group.

Level of Improvement	Complete improved	Moderate improved	Mild improved	No improved	*P value*
Insty granules	162(49.9%)	72(21.8%)	54(16.3%)	43(13%)	0.0001
Placebo	42(12.7%)	66(19.9%)	93(28.1%)	130(39.3%)	

Table 3. Comparison of acute respiratory viral infection associated with cough after treatment in Insty granules group and placebo group.

Level of Improvement	Complete improved	Moderate improved	Mild improved	No improved	*P value*
Insty granules	120(36.3%)	93(28.1%)	72(21.8%)	46(13.9%)	0.0001
Placebo	60(18.1%)	66(19.9%)	99(29.9%)	106(32%)	

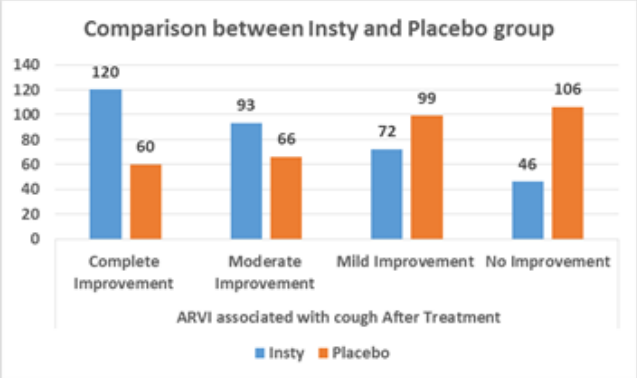

Figure 4. Comparison of ARVI associated with cough after treatment in Insty granules group and placebo group.

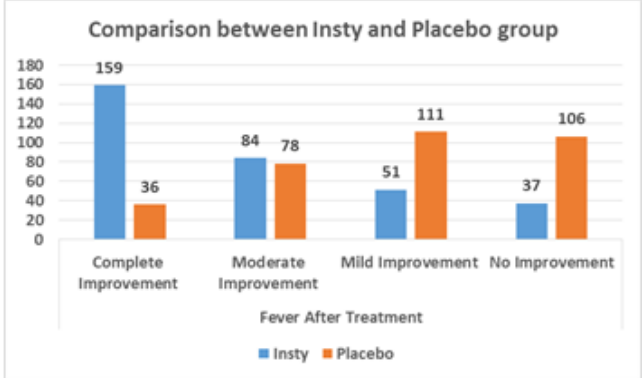

Figure 5. Comparison of fever after treatment in Insty granules group and placebo group.

FEVER

Fever symptom has been recorded in patients. Patients presenting with symptom of fever observed after treatment in both groups. In Insty granules group 48% patients show complete improvement, 25.4% show moderate improvement, 15.4% show mild improvement and 11.2% show no improvement. In placebo group 10.9% patients show complete improvement, 23.6% show moderate improvement, 33.5% show mild improvement and 32% show no improvement. The overall effects of Insty granules and placebo on fever after treatment is shown in Table **4** and Figure **5**.

RHINITIS

Rhinitis symptom has been recorded in patients. Patients presenting with symptom of rhinitis observed after treatment in both groups. In Insty granules group 40.8% patients show complete improvement, 29% show moderate improvement, 18.1% show mild improvement and 12.1% show no improvement. In Placebo group 11.8% patients show complete improvement, 23.6% show moderate improvement, 28.1% show mild improvement and 36.6% show no improvement. The overall effects of Insty granules and placebo on rhinitis after treatment is shown in Table **5** and Figure **6**.

Table 4. Comparison of fever after treatment in Insty granules group and placebo group.

Level of Improvement	Complete improved	Moderate improved	Mild improved	No improved	*P value*
Insty granules	159(48%)	84(25.4%)	51(15.4%)	37(11.2%)	0.0001
Placebo	36(10.9%)	78(23.6%)	111(33.5%)	106(32%)	

Table 5. Comparison of rhinitis after treatment in Insty granules group and placebo group.

