Pre-clinical and randomized clinical trial with bromhexine and N-acetylcysteine for COVID-19

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Abstract

Treatment options for mild to moderate COVID-19 is limited. N-acetylcysteine and bromhexine have antiviral activity and show potential as treatment options against SARS-CoV-2 infections. This study evaluates the in vitro antiviral effect of bromhexine (BMX) for SARS-CoV-2 and determines the efficacy of treatment with BMX in combination with N-acetylcysteine (NAC) to reduce clinical scores in patients with mild to moderate COVID-19. Upon evidence from pre-clinical studies, a single center randomized trial of BMX + NAC (ClinicalTrials.gov Identifier: NCT04928495) with 420 participants in total took place in Fortaleza, CE, Brazil. Out of the 420 participants 140 received placebo, 140 received NAC alone, and 140 received NAC + BMX. Patients were monitored for 10-14 days, where physicians recorded all signs and symptoms reported. Nasopharyngeal swabs and blood samples were collected for SARS-CoV-2 RNA testing during the first visit, as well as 3 and 10 days after. Blood samples were collected at first visit and 10 days after for immuno-inflammatory biomarkers measurements. Treatment with NAC + BMX reduced clinical scores and symptoms when compared to placebo group (2/26; 8% vs 7/18; 39%; p < 0.05). Fever (≥37.8°C) was reduced by NAC + BMX treatment when compared to treatment with NAC alone and placebo. This study was limited by a largely vaccinated population. Our analysis showed that BMX reduces SARS-CoV-2 infection in vitro. Clinical trial results suggested that combinatory treatment with NAC + BMX is beneficial in mild to moderate COVID-19.

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Figure 1
486 patients were evaluated for eligibility
Patients were screened for clinical signs and symptoms of COVID-19
Full consent and demographic information were obtained
66 patients were ineligible to participate in the study

420 patients were randomized

140 received N-acetylcysteine + Bromhexine
140 received N-acetylcysteine + Vitamin C
140 received Vitamin C

First visit
N = 420 (100%)
(on day 1)
During the first visit we collected clinical data, demographics, nasopharyngeal swab and blood samples
Initiation of randomized treatments for 10 days

Second visit
N = 313 (74%)
(at 3 ± 2 days)
During the second visit we collected clinical data, nasopharyngeal swab and blood samples

Third visit
N = 261 (62%)
(at 10 ± 3 days)
During the third visit we collected clinical data, nasopharyngeal swab and blood samples
Completion of randomized treatments
Figure 3
Fig 4
Figure 5

A. Headache

B. Cough

C. Rhinorrhea

D. Weakness

E. Sore throat

F. Fever

% of patients with symptom

COVID-19 patients

Control
NAC
NAC + BMX

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