RANDOMIZED DOUBLE BLIND PLACEBO CONTROLLED CLINICAL STUDY OF CYMBOPOGAN CITRATUS IN INFLUENZA

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KEYWORDS: Cymbopogan Citratus, Influenza, Lemon Grass.

ABSTRACT

Background: Influenza, or flu, is a respiratory illness that is caused by a virus. As Influenza is known to be highly contagious and thereby affecting working community at large, a natural; cost effective remedy can help sail through the course of illness with much ease. The plant Cymbopogan citratus (DC) Stapf. commonly known as Lemon grass belongs to Poaceae family and is a native of tropical countries. Various studies have been done on the plant to reveal its potential therapeutic effects. Thus this study undertook to evaluate its efficacy in the management of Influenza and its symptoms.

Methodology: Randomized double blind placebo controlled clinical study. 62 patients of age group 20-50 years, suffering from Influenza and fulfilling the diagnostic criteria were selected and randomly grouped into trial (Group I - 31 patients) and control group (Group II - 31 patients received the Placebo - Distilled water 25ml 3 times daily). Both the groups were given Paracetamol 500mg/kg body weight as rescue medicine if required.

Observation & Results: The signs and symptoms of Influenza which were exhibited in patients when subjected to the Trial medication showed good results. The quality of life in them was better compared to control group.

Conclusion: The current study helped to confirm the effect of the plant Cymbopogan citratus (DC) Stapf. in influenza. In Trial group, significantly better remission of associated signs and symptoms of influenza was found compared to control group. This would help us create an increased awareness amongst the public about the use of herbal medicines in either cure or as add on therapy in the management of Influenza.

INTRODUCTION

Influenza mostly referred as flu is an acute respiratory illness caused commonly by influenza A or B virus. It is one of the worst known pandemics which took the life of 50 million people. The respiratory secretions of infected persons contain significant numbers of influenza virus particles, so infection can be transmitted by sneezing and coughing through large particle droplets[1].

The mean period of influenza virus shedding in immune competent adult patients is about 5 days but may continue for up to 10 days or more - especially in children, elderly adults, chronic disease patients and immune compromised hosts. Typically influenza starts with the abrupt onset of high-grade fever, myalgia, headache and malaise. These symptoms are followed by symptoms of respiratory issues like unproductive cough, sore throat or nasal congestion and discharge.

The illness varies from mild to severe suffering, sometimes ending up in complications too[2]. As Influenza is known to be highly contagious and there by affecting working community at large
Inclusion Criteria: Verified cases of influenza were enrolled for the study with fever ≥100.4°F with at least one respiratory symptom of influenza which is within 48 hrs of onset.

Exclusion Criteria: Pregnant women, breast feeding ladies, suspected bacterial infections, H/o antiviral therapy, recent participation in any other clinical trial, patients with any other prior illness, who have received anti influenza and swine flu vaccination, suffering with any chronic diseases and high risk cases.

6. Randomization & Grouping: Randomly patients were grouped into trial and control group using simple random technique adopting random number generator. Group 1 contained 31 patients who received the trial drug (Arka of Cymbopogon citratus) and Group 2 contained 31 patients who received the placebo (distilled water).

7. Intervention: Written informed consent was taken from every patient recruited for the trial. Arka and distilled water were both administered in the dose of 25ml three times a day orally for a period of 5-7 days. Rescue medicine paracetamol was advised to be taken by both the groups only on having fever or any discomfort.

8. Assessment Criteria: The fever was recorded in degree Fahrenheit and other symptoms were recorded in the scoring scale of 10 to 0. Visual analogue scale was used to assess pain.

9. Follow Up and Assessment: alternate days follow up was done for 7 days and the findings were recorder.

10. Reporting of Complication/Side Effects/Adverse Events: Proper recording of adverse events in the trial group if any was done in the case sheet.