Level of Improvement	Complete improved	Moderate improved	Mild improved	No improved	*P value*
Insty granules	135(40.8%)	96(29%)	60(18.1%)	40(12.1%)	0.0001
Placebo	39(11.8%)	78(23.6%)	93(28.1%)	121(36.6%)	

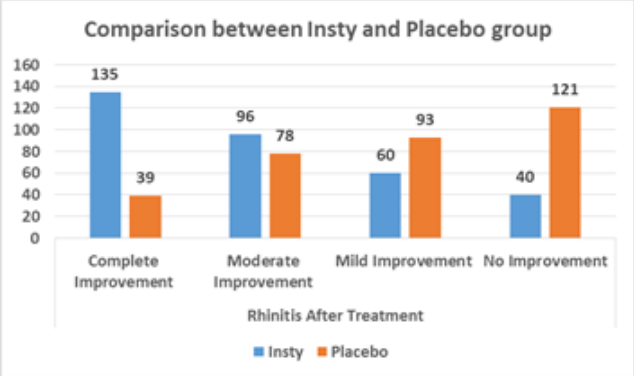

Figure 6. Comparison of rhinitis after treatment in Insty granules group and placebo group.

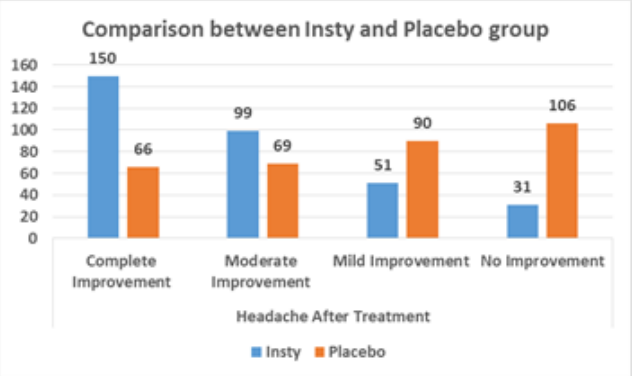

Figure 7. Comparison of headache after treatment in Insty granules group and Placebo group.

Headache

Headache symptom has been recorded in patients. Patients presenting with symptom of headache observed after treatment in both groups. In Insty granules group 45.3% patients show complete improvement, 29.9% show moderate improvement, 15.4% show mild improvement and 9.4% show no improvement. In placebo group 19.9% patients show complete improvement, 20.8% show moderate improvement, 27.2% show mild improvement and 32% show no improvement. The overall effects of Insty granules and placebo on headache after treatment is shown in Table **6** and Figure **7**.

Sneezing

Sneezing symptom has been recorded in patients. Patients presenting with symptom of sneezing observed after treatment in both groups. In Insty granules group 33.5% patients show complete improvement, 26.3% show moderate improvement, 20.8% show mild improvement and 19.3% show no improvement. In placebo group 15.4% patients show complete improvement, 20.8% show moderate improvement, 33.5% show mild improvement and 30.2% show no improvement. The overall effects of Insty granules and placebo on sneezing after treatment is shown in Table **7** and Figure **8**.

Table 6. Comparison of headache after treatment in Insty granules group and placebo group.

Level of Improvement	Complete improved	Moderate improved	Mild improved	No improved	*P value*
Insty granules	150(45.3%)	99(29.9%)	51(15.4%)	31(9.4%)	0.0001
Placebo	66(19.9%)	69(20.8%)	90(27.2%)	106(32%)	

Table 7. Comparison of sneezing after treatment in Insty granules group and placebo group.

Level of Improvement	Complete improved	Moderate improved	Mild improved	No improved	*P value*
Insty granules	111(33.5%)	87(26.3%)	69(20.8%)	64(19.3%)	0.0001
Placebo	51(15.4%)	69(20.8%)	111(33.5%)	100(30.2%)	

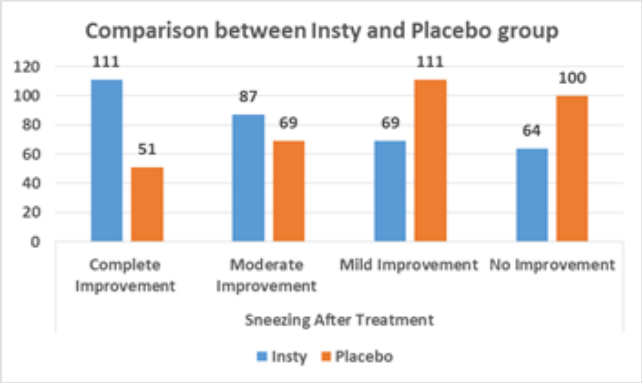

Figure 8. Comparison of sneezing after treatment in Insty granules group and placebo group.

