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PROSPECTIVE INTERVENTIONAL STUDY TO EVALUATE THE EFFECT OF SIDDHA INTERVENTION KABASURA KUDINEER AS A PROPHYLACTIC MEASURE AMONG HIGH RISK POPULATION EXPOSED TO COVID-19

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ABSTRACT

Background: Covid19 a massive threat to public health worldwide addressed the need of Clinical interventions to decrease the incidence and severity of illness. **Objectives:** Aim of the study is to assess the effectiveness of Siddha intervention- Kabasura Kudineer in prophylaxis of COVID-19 with the assessment of laboratory parameters before and after intervention. The secondary objective is observance of any Adverse Reaction due to consumption of Kabasura Kudineer. **Methods:** The subjects selected for the study are initially subjected to clinical examination, biochemical Investigation, assessment of Immune status and quality of life. Kabasura Kudineer was given to the subjects and advised to take it as per the prescribed dosage for 14 days. Subjects was observed for occurrence of mild to moderate symptoms of COVID-19. The follow-up period is another 14 days and after that, the clinical assessment was carried out. **Results:** The clinical assessment of 400 subjects enrolled showed improvement in quality of life through WHO-QOL-BREF assessment. The ISQ score is increased in all cases after the intake of Kabasura Kudineer and follow-up. There was no incidence of Covid 19 in subjects taken the Siddha intervention. Haemoglobin level of 76% Subjects taken KSK showed strong positive correlation ($r = 0.9$) and great significance ($t18 = -5.29$, $p < 0.001$) with 95% CI. The RBC count value of 56% subjects treated with KSK exhibited strong positive correlation ($r = 0.87$) and significance ($t13 = 4.41$, $p < 0.001$). **Conclusion:** No incidence of COVID-19 in high risk population of this interventional study concludes that the immunomodulatory activity of the drug may support for the prevention of Covid 19 infection.

KEYWORDS : Kabasura kudineer, Prophylactic, adverse reaction, Immunomodulatory activity.

INTRODUCTION:

The novel coronavirus disease COVID-19 is a respiratory tract infection caused by a newly emergent coronavirus, SARS-CoV-2, that was first recognized in Wuhan, China, in December 2019.[1] COVID-19 is a massive threat to public health worldwide. Despite all the advancements in the 21st century in the field of medical sciences and advanced research, health problems and diseases have again led humankind to great distress. It has witnessed three major viral outbreaks in the current century- SARS-CoV, MERS and SARS-COV-2 whereas the latter SARS-CoV-2, highlights the need for control in this highly pathogenic epidemic.

Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, Autoimmune disorders, cancer, etc more likely to develop serious illness. The SARS-Cov receptor binding domain binds with the viral hotspot of ACE receptor and thus facilitates the viral entry into human cells. Several naturally selected mutations in the SARS-CoV RBM surround these hotspots and regulate the infectivity, pathogenesis, and human-to-human transmissions of SARS-CoV.[2] Hence clinical interventions to decrease the incidence and severity of COVID-19 are needed immediately.

Although there are lot of Clinical studies are ongoing all over the world, there is a scope for alternative systems of Medicine also in these types of pandemic conditions, where masses of population are affected. Moreover Siddha system is having positive experience in the management of previous epidemic diseases like Chikungunya and Dengue. As per the Siddha classical literature of *TheranKarisal*, clinical symptoms of COVID-19 is equated to *Kabasuram*.

KabaSura Kudineer (KSK) indicated for *Kabasuram* consists of 15 herbals ingredients which individually has anti-viral and immune-modulatory activity. The studies reported that 10 phytocompounds found in KSK act as ligands to bind with viral proteins to prevent the binding of host receptors. Of these Cucurbitacin B (-112.09), Cardiofoliolide (-111.5), Apigenin (-98.84) and Pyrethrin (-92.98) were observed as more effective with less bind energies required for binding with spike proteins to prevent the fusion lead viral replication.[3] Hence KSK was found to be effective in preventing novel corona virus binding and replication.

