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Letter to the Editor

Zinc role in Covid-19 disease and prevention

Papel del zinc en la prevención y la enfermedad de COVID-19



Dear Editor,

Zinc (Zn) is a very valuable metal because of its many functions.^{1,2} It maintains the neurological, immune, reproductive, and skin systems.³ Zn involves in enzyme catalysis, protein-protein functions, and protein oligonucleotide maintenance.⁴ The intracellular Zn is connected to metallothionein (MT). This controls the Zn levels through an intracellular process.⁵ Zn modulation of MT mRNA expression is known.^{6,7}

Zn modulates mRNA levels of cytokines. It down-regulates microRNA expression and key enzymes and proteins necessary for microRNA maturation and stability.^{8–10}

Zn concentration in cells is controlled by homeostasis which helps the organism to accumulate diverse dietary Zn. Zn enables the body to make proteins and DNA. It promotes wound healing. It is important in childhood growth and development. It also has antioxidant properties. Zn is also important in cell-mediated immune function. Zn may reduce the duration of cold symptoms, support blood sugar control, improve severe and inflammatory acne, decrease heart disease risk, and slow the progression of macular degeneration.¹¹ Zn has also been shown to regulate gene transcription in cancer cells.

Zn is an anti-inflammatory and detox compound that also helps as detailed later with Covid-19 infection in prophylaxis and treatment. It may thus also improve the efficacy, as well as reduce inflammation and toxic effects of Covid-19 vaccines.

This work advocates for ensuring zinc sufficiency before and after vaccination.

The Australian Therapeutic Goods Administration in their weekly report of Covid-19 vaccine safety,¹² received 22,031 communications of adverse events from the administration of 3,613,053 doses of AZ, which is a DNA vaccine, and Comirnaty (Pfizer) which is an mRNA vaccine. In between them, there have been 210 reports of deaths following immunization. Thus, the fatality rate from receiving one dose of a two-shot vaccine is 0.01%. Because two doses are needed, and that protection from vaccines lasts less than one year,¹³ we may

estimate the fatality rate from universal vaccination of the population at 0.02% per year. This number has to be put in the context of the fatalities that could have been experienced in Australia by using more relaxed border control, less harsh lockdowns, but also better therapeutic approaches as done in countries of a similar level of health system.

Australia had a singular approach to Covid-19, targeting risk avoidance rather than risk management, and keeping the borders mostly closed. This has translated into a small percentage of infected over 14 months, 0.11%.¹⁴ Similarly remarkable is the therapeutic approach to only use Dexamethasone, and conditionally in very specific cases Tocilizumab,¹⁵ i.e. adjuvants therapies, while practically preventing the use of antivirals, as Remdesivir is only used conditionally in very specific cases and Anakinra, Favipiravir, Hydroxychloroquine, Interferon Beta-1a, and Lopinavir/Ritonavir are specifically declared not to be used for the treatment of COVID-19.¹⁵ Not a surprise if the national average case fatality rate from contracting Covid-19 is 3.03%,¹⁴ with the state of Victoria 3.99%. We may consider as an example of more sustainable restrictions but also a much better therapeutic approach the case of the United Arab Emirates. The percentage of cases over 14 months has been 5.67%.¹⁴ Then, treatment in the United Arab Emirates has been much more sophisticated, with many combinatory therapies inclusive of antivirals offered to hospitalized patients, and therapies also offered to asymptomatic off-patients in risk categories.¹⁶ Up to their case-specific discretion, physicians have the opportunity to use individual and combinatory therapies based on Chloroquine Phosphate, Hydroxychloroquine, Favipiravir, Lopinavir-Ritonavir, Camostat, Remdesivir, nebulized Interferon Alpha or Interferon Beta, Ribavirin, and adjunctive Anticoagulation, Steroids or Tocilizumab as well.¹⁶ As a result, the case fatality rate is 0.30% (10 times smaller than in Australia and 13 times smaller than in the state of Victoria). This means that with the same exposure to Covid-19 infection but also the same therapies of the United Arab Emirates, Australia could experience slightly less than 0.02% of the population being infected and perished as a result of the infection over one year. It may be added that vac-

