## High-Dose Vitamin C Infusion for the Treatment of Covid-19: Beware of Paraben Intoxication

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Dear Editor.

Vitamin C (ascorbic acid) has several favorable effects on the immune system, such as enhancing phagocyte function, interferon production, and T-lymphocyte transformation [1]. Moreover, vitamin C diminishes inflammation and lung injury by reducing hydrogen peroxide, superoxide anion, and nitric oxide levels [2]. In addition, vitamin C was shown to increase the resistance of chick embryo ciliated tracheal organ cultures to Corona virus infection [3]. Furthermore, patients with severe pneumonia were treated with vitamin C infusion at a dose of 6 g/day and this treatment was found to be associated with lower mortality and improved chest radiologic score on the 7th day [2]. In the light of this information, a phase II clinical trial (NCT04264533) was initiated in China to evaluate the effect of high-dose intravenous (i.v.) vitamin C (24g/day for 7 days) on intensive care unit (ICU) patients with severe Corona virus disease-19 (Covid-19)-associated pneumonia [4]. Nevertheless, this study has not been completed yet. Inspired by these studies, we considered administration of high-dose vitamin C for the treatment of ICU patients with severe Covid-19 pneumonia. However, as soon as we noticed the paraben component (methylparaben 4 mg, propylparaben 0.5 mg) in 500 mg i.v. vitamin C preparation in our country, we refrained from the administration of this medication. Since the content of this vitamin C preparation is adjusted to the daily recommended dosage (100-300 mg), paraben accumulation may occur when a high dose of vitamin C is administered to patients.

Parabens, which include methylparaben, ethylparaben, propylparaben, and butylparaben, are preservatives that are used in a wide range of cosmetic, pharmaceutical, and food products in limited amounts [5]. Despite the fact that parabens are rapidly metabolized to p-hydroxybenzoic acid and excreted in urine, chronic exposure to parabens have both androgenic/antiandrogenic and estrogenic/antiestrogenic effects. Moreover, parabens are carcinogenic, especially known to cause breast and skin cancer. Fertility is also thought to be impaired through chronic paraben exposure [6].

Therefore, we would like to warn our colleagues to be cautious about the ingredients of vitamin C medications in their countries, especially for paraben, before the initiation of high-dose vitamin C infusion for the treatment of Covid-19 patients.

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