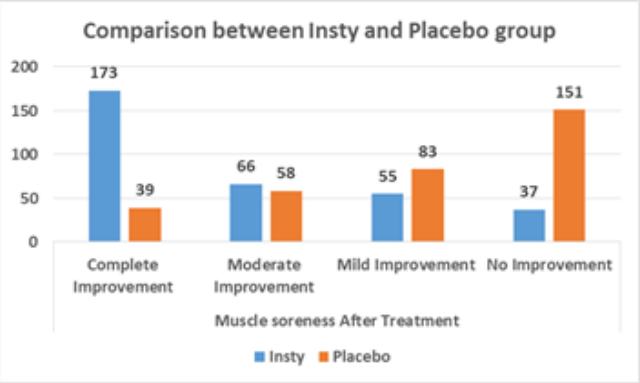

Figure 9. Comparison of muscle soreness after treatment in Insty granules group and placebo group.

Muscle Soreness

Muscle soreness symptom has been recorded in patients. Patients presenting with symptom of muscle soreness observed after treatment in both groups. In Insty granules group 52.3% patients show complete improvement, 19.9% show moderate improvement, 16.6% show mild improvement and 11.2% show no improvement. In placebo group 11.8% patients show complete improvement, 17.5% show moderate improvement, 25.1% show mild improvement and 46.6% show no improvement. The overall effects of Insty granules and placebo on muscle soreness after treatment is shown in Table **8** and Figure **9**.

Running Nose

Running Nose symptom has been recorded in patients. Patients presenting with symptom of running nose observed after treatment in both groups. In Insty granules group 36.3% patients show complete improvement, 26% show moderate improvement, 23.6% show mild improvement and 14.2% show no improvement. In placebo group 15.7% patients show complete improvement, 17.2% show moderate improvement, 27.5% show mild improvement and 39.6% show no improvement. The overall effects of Insty granules and placebo on running nose after treatment is shown in Table **9** and Figure **10**.

Table 8. Comparison of muscle soreness after treatment in Insty granules group and placebo group.

Level of Improvement	Complete improved	Moderate improved	Mild improved	No improved	*P value*
Insty granules	173(52.3%)	66(19.9%)	55(16.6%)	37(11.2%)	0.0001
Placebo	39(11.8%)	58(17.5%)	83(25.1%)	151(45.6%)	

Table 9. Comparison of running nose after treatment in Insty granules group and placebo group.

Level of Improvement	Complete improved	Moderate improved	Mild improved	No improved	*P value*
Insty granules	120(36.3%)	86(26%)	78(23.6%)	47(14.2%)	0.0001
Placebo	52(15.7%)	57(17.2%)	91(27.5%)	131(39.6%)	

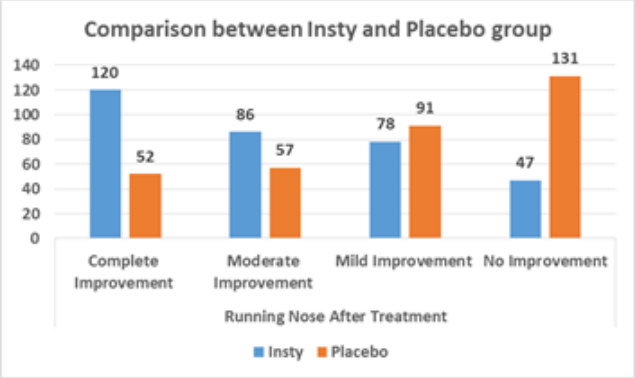

Figure 10. Comparison of running nose after treatment in Insty granules group and placebo group.

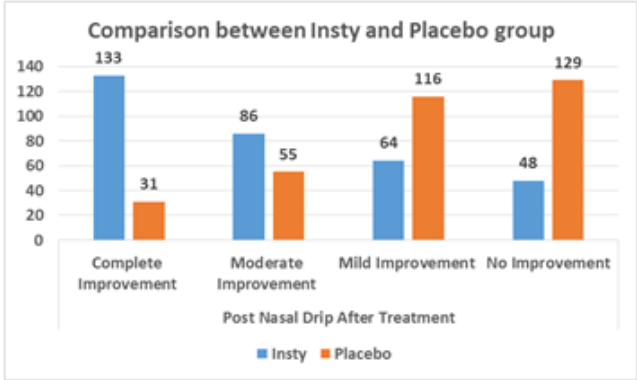

Figure 11. Comparison of post nasal drip after treatment in Insty granules group and placebo group.

