

## *Is chemoprophylaxis with ivermectin in dentistry effective at preventing COVID-19?*

### *A quimioprofilaxia com ivermectina em odontologia é eficaz na prevenção da COVID-19?*

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Due to the serious problems caused by the COVID-19 pandemic, several publications have proposed prevention protocols for infection by Sars-CoV-2 [1-4]. This has led dentists to seek information on chemoprophylaxis, since dental staff must provide care for patients with urgent need [5].

Ivermectin has antiviral effects on viruses whose genetic material is DNA and those the present RNA, as is the case of the novel coronavirus [6]. The most widely accepted mechanism of action for ivermectin is the inhibition of the nuclear importation of viral proteins mediated by the heterodimer importin  $\alpha/\beta 1$ , which are indispensable to the replication of RNA viruses [7].

Caly et al. [8] demonstrated the effect of ivermectin on Sars-CoV-2. The authors found that the continuous use of 5 microM of ivermectin for two days in an isolated culture of Vero/hSLAM cells infected with Sars-CoV-2 killed the novel coronavirus nearly completely [8]. Despite this

promising discovery, the activity of ivermectin has not yet been clinically proven in humans.

Regarding pharmacokinetics, in its daily release on evidence related to COVID-19 [9], the Brazilian Health Ministry presented a study in which the authors report that doses that produce inhibitory concentrations of SARS-CoV-2 cannot be achieved in humans, as the maximum dose permitted by the US Food and Drug Administration (FDA) is 200 mg/kg [10] and safe therapeutic doses reach blood levels in the range of 20 to 80 ng/ml [11] Caly et al. [8] report that ivermectin has an in vitro inhibitory concentration (IC50) of SARS-CoV-2 35 fold higher than the maximum plasma concentration (Cmax) reached after the oral administration of the approved dose of ivermectin for administration to humans [8] This observation limits the execution of tests on humans and suggests a low likelihood of success regarding the treatment of COVID-19 [12,13].

After noting an increase in the consumption of ivermectin, the FDA warned the population regarding the

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side effects and to not use veterinary products, not to use products of a dubious origin, not to take the medication without a medical prescription and only take drugs dispensed by pharmacists at regulated pharmacies [14]

Ivermectin is considered safe, with few side effects when taken orally [6] However, its concomitant use with another antiviral medication is associated with neurotoxicity [15] The Brazilian Society of Pneumology and Phthisiology reports that there is no scientific evidence that ivermectin, chloroquine or hydroxychloroquine, either alone or in combination, is capable of avoiding the installation of the disease in non-infected individuals [16] There are four ongoing studies that are expected to be concluded between August and December 2020, the results of which could lead to changes in the recommendations if clinical benefits are demonstrated [17]

The administration of ivermectin in hospitalized patients has been associated with a shorter hospital stay and a reduction in the mortality rate [18]. To date, however, there is no robust scientific evidence attesting to the effectiveness and safety of ivermectin as chemoprophylaxis for COVID-19.

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