15 zinc COVID-19 studies

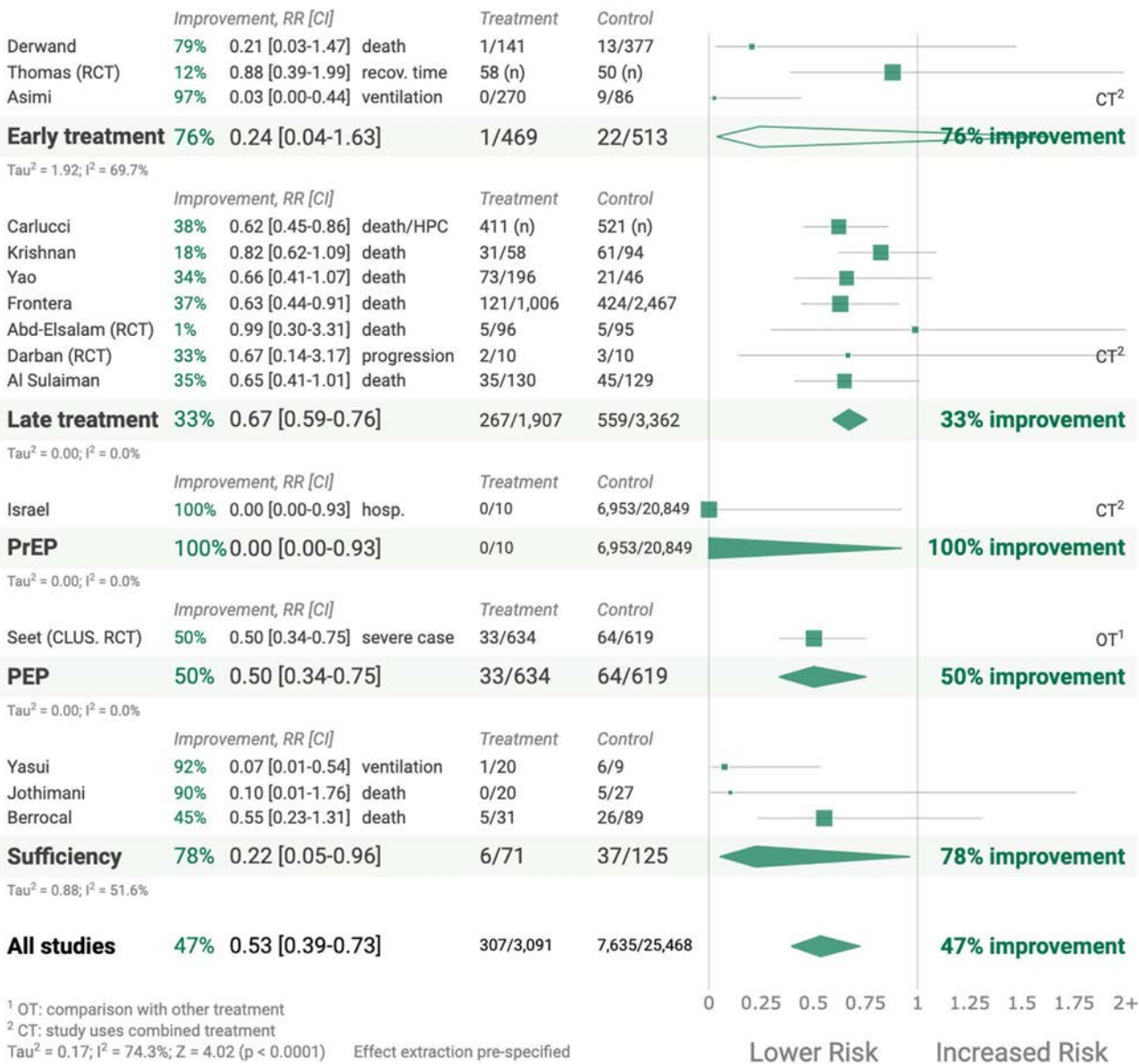


Fig. 1 – Summary of Covid-19 Zinc studies from 17.

cines do not offer 100% protection, especially against variants, as admitted by the Australian government when they write there are currently no grounds for an exemption from restrictions based on a person being vaccinated against Covid-19. Zinc and Covid-19 infection.

Zn is certainly not a 100% effective therapy for Covid-19 infection. However, it has been shown that Zn help with Covid-19 infection. Zn deficiency has been associated with more serious consequences of Covid-19 infection. Zn supplementation is important in the prevention,¹⁷ as well as the treatment in conjunction with antivirals such as Chloroquine or Hydroxychloroquine.¹⁷ Regarding Zn Covid-19 studies,¹⁷ reports of 15 studies where it is shown Zn supplementation matters in different phases of Covid-19 infection (Fig. 1).