CTR registration number: Trial REF/2016/10/012456

Observations
- A total of 31 patients in both groups in each group were enrolled. Group I-31 patients received trail drug and Group II-31 patients received the Placebo (Distilled water 25ml 3 times daily).
- There were 15 male and 16 female in Group I and 19 male and 12 female in Group II.
- The age group of patients in Group I belonged to 21 to 50, whereas 28 to 50 in Group II.
- Fever being the main symptom, the temperature in the two groups ranged from a minimum of 100.6°F to maximum of 103°F in Group I and 101°F to 103°F in Group II.
There was a drop in mean temperature in both groups seen before and after the treatment. (See details in Table 01 and Graph 1).

The details of temperature of all the 31 patients of the two groups is charted in table 03 & 04 and graph.

Other associated symptoms were recorded in the scoring scale of 10-0 and visual analogue scale for pains, details of their mean value of all 31 patients in each group is charted in Table 04 and diagrammatically represented in graph 04.

Results

The signs and symptoms of Influenza showed improvement in patients when subjected to the Trial medication. The faster remissions of associated symptoms were seen in the trail group compared to the controlled group. The current study helped to prove the effect of Cymbopogon citratus (DC) Stapf in the disease influenza. This would help us create an increased awareness amongst the public about the use of herbal medicines in either cure or as add on therapy in the management of Influenza.

### Table 1: Showing parameters

| Parameters          | Group I | Group II |
|---------------------|---------|----------|
| Number of samples:  | 31      | 31       |
| Age                 | 21-50   | 28-50    |
| Gender              |         |          |
| Male                | 15      | 19       |
| Female              | 16      | 12       |
| Fever (Min- max)    | 100.6-103 | 101-103 |
| Fever (Mean in Degree F) |     |
| Before treatment    | 101.67  | 101.93   |
| After treatment     | 99.60968 | 99.74839 |

### Table 2: Showing Temperature changes of the two groups, before and after treatment

| Subjects | Fever (in Degree F) | Subjects | Fever (in Degree F) |
|----------|---------------------|----------|---------------------|
| 1        | 102.2 100           | 1        | 102.2 100           |
| 2        | 101 100             | 2        | 102 100.2           |
| 3        | 100.8 99            | 3        | 102.8 100           |
| 4        | 102.6 100           | 4        | 102.4 100           |
| 5        | 100.6 100           | 5        | 101.8 99            |
| 6        | 102.5 100.1         | 6        | 102.2 100           |
| 7        | 100.6 98.6          | 7        | 101.2 100           |
| 8        | 102 99              | 8        | 102 100.2           |
| 9        | 101 99              | 9        | 101 99              |
| 10       | 101.8 100           | 10       | 102 98.8            |
| 11       | 102 100.2           | 11       | 102.6 100           |
| 12       | 102 100             | 12       | 101.2 100           |
| 13       | 103 100             | 13       | 101.8 99.2          |
| 14       | 102 100             | 14       | 101.6 100.1         |
| 15       | 101.6 99            | 15       | 102.1 100           |
| 16       | 102 100             | 16       | 102 100             |
| 17       | 100.9 99            | 17       | 101.8 99.8          |
| 18       | 100.8 99.8          | 18       | 101 100             |
| 19       | 101.8 99.6          | 19       | 103 99              |
| 20       | 101 100             | 20       | 102.4 100           |
| 21       | 102.8 99            | 21       | 102.2 99.6          |
| 22       | 102 98              | 22       | 102 100             |
| 23       | 100.6 98.6          | 23       | 102 99              |
| 24       | 101.2 100           | 24       | 102 100.1           |
### Table 3: Showing mean of the grades in associated symptoms of the two group, before and after treatment on a scoring scale of 0-10

| Associated Symptoms - (Average/ Mean) | Extreme coldness (chills shivering, shaking (rigor)) | Cough | Nasal congestion | Running nose | Sneezing | Fatigue | Irritated, watering eyes | Redness in eyes/face/mouth/throat/nose | Body aches | Pain in Joints | Throat Ache | Headache |
|--------------------------------------|-----------------------------------------------------|-------|-----------------|-------------|---------|--------|--------------------------|-------------------------------------|-----------|--------------|-----------|----------|
| Before treatment                     | 0.7742                                              | 1.19  | 0.29032         | 2.67742     | 1.903   | 0.484  | 0                         | 0.29032                                           | 1.90323   | 0.8065       | 0.6129    | 1.871    |
| After treatment                      | 0                                                  | 0     | 0               | 0           | 0       | 0      | 0                        | 0                                                  | 0         | 0            | 0         | 0        |
|                                      |                                                     |       |                 |             |         |        |                           |                                                     |           |              |           |          |
### Statistical Analysis of the study

