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# Role of Budesonide in Corona Virus Disease: Systematic Review

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**ABSTRACT:**
**Background:** The current COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, raises important questions as to whether pre-morbid use or continued administration of inhaled corticosteroids (ICS) affects the outcomes of acute respiratory infections due to coronavirus.
**Purpose of study:**Inhaled budesonide is a low cost, safe (time censored), effective (number needed to treat of eight) simple and widely available therapeutic option, which can be of great help around the world, particularly in low-income and middle-income countries. Several potential mechanisms might underlie these clinical observations.
**Results:** Inhaled budesonide in early Covid-19 infection significantly reduced the likelihood of requiring urgent care, emergency department consultation and hospitalization.
**Conclusion:** The budesonide group reported greater wellbeing of the patients. Also scales down the need for urgent medical care and reduces recovery time, if given early to Covid-19 patients with mild symptoms.
**Key Words:** Budesonide, COVID, Corona Virus.

## INTRODUCTION

The current COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, raises important questions as to whether pre-morbid use or continued administration of inhaled corticosteroids (ICS) affects the outcomes of acute respiratory infections due to coronavirus[1]. In most individuals, infection with SARS-CoV-2 is either

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asymptomatic or produces mild illness (COVID-19) that resolves spontaneously; yet, a small proportion of patients with COVID-19 develop severe disease, require hospitalisation (often in a critical-care setting) and die. COVID-19 has an initial period characterised by cough and fever, followed after around 8 days in approximately 20% of patients by the development of dyspnoea with pulmonary infiltrates in about 10% [2,3]. Approximately a quarter of patients admitted to hospital developed acute respiratory distress syndrome (ARDS) after a median of 10.5 days after symptom onset [3]. A dysregulated type I interferon response to SARS-CoV-2 with overproduction of proinflammatory cytokines seems to be a key pathogenic mechanism underlying progression to severe COVID-19 and death. Thus, controlling this excessive inflammatory response might potentially prevent disease progression. Inhaled budesonide is a low cost, safe (time censored), effective (number needed to treat of eight), simple, and widely available therapeutic option, which can be of great help around the world, particularly in low-income and middle-income countries [4]. Several potential mechanisms might underlie these clinical observations. First, inhaled corticosteroids (including budesonide) have been used successfully for decades to down regulate the excessive inflammation that characterises several chronic airway diseases such as asthma and COPD,So it is plausible that inhaled budesonide might have contributed to control the inflammatory response in early COVID-19, as systemic dexamethasone seems to do in patients with severe COVID-19. In the context of the current pandemic, it was noted that patients with asthma and COPD appear to be under-represented among COVID-19-infected individuals seeking emergency care, and it was hypothesised that the chronic use of inhaled corticosteroids might have controlled the excessive inflammatory response induced by SARS-CoV-2 in these individuals [1,5].

## MATERIAL & METHODS:

We undertook a rapid systematic review to evaluate the role of budesonide in covid-19 patients. The review was conducted using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist in April 2020 . We searched PubMed, EMBASE, Scopus and Google Scholar for relevant studies on (COVID-19 or SARS or MERS or coronavirus) and budesonide.

## RESULTS:

Inhaled budesonide in early Covid-19 infection significantly reduced the likelihood of requiring urgent care, emergency department consultation and hospitalization. Table 1 shows the ressearch based review of inhaled budesonide and its effect on corona virus diseases.

**TABLE 1: DATA BASED RESEARCH REVIEW ON ROLE OF INHALED BUDESONIDE IN CORONA VIRUS DISEASE**

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| S.NO. | STUDY TYPE | AUTHOR DETAILS | DURATION | SAMPLE | RESULTS |
|---|---|---|---|---|---|
| 1 | Inhaled budesonide in the treatment of early COVID-19 illness (STOIC): a phase 2, open-label, randomised controlled trial | Sanjay Ramakrishnan from the Nuffield department of Clinical Medicine, University of Oxford, UK | From July 16 to December 9, 2020 | 146 participants were randomly assigned — 73 to usual care and 73 to budesonide. | The study concluded that the use of inhaled budesonide in early mild cases has a 90 per cent chance of preventing hospitalization |
| 2 | Inhaled budesonide in early treatment reduces need for urgent medical care,Lancet study | MascarenhasAnuradha. | April 22,2021 | | Inhaled budesonide in early Covid-19 infection significantly reduced the likelihood of requiring urgent care, emergency department consultation and hospitalisation, the study results showed. |
| 3 | Budesonide shortens recovery time in patients not admitted to hospital. | Elisabeth Mahase.Covid-19 | 25 March 2021 | 751 people in the budesonide group (800 µg twice a day for 14 days) and 1028 in the usual care group who were SARS-CoV-2 positive | Inhaled budesonide reduced the time to recovery by a median of three days in people with Covid-19 with risk factors for adverse outcomes |

