

COVID-19 and beta glucans: Pilot study shows two strains can help control biomarkers of clinical severity

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The significant and steady decrease in IL6 and D-Dimer substantiate the anti-inflammatory and anti-coagulation benefits of beta glucans. ©GN Corporation

A pilot study in India has reported that intake of two strains of beta glucans can lower cytokine storm and coagulopathy biomarkers in COVID-19 patients.

The mild symptoms of COVID-19 involve fever, cough or runny nose, but cytokine storm and coagulopathy have been linked to the onset of severe cases of COVID-19 which required oxygen, ventilation and may led to organ failure and death. Patients with co-morbidities are prone to a rapid progression of the disease.

Cytokine storm is identified by the increase in biomarkers such as IL6, C-reactive protein (CRP), the neutrophil to lymphocyte ratio (NLR), and the decrease of lymphocyte to CRP ratio (LCR) and the leukocyte-CRP ratio (LeCR).

Coagulopathy is assessed by the increase in D-Dimer and ferritin.

Worldwide, several pharmacological interventions involving zinc, ascorbic acid, anti-coagulants and steroids have been administered to control these biomarkers but they tend to have associated side effects.

“There have been reports of bleeding diathesis after anti-coagulants, and the appropriate timing for administration of these pharmacological agents are still being debated. At this hour, a safer and more efficient interventional strategy to modulate the immune system to prevent or tackle the cytokine storm and to manage the coagulopathy cascade is needed,” researchers said in a study published on the preprint server medRxiv.

In this study, they studied the effect of two strains of beta-glucans, produced by *Aureobasidium pullulans* (AFO-202 and N-163 strains) as an alternative adjunct treatment in patients with COVID-19.

In basic, translational and clinical studies, AFO-202 has been found to be an immune enhancer whereas N-163 has been found to have anti-inflammatory, anti-fibrotic and immuno-modulatory potentials, according to one of the authors, Dr Samuel JK Abraham.

For this study, Japan-based firm GN Corporation provided the AFO-202 and N-163 strains. The former is marketed under the brand Nichi-Glucan, and comes in granule form.

The latter is available under the brand Nichi-Glucan-REFIX and comes in gel form.

GN Corporation had initially planned for a clinical trial on [Nichi-Glucan](#) earlier this year, but due to logistical issues, the trial was not initiated.

This current study is the first trial it has conducted on beta-glucans, according to Abraham, who is also head of R&D at GN Corporation.

The study is now being peer reviewed.

Study design

A total of 24 COVID-19 positive patients were recruited (18 to 62 years old), and randomly divided into three groups (n=8 each). Subjects with or without co-morbidities were enrolled, they had mild to moderate COVID-19 symptoms but required hospitalisation, those who required intensive care were excluded.

Group 1 was the control, receiving the standard treatment of Remdesivir, Solumedrol, Clexane and broad spectrum antibiotic bronchodilators.

Group 2 received the standard treatment along with AFO-202 beta glucan supplement (3g/day) for 30 days.

Group 3 received standard treatment along with AFO-202 beta glucan (3g/day) and N-163 beta glucan (10g/day) also for 30 days.

The primary outcome was improvement in the clinical symptoms of COVID-19 which was the time taken for improvement and complete recovery.

The secondary outcome was mortality, progression to critical care admission, oxygen/life-support and tests for biochemical parameters such as D-Dimer, IL6, erythrocyte sedimentation rate (ESR), CRP, NLR, LCR and LeCR.

The average duration of stay in the hospital was not statistically different across all three groups, at 4.25 days in group 1, 4.75 days in group 2 and 4.125 days in group 3.

There was no mortality in any of the groups. None of the subjects required ventilation.

Cytokine storm control

IL-6 levels have been reported to be significantly elevated and associated with adverse clinical outcomes in COVID-19.

In the control group, IL6 values decreased from an average of 7.395 pg/ml to 3.16 pg/ml in day 15 but increased to 55.37 pg/ml at day 30.

However, in group 2 and 3, IL6 levels steadily decreased from day 15 to 30. The results were statistically significant ($p=0.0214$).

Hence, the IL-6 values only decreased to normal values in the beta glucan groups.

Other significant predictors of severity in COVID-19 such as NLR, LCR and LeCR were also maintained at normal range in the beta glucan groups.

Coagulopathy control

D-dimer is a good predictor of mortality in COVID-19 patients, where a D-dimer level greater than 0.5 $\mu\text{g/ml}$ is associated with severe infection, and a value greater than 1 $\mu\text{g/ml}$ is associated with increasing odds of in-hospital death in patients with COVID-19.

The D-Dimer values in group 1, which was on average 751 ng/ml at baseline, decreased to 143.89 ng/ml on day 15, but increased to 202.5 ng/ml on day 30.

In groups 2 and 3, D-Dimer levels decreased on day 15 and remained at normal levels until day 30. This was statistically significant ($p=0.013$).

Two strain power

The significant and steady decrease in IL6 and D-Dimer substantiate the anti-inflammatory and anti-coagulation benefits of beta glucans.

"We are excited about the findings to see the control of IL-6 and D-Dimer in COVID-19 patients, which are biomarkers of cytokine storm and coagulopathy and plan to collaborate with organisations, who can take this concept to a vaccine adjuvant product to help the vulnerable population," Dr Abraham said.

GN Corporation recently launched the Nichi-Glucan REFIX supplement.

At the moment, it does not have a product containing both types of beta glucans.

GN Corporation is now studying the effect of these two Nichi Glucans on gut microbiome and metabolomics.

Future studies

As this is a pilot clinical study, researchers say larger multi-centric clinical trials are warranted to validate the findings and recommend beta-glucans as an adjunct in the management of COVID-19 and the ensuing long COVID-19 syndrome.

"We conducted this study at the time of a decline in the second wave in India when infection due to the delta variant of SARS-CoV2 virus was gradually emerging as a threat with increased contagiousness,

We have not studied genomic sequencing in the subjects to identify the delta variant virus, and this needs further evaluation to study the efficacy of the beta glucans against emerging variants," researchers said.

<https://doi.org/10.1101/2021.08.09.21261738>

“Beneficial Effects of novel *Aureobasidium Pullulans* strains produced Beta-1,3-1,6 Glucans on Interleukin-6 and D-Dimer levels in COVID-19 patients; results of a randomized multiple-arm pilot clinical study”

Authors: Kadalraja Raghavan, Samuel JK Abraham, et al.