Zinc supplementation during SARS-CoV-2 acute infection results in better outcomes: a randomized clinical trial

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Background

Hi ha escassa evidència sobre l'impacte de l'afectació alta The immune system is markedly susceptible to changes of zinc levels and this might imply a different response against infection. Prior evidence suggests some benefit on viral infection prognosis after zinc supplementation. We aim to study the efficacy of zinc supplementation in SARS-CoV-2 infection outcomes.

Methods

This is an unicenter prospective, randomized clinical trial where adult patients admitted with moderate SARS-CoV-2 infection without end-organ failure were randomized to standard of care plus oral zinc for 14 days (a single tablet once daily containing 83.9mg of zinc acetate equals to 25mg of zinc element) (zSoC) (n =37) or standard of care alone (SoC) (n = 34). Exclusion Criteria: i) SARS CoV-2 vaccinated patient, ii) pregnant or breast-feeding; iii) inability to take oral medication; iv) life expectancy <72 hours at hospital admission. The primary combined outcome was death due to SARS-CoV-2 or intensive care unit (ICU) admission after randomization. Secondary outcomes included length of hospital stay (LoS) and time to clinical stability (defined as: oxygen saturation >94% [FiO2 21%], normalized level of consciousness [baseline], HR <100rpm, systolic BP> 90mm Hg, Temperature <37.2°C). Student's t test for continuous variables and Fisher's exact test for categorical variables were used. Wilcoxon–Mann–Whitney test generalized Odds ratio (ORs) and 95% confidence intervals (CIs) were presented to compare the differences in outcomes between SoC and zSoC. A logistic regression model was fitted after adjusting by age, sex, severity and comorbidity to study the ORs of the primary outcome between groups SoC and zSoC.

Conclusions

Daily zinc supplementation with 83.9mg of zinc acetate for 14 days during the acute phase of SARS-CoV-2 infection resulted in lower rates of severity (less death and ICU admission) and faster clinical recovery along with shorter hospital stay.

Results

Seventy-one participants were recruited. No significant differences in terms of age, gender and comorbidities nor in SoC were found between groups (Table 1). 14-day Mortality was 2.90 % (2 participants) in the SoC group and none in zSoC. ICU admission rates were, respectively, 8 (23%) and 1 (2.7%) (OR: .098; 95% CI .013–.766). The principal combined outcome was in 8 participants (23%) in SoC and in 2 (5.4%) in zSoC (OR: 0.18; 95% CI .03–.946). In a logistic regression model adjusting by age, sex, comorbidity and severity the OR for the combined outcome in those in zSoC was 0.091 (95% CI: 0.007-0.913; p=0.045). LoS was shorter in zSoC (6.9 days (SD 6.1) vs 12.7 (SD 11.6); p=0.013) respectively. Time to clinical stability was significantly shorter in zSoC (5 days (SD 6.1)) compared to SoC 11.9 (SD 9.1); p=0.005. No significant differences in changes in inflammatory markers were found among groups. No severe adverse events were observed during the study. Figure 1 shows changes in the WHO severity score at baseline and day 7.

Flow diagram.
Recruitment of parcticipants

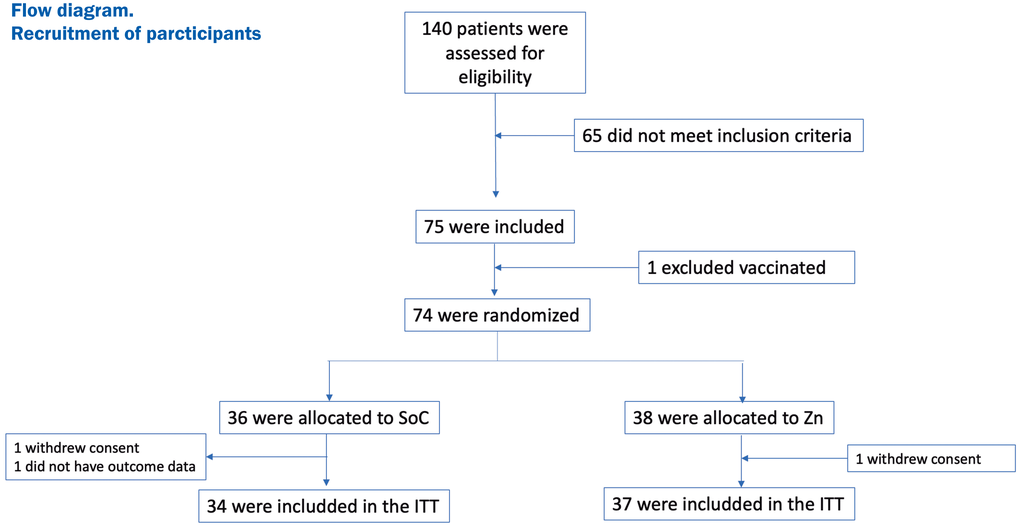

Figure 1. Changes in WHO severity score for COVID-19. In Standard of care (SoC) and Zinc supplemented group (zSoC)