**General Linear Model**

#### Descriptive Statistics

| Groups  | Mean | Std. Deviation | N  |
|---------|------|----------------|----|
| Trial   | .00  | .000           | 31 |
| Control | .39  | 1.230          | 31 |
| Total   | .19  | .884           | 62 |
| Trial   | .00  | .000           | 31 |
| Control | .06  | .359           | 31 |
| Total   | .03  | .254           | 62 |

#### Tests of Within-Subjects Effects

| Measure | Type III Sum of Squares | df | Mean Square | F    | Sig. |
|---------|--------------------------|----|-------------|------|------|
| Change  | .806                     | 1  | .806        | 3.614| .062 |
| Change * groups | .806 | 1 | .806 | 3.614 | .062 |
| Error (change) | 13.387 | 60 | .223 |

The above table shows there is no significant difference found between the parameter of irritability between the trial group and control group.

#### Profile Plots

![Profile Plot](image)

#### T-Test

| Groups | N  | Mean | Std. Deviation | Std. Error Mean |
|--------|----|------|----------------|-----------------|
| Trial  | 31 | .00  | .000           | .000            |
| Control| 31 | .61  | 1.706          | .306            |

| t-test for Equality of Means |
|-----------------------------|
| t  | df | Sig. (2-tailed) | Mean Difference |
|----|----|-----------------|-----------------|
| Irrit_remission | -2.000 | 60 | .050 | -.613 |
The above table shows there is significant difference found between the parameter of fatigue remission with P value 0.050. The trial group was significantly better in irritability remission than control group.

**General Linear Model**

| Measure: MEASURE_1 | Type III Sum of Squares | df | Mean Square | F   | Sig.  |
|--------------------|--------------------------|----|-------------|-----|-------|
| Change             | 2.613                    | 1  | 2.613       | 7.003 | .010  |
| Change * groups    | .000                     | 1  | .000        | .000 | 1.000 |
| Error (change)     | 22.387                   | 60 | .373        |     |       |

The above table shows there is no significant difference found between the parameter of redness in between the trial and control group

**Profile Plots**

The above table shows there is no significant difference found between the parameter of redness remission with the trial group and control group with P value 0.650

**General Linear Model**

| groups          | Mean | Std. Deviation | N  |
|-----------------|------|----------------|----|
| Redness_rem      |      |                |    |
| Trial            | .32  | 1.013          | 31 |
| Control          | .45  | 1.207          | 31 |
| Total            | .39  | 1.107          | 62 |

The above table shows there is no significant difference found between the parameter of Pete_rash_BT with the trial group and control group with P value 0.650

**General Linear Model**

| groups          | Mean | Std. Deviation | N  |
|-----------------|------|----------------|----|
| Pete_rash_BT    |      |                |    |
| Trial           | .00  | .000           | 31 |
| Control         | .00  | .000           | 31 |
| Total           | .00  | .000           | 62 |

The above table shows there is no significant difference found between the parameter of Pete_rash_at with the trial group and control group with P value 0.650
Tests of Within-Subjects Effects

Measure: MEASURE_1

| Source               | Type III Sum of Squares | df | Mean Square | F    | Sig. |
|----------------------|-------------------------|----|-------------|------|------|
| Change               | Sphericity Assumed      | .000 | 1 | .000 | .  | .  |
| Change * groups      | Sphericity Assumed      | .000 | 1 | .000 | .  | .  |
| Error (change)       | Sphericity Assumed      | .000 | 60 | .000 | .  | .  |

The above table shows no change.