Post Nasal Drip

Post Nasal Drip symptom has been recorded in patients. Patients presenting with symptom of post nasal drip observed after treatment in both groups. In Insty granules group 40.2% patients show complete improvement, 26% show moderate improvement, 19.3% show mild improvement and 14.5% show no improvement. In placebo group 9.4% patients show complete improvement, 16.6% show moderate improvement, 35% show mild improvement and 39% show no improvement. The overall effects of Insty granules and placebo on post nasal drip after treatment is shown in Table **10** and Figure **11**.

Comparison of treatment before and after

The comparison is made by using paired sample t-test and *p* value is analyzed. Test drug is more significant in controlling the symptoms of cold and flu than placebo drug.

DISCUSSION

Common cold viruses and flu infections are the foremost causes of physician visits in the United States, affecting a significant portion of the population. The common cold, though comparatively minor in symptomatology and for a significant number of days of work lost or school. Influenza, although in the USA accounts for annually 36,000 deaths, it is as a preventable disease and vaccines and antiviral drugs may be useful in the prevention and treatment of influenza. However, scope and efficiency of these agents are inadequate. Therefore, most of the orthodox interventions for colds and flu are prescribed for the symptomatic relief with over the counter drugs (OTC) medications. Natural therapies in the form of dietary supplements, immunostimulants and antiviral botanicals can maintain the body's natural defenses. This may lead to decrease in the incidence of influenza and cold, shortens the duration, decreases the

Table 10. Comparison of post n nasal drip after treatment in insty granules group and placebo group.

Level of Improvement	Complete improved	Moderate improved	Mild improved	No improved	*P value*
Insty granules	133(40.2%)	86(26%)	64(19.3%)	48(14.5%)	0.0001
Placebo	31(9.4%)	55(16.6%)	116(35%)	129(39%)	

Intensity of symptoms and prevent complications [9]. The positive results of this study for the Insty granules correspond with the pharmacological actions of herbs present in the Insty granules. The results of this study proved the advantage of the treatment with the fixed fluid extract combination of herbs in cold and flu that was evidently superior to placebo. The tolerability of Insty granules was very good and comparable to placebo, no adverse events were reported. In conclusion our results show that Insty granules was very effective in the treatment of cold and flu when compared to placebo.

REFERENCES

1. Rosenstein N, Phillips WR, Gerber MA, Marcy SM, Schwartz B, Dowell SF. The common cold-principles of judicious use of antimicrobial agents. Pediatrics. 1998; 101 (Supplement 1):181-4.
2. Fendrick AM, Monto AS, Nightengale B, Sarnes M. The economic burden of non-influenza-related viral respiratory tract infection in the United States. Ann Intern Med. 2003; 163(4):487-94.
3. National Institute of Allergy and Infectious Diseases. Common cold. 2013. [Available from: http://www.niaid.nih.gov/topics/commoncold/Pages/default.aspx.
4. Turner RB. Epidemiology, pathogenesis, and treatment of the common cold. Ann Allergy Asthma Immunol. 1997; 78(6):531-9.
5. National Hospital Ambulatory Medical Care Survey. Outpatient Department Summary. 2010. [Available from: http://www.cdc.gov/nchs/data/ahcd/nhamcs_outpatient/2010_opd_web_tables.pdf.
6. Ebell MH, Lundgren J, Youngpairoj S. How long does a cough last? Comparing patients' expectations with data from a systematic review of the literature. Ann Fam Med. 2013; 11(1):5-13.
7. Winther B, Gwaltney JM, Jr., Mygind N, Turner RB, Hendley JO. Sites of rhinovirus recovery after point inoculation of the upper airway. JAMA. 1986; 256(13):1763-7.
8. Mossad SB. Treatment of the common cold. BMJ. 1998; 317(7150):33-6.
9. Roxas M, Jurenka J. Colds and influenza: a review of diagnosis and conventional, botanical, and nutritional considerations. Altern Med Rev. 2007; 12(1):25-48.