## DISCUSSION:

Inhaled budesonide in early Covid-19 infection significantly reduced the likelihood of requiring urgent care, emergency department consultation and hospitalization.In vitro studies have suggested that corticosteroids may impair antiviral innate immune responses [6,7] and that ICS use leads to delayed virus clearance [9]. Other studies, however, have shown normal responses in patients on ICS [10]. It is important to note that most studies have been carried out with rhinovirus and there may be differences in the response to other viruses. Sanjay Ramakrishnan from the Nuffield department of Clinical Medicine, University of Oxford, UK, and lead author of the study, said the phase 2 clinical trial was done in the community in Oxfordshire, UK and the aim was to evaluate the efficacy of the widely used inhaled glucocorticoid budesonide in individuals with early Covid-19 infection in the community[11]. The onset of Covid-19 is usually mild, providing a potential window to intervene before the development of severe disease. From July 16 to December 9, 2020, 146 participants were randomly assigned — 73 to usual care and 73 to budesonide. The study results showed that inhaled budesonide significantly reduced the risk of urgent care visit, emergency department assessment or hospitalisation versus the usual care arm by 91 percent. the trial participants were people with mild symptoms and did not include those with severe symptoms or hospitalisation. The study concluded that the use of inhaled budesonide in early mild cases has a 90 per cent chance of preventing hospitalization [11.12]. In the Lancet study, patients in the budesonide arm received a budesonide dry powder inhaler at a dose of 800 µg twice a day. Participants, administered budesonide, were asked to stop taking the inhaler when they felt they had recovered or if they had a primary outcome . Inhaled budesonide was taken for a median duration of seven days in the study. In the other group, the usual care was supportive therapy, with the National Health Service (NHS) advising patients with Covid-19 symptoms to take antipyretics for symptoms of fever (products containing paracetamol, or non-steroidal anti-inflammatories such as aspirin and ibuprofen) and

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honey for symptoms of cough. Inhaled budesonide in early Covid-19 infection significantly reduced the likelihood of requiring urgent care, emergency department consultation and hospitalisation, the study results showed.[4] In another updated interim, analysis (published in medRxiv preprint by authors from the same group at Nuffield Department of Clinical Medicine and Nuffield Department of Primary Care Health Sciences, University of Oxford) showed that inhaled budesonide reduced the time to recovery by a median of three days in people with Covid-19 with risk factors for adverse outcomes[18]. The interim analysis, based on data collected up to 25 March 2021, involved 751 people in the budesonide group (800 µg twice a day for 14 days) and 1028 in the usual care group who were SARS-CoV-2 positive. It found that the median time to self-reported recovery for people taking inhaled budesonide was 3.011 days shorter compared with usual care (95% Bayesian credible interval 1.134 to 5.410 days), with a high probability (0.999) of being superior to the usual standard of care[18]. Around one third (32%) of people taking inhaled budesonide recovered in the first 14 days post-randomisation and remained well until 28 days, compared with just over one fifth (22%) in the usual care group. The budesonide group also reported greater wellbeing after two weeks (mean difference in WHO-5 wellbeing score +3.37, 95% confidence interval 0.97 to 5.76, P=0.006). A rapid systematic review was done to evaluate whether pre-morbid use or continued administration of inhaled steroids is a risk factor for adverse outcomes in acute respiratory infections due to COVID-19, SARS or MERS. The review was conducted using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist in March 2020 [21]. In total 771 publications were identified by the search strategies. The abstracts of these publications were screened by two reviewers (D.M.G. Halpin and D. Singh) and 59 publications were identified for full text review. Following examination of the full texts including translations of those in Chinese, no publications were identified as having data on prior ICS use in patients with SARS, MERS or COVID-19 infection. A few studies did report the prevalence of comorbidities, including chronic respiratory disease and occasionally specifically asthma or COPD, but in general studies provided little or no information about patients' pre-morbid health or medication.[22,23] Even if data on the prevalence of ICS use had been available, their interpretation would have been impossible without also having data on the severity of the underlying respiratory disease to allow adjustment for this as a confounding factor.

## CONCLUSION

The steroids in Covid-19 (STOIC) trial potentially provide the first easily accessible effective intervention in early treatment of Covid-19. Inhaled budesonide in early Covid-19 infection significantly reduced the likelihood of requiring urgent care, emergency department consultation and hospitalization. The budesonide group also reported greater wellbeing of the patients after two weeks . Inhaled Budesonide, a steroid used to treat asthma, if given early to Covid-19 patients with mild symptoms, scales down the need for urgent medical care and reduces recovery time.

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