Profile Plots

T-Test

Group Statistics

| groups               | N  | Mean | Std. Deviation | Std. Error Mean |
|----------------------|----|------|----------------|-----------------|
| Pete_rash_remission  |    |      |                |                 |
| Trial                | 31 | .00  | .000a          | .000            |
| Control              | 31 | .00  | .000a          | .000            |
| a. t cannot be computed because the standard deviations of both groups are 0. |

General Linear Model

Descriptive Statistics

| Groups              | Mean | Std. Deviation | N  |
|---------------------|------|----------------|----|
| Bodyache_BT         |      |                |    |
| Trial               | 1.90 | 2.226          | 31 |
| Control             | 3.19 | 2.212          | 31 |
| Total               | 2.55 | 2.295          | 62 |

| Bodyache_AT         |      |                |    |
| Trial               | .00  | .000           | 31 |
| Control             | .00  | .000           | 31 |
| Total               | .00  | .000           | 62 |

Tests of Within-Subjects Effects

Measure: MEASURE_1

| Source               | Type III Sum of Squares | df | Mean Square | F    | Sig. |
|----------------------|-------------------------|----|-------------|------|------|
| Change               | 201.323                 | 1  | 201.323     | 81.742 | .000 |
| Change * groups      | 12.903                  | 1  | 12.903      | 5.239 | .026 |
| Error (change)       | 147.774                 | 60 | 2.463       |      |      |

The above table shows there is significant difference found between the parameter of body pain in between trial and control group. The trial group was found to be significantly better than control group.

Profile Plots
T-Test

| Group Statistics |
|------------------|
| **Groups**  | **N** | **Mean** | **Std. Deviation** | **Std. Error Mean** |
| Bodyache_remission | Trial | 31 | 1.81 | 1.815 | .326 |
|                 | Control | 31 | 3.71 | 2.003 | .360 |

| Independent Samples Test |
|---------------------------|
| **t-test for Equality of Means** |
| **Bodyache_remission** | **t** | **df** | **Sig. (2-tailed)** | **Mean Difference** |
|                          | -3.920 | 60 | .000 | -1.903 |

The above table shows there is significant difference found between the parameter of fatigue remission. The trial group was significantly better in body ache remission than control group.

General Linear Model

| Descriptive Statistics |
|-------------------------|
| **groups**  | **Mean** | **Std. Deviation** | **N** |
| Pain_BT      | Trial     | .81 | 1.515 | 31 |
|              | Control   | 1.33 | 1.768 | 30 |
|              | Total     | 1.07 | 1.652 | 61 |
| Pain_AT      | Trial     | .00 | .000 | 31 |
|              | Control   | .00 | .000 | 30 |
|              | Total     | .00 | .000 | 61 |

| Tests of Within-Subjects Effects |
|----------------------------------|
| **Measure: MEASURE_1** |
| **Source** | **Type III Sum of Squares** | **df** | **Mean Square** | **F** | **Sig.** |
| Change     | 34.903 | 1 | 34.903 | 25.821 | .000 |
| Change * groups | 2.116 | 1 | 2.116 | 1.566 | .216 |
| Error (change) | 79.753 | 59 | 1.352 | |

The above table shows there is no significant difference found between the parameter of pain in between the trial and control group.

Profile Plots

T-Test

| Group Statistics |
|------------------|
| **Groups**  | **N** | **Mean** | **Std. Deviation** | **Std. Error Mean** |
| Pain_remission | Trial | 31 | .84 | 1.485 | .267 |
|                | Control | 31 | 1.97 | 2.415 | .434 |

| Independent Samples Test |
|---------------------------|
| **t-test for Equality of Means** |
| **Pain_remission** | **t** | **df** | **Sig. (2-tailed)** | **Mean Difference** |
|                      | -2.217 | 60 | .030 | -1.129 |
The above table shows there is significant difference found between the parameter of pain remission with P value 0.030. The trial group was significantly better in body ache remission than control group.

