




## LETTER TO THE EDITOR

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# Ivermectin for COVID-19 prophylaxis

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### Dear Editor,

With the advent of COVID-19 globally, many doctors have begun to review the medications that are already available to treat and/or protect against the infection.<sup>1</sup> One of these drugs is the antiparasitic ivermectin. The first clinical trial was registered by Zagazig University in May, 2020; and hence, it has been adopted in several studies.<sup>2-5</sup>

Ivermectin is one of the medicines previously listed by WHO as one of essential drugs; and approved by US Food and Drug Administration (FDA) as an anti-parasitic drug.<sup>6</sup> It is a 50-years-old generic drug. It has been used with a long history of safety for about 4 billion times around the world.<sup>7</sup> It has been widely administered against many parasitic diseases including strongyloidiasis, onchocerciasis and lymphatic filariasis.<sup>8</sup> Ivermectin is an inexpensive, readily available drug that is well-accepted for use by some health authorities around the world on large scales. It can also be easily taken by mouth. Moreover, ivermectin administered even with a high dose up to 2000 µg/kg is well-tolerated. Such dose represents up to 10 times the highest FDA-approved dose of 200 µg/kg.<sup>9,10</sup> Despite the evident

safety of ivermectin, it is contraindicated in patients with blood-brain barrier (BBB) leakage such as in cases of meningitis.<sup>11</sup> Regarding its use for pregnant women, infants and children below than 15 kg body weight, there is insufficient evidence for safety.<sup>12,13</sup> Therefore, its use for those categories of people might be avoided.

It has been promoted to be used in large scales in India with great success.<sup>14</sup> Moreover, it has been investigated in countries of Latin America, South Africa and others with encouraging reports. Meanwhile, it has been taken up by self-medicated individuals in many countries including USA. Although, it is not WHO or FDA-approved drug for COVID-19, a recent study stated that there is an increase in use of ivermectin by American citizens during pandemic period that peaked in January 2021 with a relative increase of 989%.<sup>15</sup> This might be an important factor other than the widespread distribution of vaccines in reducing the number of cases of COVID-19. At the same time, use of ivermectin in Peru resulted in an approximately 14-fold decrease in excess deaths versus a 13-fold increase with reversed ivermectin policy.<sup>7</sup>

Ivermectin could be taken at home under medical supervision at appearance of the first signs of

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COVID-19, and it can also be given to individuals who are in close contact with confirmed cases. It might significantly reduce COVID severity and progression especially if administered as early as possible. Subsequently, the numbers of cases could be reduced; and therefore, fewer patients will need to be hospitalized. Its use in protection might also be based on the reports stating that it is of great benefit in treating cases of mild and moderate cases. However, no benefit for use has been reported for use in severe cases who are in need for mechanical ventilation.<sup>16</sup>

In vitro studies, ivermectin has been observed to inhibit the replication of SARS-CoV-2 “the virus causing corona”. It is considered a host-directed antiviral agent so it can be of a broad-spectrum antiviral including viruses causing Zika, dengue, HIV and yellow fever.<sup>17</sup> It has been stated that ivermectin could prevent protein of virus from entering host cell nucleus.<sup>18</sup> Moreover, its binding with SARS-CoV-2 spike protein is non-epitope specific. Therefore, it might be effective for combating the mutations and different variants of the SARS-CoV-2.<sup>7</sup> Moreover, Zaidi and Dehgani-Mobarakhi explained 20 different mechanisms for ivermectin against viruses including direct actions on the virus as well as effect on the host cells to resist viral replication and to target the virus-induced inflammation.<sup>19</sup> They added that it is of worthy attention to repurpose another approved drug such as ivermectin in order to overcome the new mutant strains of coronavirus and the potential re-emergence of novel viruses. In a report issued by England Ministry of Health on 9 July 2021, it has shown that the numbers of deaths due to the delta variant of the virus were higher among vaccinated persons compared to nonvaccinated cases with sample numbers of 118 versus 92, respectively.<sup>20</sup> This means that the current vaccines may not be effective against new strains of virus.

We call on the experts of WHO to reconsider their advice against use of ivermectin for COVID-19; and instead, they might recommend its urgent investigation especially since WHO has been previously declared that it could be used for mass treatment and prophylaxis in other diseases.<sup>6,21</sup> The attribution of WHO advice against ivermectin use in the current pandemic has been based on argument of insufficient evidences. Despite such advice of WHO, many governments have turned to it for combating the pandemic. However, we see no convincing reason to reject use of ivermectin in the current pandemic despite its high efficacy, safety and ease of its trials and confirmation of its positive effects. Meanwhile, testing of its effectiveness is so easy and doesn't require facilities except to accept volunteers to participate in the investigations without reported health risks or even economic burden.

It is emphasized that no drug or vaccine can be said to eliminate or protect from infections without proper

clinical trials. In this context, Bryant et al. performed a meta-analysis of 15 clinical trials conducted up to April 25, 2021 for investigation of efficacy of ivermectin.<sup>22</sup> They concluded that ivermectin could be of great impact in combating SARS-CoV-2 pandemic. Moreover, a recent study conducted by French Pasteur Institute confirmed the good effective role of ivermectin against COVID-19 infection.<sup>23</sup> Accordingly, we agree the opinion of other authors that apparent efficacy, safety and low cost of ivermectin could be an important cause for its significant role in control of the current pandemic globally.<sup>22</sup>

Meanwhile, many encouraging news have come from almost all countries and governments adopting ivermectin for prophylaxis with a dramatic drop in the number of cases. These countries include India, Peru, Mexico, South Africa, Brazil and other countries.<sup>24</sup> Moreover, it has been approved for use against COVID-19 in many other countries including Honduras, Slovakia and Czech Republic.<sup>25</sup>

Some authors have endorsed the use of a prophylactic weekly dose of ivermectin to protect health care workers from infection with the coronavirus.<sup>26</sup> Meanwhile, a group of expert physicians named Front Line COVID-19 Critical Care Alliance reviewed the effects of ivermectin on COVID-19 infections; and concluded that it has showed a strong evidence of therapeutic efficacy and is recommended for prophylaxis and therapy of SARS-CoV-2 infection.<sup>27</sup> In a previous report, we proposed use of ivermectin in mass prophylaxis by administering one or more doses to all members of community at the same time.<sup>5</sup> However, if this is difficult to be adopted by health authorities, ivermectin might be administered at regular intervals for health care members, and as a single booster dose if contact with patients is suspected. Urgent prospective studies on large numbers of cases are recommended to determine the exact protocol and doses to be used in the current pandemic.

## Conclusions

Use of ivermectin on a wide scale is very safe as previously stated by WHO in control of some parasitic diseases. It has been tested by numerous clinical trials and researches as a therapeutic and prophylaxis for the current pandemic. It can provide a temporary protection but not prolonged immunization. It might protect people from infection at when exposed to cases of COVID-19. In addition, it eliminates the infections in the early stages of the disease. Even in vaccinated individuals who have had COVID-19 infection, they can use it for treatment. To be effective in COVID-19 prophylaxis, it is suggested to be given to all members of community at the same time. Otherwise, it may be taken when contact with COVID-19 patients or disease-carriers. It is also a call to WHO and US FDA to re-consider their advice against use of ivermectin in prophylaxis of the current pandemic.

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