The molecular docking studies on Anti-viral effects phytocompounds from Kabasura kudineer on SARS-CoV-2 shows the compounds inhibiting COVID-19, giving the better energy score compared to synthetic drugs. Based on the binding energy score, these compounds can be used to develop effective antiviral drugs.[4]

The antiviral activity of KSK against SARS-CoV-2 was assessed in Vero E6 cells and followed by an RT-PCR assay. KSK significantly inhibited SARS-CoV-2 replication in Vero E6 cells. These data indicate that KSK prevents the attack of its virus, rendering the use of these a novel COVID-19 infectious diseases strategy.[5]

KSK was analyzed for the determination of organoleptic characters, preliminary phytochemical analysis, physico- chemical analysis, TLC photo documentation and HPTLC fingerprint studies.[6] Toxicological studies on KSK showed that it is safe.[7]

Recent studies confirmed that KSK has immunomodulatory and thrombolytic properties in vitro models.[8] Study results showed that KSK manipulates its anti-inflammatory effects mainly through blocking the TLR mediated NF- B signal transduction pathways. KSK could be a potential therapeutic drug for alleviating excessive inflammation in many inflammation-associated diseases like COVID-19.[9] Moreover certain studies proved the significant anti-inflammatory antipyretic and antibacterial activity of kabasura kudineer choornam.[10]

There is a need of clinical studies to address the current challenges of COVID-19, hence an attempt to evaluate Siddha Intervention -*Kabasura Kudineer* as a prophylaxis for COVID-19 infection in healthy adult volunteers or high risk population appearing in the OPD of Siddha Regional Research Institute, Thiruvananthapuram and in high risk areas of Thiruvananthapuram was initiated.

Objective Of The Study:

The objective of the study is to assess the effectiveness of Siddha intervention- Kabasura Kudineer in prophylaxis of COVID-19 with the assessment of laboratory parameters before and after intervention.

The secondary objective is the evaluation of occurrence of adverse drug reaction due to consumption of Siddha Intervention *Kabasura Kudineer.*

Methods:

This is the Prospective Interventional study with Siddha intervention Kabasurakudineer as a prophylactic measure among high risk population exposed to COVID-19 conducted by Siddha Regional Research Institute, Thiruvananthapuram after receiving approval from IHEC and registration in Clinical trial registry.

The participants of the study are adult Male or Female above the age of 18 years to 68 years living in high risk areas. Subjects who are ready to provide written informed consent and who are willing to participate and follow the protocol requirements of the clinical study are included in the study. At the screening visit subject's clinical assessment was done to exclude the presence of any medical or surgical condition that may need immediate medical or surgical intervention.

The Subjects were educated and informed of the common measures to be taken as per the guidelines of Central/State/local health authorities to prevent the spread of the disease. The subjects selected for the study are initially subjected to clinical examination, biochemical Investigation, assessment of Immune status and quality of life.

Siddha Intervention *Kabasura Kudineer* – 60 ml Once a day (Morning - just before the Breakfast) was given to the subjects and advised to take it as per the prescribed dosage for 14 days and submit the drug compliance form. Subjects was observed for fever, sore throat, cough, body pain etc. and other health related mild to moderate symptoms of COVID-19. The follow-up period is another 14 days and after that, the clinical assessment was carried out. The health status and the immunity of the subjects was assessed after the follow-up phase using WHO-QOL-BREF Scale and ISQ During the visits of Clinical assessment, vitals were checked, any ADR occurred during the period was also be recorded.

The study was conducted, recorded and reported in accordance with GCP-ASU guidelines laid down for ASU drugs and the ICMR Ethical guidelines for biomedical research on human participants' amendment in 2006. During the conduct of the clinical study, rights, safety and wellbeing of the study participants was given prime importance. The study drug was prepared with compliance to Good Manufacturing practices (GMP) as applicable for Siddha products in India.

Outcome:

The main parameter for outcome is the "incidence of COVID-19 cases in interventional group".

The data of biochemical parameters was evaluated; the Immune status and quality of life in subjects included for the study were assessed to confirm the prevention of Covid-19 with Siddha intervention.

Data Analysis:

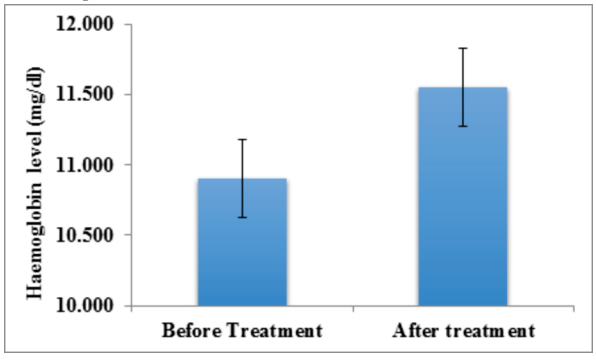
Based on the data collected the statistical analysis will be taken up on test subjects before and after the study. Clinical symptoms and Laboratory parameters was subjected to statistical analysis using Statistical Package for Social Sciences (SPSS) 17.0 version with appropriate statistical methods.