Israel et al.¹⁸ present a case-control study in a large population. Lower risk of hospitalization is associated with calcium + zinc supplements. Al Sulaiman et al.¹⁹ propose a retrospective study of ICU patients showing lower mortality with zinc treatment. Asimi et al. (Velija and Al)²⁰ propose a retrospective study of Hashimoto's thyroiditis outpatients, with those taking vitamin D, zinc, and selenium, showing significantly lower hospitalization with treatment. Seet et al.²⁴ report improvements in prophylaxis with lower serious cases, lower symptomatic cases, and lower confirmed cases of Covid-19 with all treatments (ivermectin, HCQ, PVP-I, and Zinc + vitamin C) compared to vitamin. Thomas et al.²² report a small RCT showing faster recovery with zinc and with vitamin C. Darban et al.²³ report a small RCT with 2 ICU patients, 10 treated with high-dose vitamin C, melatonin, and zinc,

not showing significant differences. Frontera et al.²⁴ propose a retrospective study of hospitalized patients showing 37% lower mortality with HCQ + zinc. Berrocal et al.²⁵ report a small retrospective study of hospitalized patients showing zinc deficiency associated with a higher ICU admission rate. Derwand et al.²⁶ report a retrospective study showing 79% lower mortality and 82% lower hospitalization with early HCQ + AZ + Zn. Jothimani²⁷ shows Covid-19 patients had significantly lower zinc levels. Yasui et al.²⁸ show in a retrospective study as significantly lower serum zinc levels are associated with severe Covid-19 cases. Yao et al.²⁹ show as Zn helps with the survival of hospitalized patients. Krishnan et al.³⁰ show in a small retrospective study of mechanically ventilated patients lower mortality with vitamin C, vitamin D, HCQ, and zinc treatment. Carlucci et al.³¹ show as the addition of Zn to HCQ + AZ reduces mortality, ICU admission, and the need for ventilation. Similar results are proposed by,³² evidencing a correlation between Zn deficiency and more serious outcomes of Covid-19 infection.

Here we argue as Zn supplementation may also be used as a preventive anti-inflammatory and de-toxic treatment during Covid-19 vaccination. These vaccines may generate local and systemic inflammatory responses. There may be also toxic effects of synthetic nucleosides and delivery components. Some Covid-19 mRNA vaccines use novel adjuvants such as lipid or polymer-based nanoparticles to protect and stabilize the mRNA and improve uptake.^{33,34} The toxicological implications of the use of these substances have been only marginally considered.

Zn is one substance that may help to mitigate the damage from Covid-19 vaccines and is thus worth considering in times of mass vaccination against Covid-19. Normal serum Zn is 0.66–1.10 mcg/mL.³⁵

Supplementation by vitamins and minerals, in general, may also help to make vaccines more effective. Supplementation with Vitamins B6 and E, Zn, and selenium in elderly people improves their immune system response to challenges.³⁶ Vaccinated individuals with Vitamin D deficiency were less protected against the flu.³⁷ Vitamin E supplementation to elderly people increases the number of antibodies after vaccination for hepatitis B and tetanus.³⁸ People over 60 years of age are often deficient in Zn, and other minerals such as selenium.³⁹

Some degree of inflammation is required for the body to produce a correct immunological response to a vaccine, and thereby a protective antibody titer in the end. Suppressing inflammation might therefore negatively affect the effectiveness of vaccination. Nothing in the literature supports the specific use of Zn to prevent damage from vaccines, increase the efficacy of vaccines, but also reduces the efficacy of vaccines, as the subject has not been covered yet by any trial. Monitoring of Zn levels before and after administration of vaccines is therefore mandatory, to be reported in the database of adverse effects from the vaccine, together with information about infection and recovery after vaccination.

This contribution has analyzed the impact of Zn supplementation on the severity of Covid-19 infection, as well as the efficacy and the adverse events of vaccinations for Covid-19 infection. Zn supplementation helps to prevent more serious consequences from Covid-19 infection. It is unlikely that Zn

supplementation may increase or reduce the efficacy of Covid-19 vaccines. More likely, Zn supplementation may mitigate the vaccine adverse events. It is suggested to control Zn levels and use supplementation to address Zn deficiency before and after being vaccinated for Covid-19 infection, especially for those above 60 years of age. While a proof of principle linking Zn serum levels to Covid-19 vaccines' response is missing, as there are no specific data available, supplementation for sufficiency certainly has a minimal cost and no side effects.

Conflict of interest

The authors have no conflict of interest to declare.

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