

Metformin: A Novel Adjuvant Drug in Covid Battle Oral Hypoglycemic Drug with Antiviral & Antifungal Effects

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Background

Since last many months it is evident that hyperglycemia (high sugars) in Covid-19 infection has caused worst prognosis and has increased the risk of death in non-diabetic patients as well [1,2]. Not only virus entry but later on the replication is also amplified due to hyperglycemia. Acute hyperglycemia is usually associated with surge of inflammatory mediators [3]. This may lead to “cytokine storm” in the COVID-19. The vital step of binding of SARS-CoV-2 to ACE2 receptors [4] requires glycosylation which is associated with hyperglycemia. Steroids are to be given for life saving indications, but they are associated with temporary, acute hyperglycemia even in non-diabetic patients. Many studies have depicted that the presence of active inflammation and steroid-induced hyperglycemia led to cardiovascular complications [4]. The incidence of mucor mycosis has suddenly increased in post covid infection phase. The various predisposing factors for this are uncontrolled diabetes, long-term corticosteroids, immunosuppressive therapy, renal failure, cirrhosis, burns, and malnutrition [5].

Need of Hour

A drug is needed which will reduce hyperglycemia as well reduce viral activity and helpful in dreaded complication like mucor mycosis.

Balanced Approach

The prompt control of hyperglycemia will hamper the release of cytokines. Judicious and timely use of steroids, prevention and con-

trol of hyperglycemia in Covid-19 infected patients is one of the important lifesaving approaches. It will improve the prognosis.

Metformin

- Metformin, a novel drug can be helpful in reversing hyperglycemia.
- It has antiviral properties too, at molecular level.
- Metformin by its antifungal actions may help in the treatment of mucor mycosis.
- It is readily available and cost effective. And moreover-
- It is widely used with good margin of safety in non-diabetic patients.

Metformin in Diabetes: It is the most widely used oral hypoglycemic agent for type 2 diabetes.

Metformin in Non-Diabetics: It is safely used in non-diabetic indications like polycystic ovary syndrome, cardiovascular disease and various cancers.

Possible Antifungal Role of Metformin in Prevention of Mucor Mycosis: Metformin is well studied for its antifungal actions on *Candida glabrata*. Early diagnosis, aggressive surgical treatment and use of antifungal, Amphotericin -B are the key points in the management [6-8]. Shuying, et al. [9] has shown metformin to potentiate antifungal actions of Amphotericin B [9].

Metformin use Against other Viruses: Metformin has shown the inhibition of viral replication through AMPK activation [10]. Already

it is studied in the treatment of HCV, ZIKA, HIV, HBV and Influenza [11-14]. Possible antiviral role of metformin in Covid 19 treatment:

- a. Metformin activates AMPK and inhibits mTOR pathway.
- b. Such inhibition in Influenza14 and MERS CoV infection15 is well studied.
- c. It helps in prevention of viral replication.
- d. It would be definitely useful for covid 19 as well. Such usage must be encouraged and trials in that direction must be expedited [15-18].

Conclusion

The above discussion indicates the possible promising role of metformin as an adjuvant drug. It reduces hyperglycemia; it is the first line choice in type II diabetes. It has antiviral and antifungal actions and enhances the action of Amphotericin B which is a choice of treatment in mucor mycosis. Urgent trials and recommendations for its broad-spectrum usage as adjuvant are needed.

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