RESULTS & DISCUSSION

Between June 2020 and December 2020, around 400 cases fulfilling the inclusion criteria were enrolled for the study. The clinical assessment of 400 subjects enrolled showed improvement in quality of life through WHO-QOL-BREF assessment. The ISQ score is increased in all cases after the intake of *Kabasura Kudineer* and follow-up. There was no incidence of Covid 19 in subjects taken the Siddha intervention.

The limited participants only were interested in laboratory Investigation, i.e 25 Patients investigated before and after the trial, 60 Patients before the trial. The laboratory investigation parameters carried out in subjects included in the study are CBC (Complete Blood Count), ESR and RBS(Random Blood Sugar). There is slight variation in the biochemical parameters of subjects enrolled for the study.

Out of the 25 people who completed 14 days of treatment, 19 people(76%) showed an increase in the Hemoglobin%. That is the Haemoglobin level of 76% Subjects taken KSK showed strong positive correlation ($r = 0.9$) and great significance ($t_{18} = -5.29$, $p < 0.001$) with 95% CI. Three out of 25 people had same Hb% before and after treatment. In four out of 25 cases a mild drop in Hb% was noted.

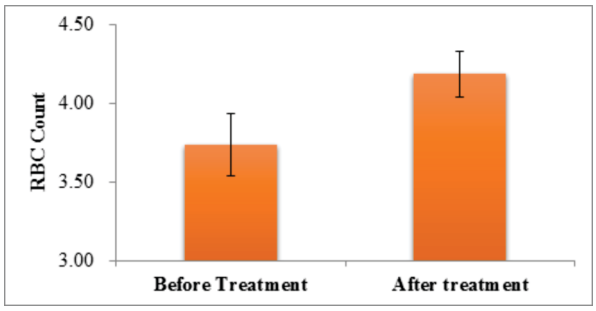


Similarly 56% (14 out of 25) of the study population had a visible change of increase in the RBC count after completing the treatment. That is the RBC count value of 56% subjects treated with KSK exhibited strong positive correlation ($r = 0.87$) and significance ($t_{13} = 4.41$, $p < 0.001$).

4/25 people had the same RBC count before and after treatment whereas in 7 out of 25 cases there was a mild dip in RBC count.

In most of the cases the total count (TC) was within normal limits prior to and after completion of treatment. But a few patients (3/25) who had leucopenia (<4000cells/cmm) before starting the treatment showed normal WBC count after

completion of the treatment. Out of the 25 cases evidence of thrombocytopenia was not seen among any persons, although 6/25 persons who had platelet count between 1.5 lakhs and 2 lakhs at the initiation of treatment showed a mild elevation in count to more than 2 lakhs after completion of treatment.



13/25 had an elevated ESR count of >20mm/hour before starting the treatment. Of these 11/25 persons showed a slight reduction in ESR rate at the end of treatment, eventhough it hasn't reached the baseline. 5/25 cases showed a mild increase in the sedimentation rate after completion of treatment. Random blood sugar doesn't show much change with treatment, 4/25 cases showed an increase in RBS after treatment compared to that before and 3/25 cases had a drop in RBS after treatment.

So in order to conclude the laboratory findings of patients before and after treatment, the hemoglobin and RBC count of the cases improved after completing the 14 days prophylactic medication. A few of the patients with leucopenia showed an increase in WBC count after completion of medication. Although platelet count was normal for all cases a slight increase in the platelet count was noted after 14 days. ESR also showed a mild dip for majority of the people but doesn't reach the normal value.There is no adverse drug reaction / adverseeffects reported by the subjects taken *Kabasura Kudineer* for 14 days.

According to the foregoing reviews, the mammalian erythrocytes has the ability to interact with inflammatory molecules in the blood, thereby regulating immune response. The Internal components of erythrocytes such as hemoglobin and heme are also formidable facets of innate immunity, capable of generating antimicrobial reactive oxygen species (ROS) to defend against invading hemolytic microbes, as well as promoting pathologic inflammatory and auto-immune responses.[11] One important immunomodulatory property of human erythrocytes is their propensity to bind a wide variety of chemokines.[11] Hence in this study the improvement in HB and RBC count of patients may help to improve the immunity and prevent the COVID infection.

CONCLUSION:

This prophylactic Siddha Interventional study in high risk population exposed to COVID-19, explores that *Kabasura kudineer* intake for fourteen days can prevent the incidence of Covid19. The laboratory investigation of the included cases showed improvement in hemoglobin and RBC count. Increase in hemoglobin may boosts oxygen supply to damaged cells, tissues and organs thereby strengthening the body's immune system. The immunomodulatory activity of the drug may support for the prevention of Covid infection.

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