**General Linear Model**

| Descriptive Statistics | groups | Mean | Std. Deviation | N   |
|------------------------|--------|------|----------------|-----|
| Headache_BT            | Trial  | .35  | .950           | 31  |
|                        | Control| .29  | 1.006          | 31  |
|                        | Total  | .32  | .971           | 62  |

The above table shows there is no significant difference found between the parameter of throat pain remission in between the trial and control group.

**Profile Plots**

![Profile Plots](image)

**T-Test**

| Group Statistics | groups | N | Mean | Std. Deviation | Std. Error Mean |
|------------------|--------|---|------|----------------|-----------------|
| Throat_remission | Trial  | 31 | .48  | 1.151          | .207            |
|                  | Control| 31 | .35  | 1.142          | .205            |

The above table shows there is no significant difference found between the parameter of throat pain remission in between the trial and control group.

**General Linear Model**

| Descriptive Statistics | Groups | Mean | Std. Deviation | N |
|------------------------|--------|------|----------------|---|
| Headache_BT            | Trial  | 1.87 | 2.109          | 31|
|                        | Control| 1.16 | 2.018          | 31|
|                        | Total  | 1.52 | 2.078          | 62|

The above table shows there is no significant difference found between the parameter of throat pain remission in between the trial and control group.

**General Linear Model**

| Descriptive Statistics | Groups | Mean | Std. Deviation | N |
|------------------------|--------|------|----------------|---|
| Headache_AT            | Trial  | .00  | .000           | 31|
|                        | Control| .00  | .000           | 31|
|                        | Total  | .00  | .000           | 62|
The above table shows there is no significant difference found between the parameter of headache remission in between the trial and control group.

**Profile Plots**

![Profile Plot Image]

**T-Test**

**Group Statistics**

| groups         | N  | Mean | Std. Deviation | Std. Error Mean |
|----------------|----|------|----------------|-----------------|
| Trial          | 31 | 1.65 | 1.582          | .284            |
| Control        | 31 | 1.29 | 2.101          | .377            |

**Independent Samples Test**

| t-test for Equality of Means | t | df | Sig. (2-tailed) | Mean Difference |
|------------------------------|---|----|-----------------|-----------------|
| Headache remission           | .751 | 60 | .455            | .355            |

The above table shows there is no significant difference found between the parameter of headache remission in between the trial and control group.

**DISCUSSION**

The efficacy of the drug *Cymbopogon citrates* (DC.) Stapf in Influenza may be attributed to its pharmacological properties like Rasa Panchaka namely Katu, Tikta Rasa, Laghu Teekshna Guna, Katu Vipaka, Ushna Veerya and Karas like Swedajanana, Jwaraghana, Deepana Paachana, Ruchya, Vatashamana, Shleshmaghna as mentioned in the Ayurveda classics [7]. The phyto constituents present in the drug like alkaloids, saponins, tannins and flavonoids are also supportive for the therapeutic activity of the drug. As there is faster remission seen in the trial group with respect to the associated symptoms of influenza this drug can be tried on a bigger sample size to prove its effectiveness on a wider scale. The drug being abundantly available makes it even more cost effective. Hence as shown in the current study due its better tolerance amongst the patients it can be aptly used as add on therapy in the management of influenza cases.

**CONCLUSION**

In Trial group, significantly better remission of associated signs and symptoms of influenza was found compared to control group. As paracetamol was used as rescue medicine in both the groups, no much significant difference was found between the trial and control group in the reduction of fever. The current study helped to confirm the effect of the plant *Cymbopogon citrates* (DC) Stapf in the disease influenza and proved to help sail through the course of illness with much ease.

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Graph 1: Showing - Changes in temperature in the two groups: before and after treatment

Graph 2: Showing - Changes in temperature of subjects in Group I: before and after treatment

Graph 3: Showing - Changes in temperature of subjects in Group II: before and after treatment
Graph 4: Showing - Baseline characteristics of 62 patients their symptoms, who were randomized to receive the drug (Group I) and Placebo (Group II)