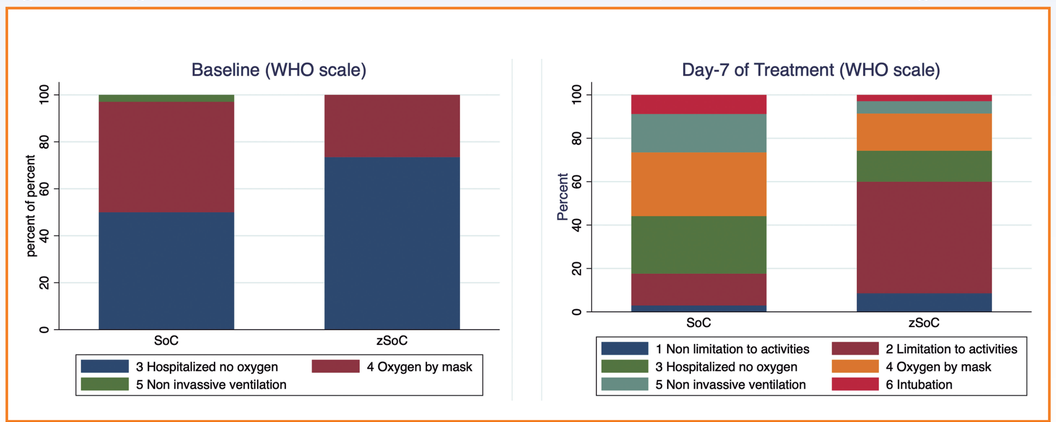

Table 1. Population Characteristics at inclusion

	Zinc	SoC
Age median (IQR)	52 (43-58)	53 (36-66)
Male gender, n (%)	22 (61%)	20 (59%)
Active smoking, n (%)	6 (16%)	4 (12%)
High Blood Pressure, n (%)	13 (35%)	9 (26%)
Type 2 Diabetes Mellitus, n (%)	5 (13%)	6 (17%)
COPD, n(%)	1 (2.7%)	1 (2.9%)
Charlson comorbidity Index		
No comorbidity (0-1) n,(%)	30 (81%)	26 (76%)
Mild Comorbidities (2-3),n(%)	4 (11%)	6 (16%)
Highly comorbid (>3), n(%)	3 (8%)	2 (5%)
Blood parameters		
C-Reactive Protein mg/dl, median (IQR)	5.7 (1.1-9.7)	5.4 (1.3-5.8)
IL-6 , median (IQR)	8 (2.1-22.5)	12 (4-50)
D-Dimer UI/l , median (IQR)	410 (345-690)	470 (350-800)
Zinc mg/dl, median (IQR)	83 (72-95)	89 (70-102)
PaO2/FiO2	291 (235-302)	257 (233-313)
MEWS-Severity score, median (IQR)	4 (3-5)	3 (2-4)
Treatments		
Dexamethasone, n (%)	37 (100%)	34 (100%)
Tocilizumab, n (%)	6 (16%)	7 (20%)
Low-Weight Heparin, n (%)	33 (89%)	31 (91%)

Table 2. Changes over time in blood biomarkers.

	Zinc		SoC	
	Baseline	Day-14	Baseline	Day-14
Zinc mg/dl, median (IQR)	83 (72-95)	129 (113-148)	89 (70-102)	124 (107-135)
C-Reactive Protein mg/dl, median (IQR)	5.7 (1.1-9.7)	0.32 (0.06-1.3)	5.4 (1.3-5.8)	0.32 (0.06-0.6)
IL-6, median (IQR)	8 (2.1-22.5)	6 (2.3-11.6)	12 (4-50)	5.3 (2.6-13.2)
D-Dimer UI/l, median (IQR)	410 (345-690)	450 (260-860)	470 (350-800)	570 (330-975)

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