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Short Communication

Outcome of ivermectin and doxycycline in cancer patients with COVID-19: A positive experience in Bangladesh

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The world, today, is facing an immense challenge with the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection known as coronavirus disease 2019 (COVID-19). Bangladesh is the 16th ranked pandemic part of the world with 244,020 cases diagnosed and 3234 deaths to date.[1] At present, no FDA approved remedies are available to defeat this deadly disease. Ivermectin, an antiparasitic drug, has been found to inhibit the replication of the SARS-CoV-2 virus *in vitro*.[2] When combined with doxycycline, an antibacterial drug, ivermectin showed encouraging activity in reducing viral load, possible molecular mechanisms of which have been proposed very recently.[3,4] Globally, a number of clinical trials are going on to explore the activity of these two widely used FDA approved drugs as a potential therapy for SARS-CoV-2 infection.

Although no systematic data are available, several studies including the European Society for Medical Oncology and the National Institute for Health and Care Excellence guidelines have reported that cancer patients are more vulnerable to develop COVID-19 infection.[5] We sought to investigate the effectiveness of ivermectin plus doxycycline in COVID-19-positive cancer patients in a tertiary care cancer center of Dhaka city in Bangladesh.

This is a case series conducted at the Oncology and Radiotherapy Centre of Square Hospital, Bangladesh. A total of eight patients were treated with ivermectin and doxycycline combination to date, who met the eligibility criteria. The primary outcome was treatment response and the secondary outcome was treatment-related toxicity. Inclusion criteria included in this study were patients with any stage of solid malignancies or lymphoma proved by pathology; active disease being treated with chemotherapy and/or radiotherapy, biological agent, hormone therapy, or immunotherapy in neoadjuvant, adjuvant, concurrent or palliative setting; ECOG performance status 0–2; age between 18 and 75 years; RT-PCR positive for SARS-CoV-2; have any of the symptoms of temperature ≥37.5°C, cough, or sore throat; and provided informed written consent. The exclusion criteria were allergy to ivermectin or doxycycline; received ivermectin, doxycycline, hydroxychloroquine, or chloroquine phosphate within the past 4 weeks; a history of chronic heart, liver, or kidney diseases; pregnant or lactating women; multiple primary malignancies; and joined in other clinical trials.

When came to our outpatient department for their scheduled cancer treatment, RT-PCR for COVID-19 was done as per the routine protocol of the hospital. No patient was found to be

impaired immune systems, that is, no leukocytopenia, thrombocytopenia, or not receiving immunosuppressants. All presented with mild symptoms of COVID-19 [Table 1]. Scheduled treatment (chemotherapy and/or radiotherapy) was postponed, once COVID-19 was confirmed and started tablet ivermectin (12 mg for patients with 80 kg weight and 18 mg for those with above 80 kg weight) single dose and Tablet doxycycline (100 mg) twice daily for 5 days. Parallelly, the patients received supportive management for their symptoms. On day 6, nasal swabs were collected for RT-PCR for SARS-CoV-2 which appeared negative for all patients, and the consecutive test was done on day 7 also appeared negative. All patients became free from the symptoms of COVID-19 after this period. Then, their cancer treatment was resumed with intensive surveillance. There was no reported toxicity of epigastric distress, abdominal discomfort, vomiting, diarrhea, or skin rash.

The World Health Organization estimated that the period of this viral shedding is up to 9 days and 20 days for the patients with mild symptoms and for those who are hospitalized, respectively.[1] We report data of eight SARS-CoV-2-infected cancer patients who were treated with ivermectin and doxycycline combination and recovered in 6 days only. In addition, our patients remained non-infectious to other people in the hospital as the successive two PCR tests were negative. Ongoing oncological managements were not compromised for any of the patients, except the 5-day treatment delay over the duration of ivermectin plus doxycycline therapy. All patients were able to complete the remainder of their chemotherapy and/or radiotherapy without any serious adverse events.

Managing cancer patients are challenging in the era of COVID-19 of today. Despite the fact that the risk/benefit ratio of cancer treatment is important without imposing the patients of being further immunosuppressed and seriously ill from SARS-CoV-2 infection, cancer-related mortality must not be ignored. Especially for curable cancers, the continuation of active oncological management is crucial to achieve cure and survival benefits. Alteration of treatment regimens, switching to oral treatment, long-term treatment breaks all can seriously threaten the treatment outcome of cancer patients even for those who are in palliative settings. Ivermectin plus doxycycline therapy, though tested in a very small number of patients in our study, resulted in very promising activity against COVID-19, and this is the first-ever data yield from cancer patients. We believe that our preliminary findings could be used as a building block for future large-scale studies, and randomized controlled trials including only cancer patients are warranted to validate the efficacy of this therapy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Table 1: Characteristics of COVID-19-infected cancer patients treated with oral ivermectin plus doxycycline.

Patient	Diagnosis	Stage	Age	Comorbidity	Ongoing cancer treatment	COVID-19 symptoms
Case 1	Gestational trophoblastic tumor	FIGO[a] Prognostic score III	35	Nil	2 weekly intramuscular methotrexate	Fever
Case 2	Breast cancer	IIB	60	Nil	Adjuvant chemotherapy with doxorubicin and cyclophosphamide	Fever
Case 3	Head and neck cancer	II	60	DM[b], HTN[c]	Definitive CCRT[d] with weekly cisplatin	Fever and cough
Case 4	Breast cancer	IIB	40	Nil	Adjuvant chemotherapy with doxorubicin and cyclophosphamide	Fever and mild cough
Case 5	Breast cancer	IIIC	62	DM[b]	Adjuvant chemotherapy with epirubicin and cyclophosphamide	Fever
Case 6	Lung cancer	IIIC	70	HTN[c]	CCRT[d] with weekly paclitaxel and carboplatin	Fever and cough
Case 7	Biliary tract cancer	IIIB	67	DM[b], HTN[c]	Adjuvant chemotherapy with 4 weekly gemcitabine	Fever
Case 8	Breast cancer	IIIC	53	Nil	Adjuvant endocrine therapy with letrozole	Fever, mild cough

[a]FIGO: International Federation of Gynecology and Obstetrics, [b]DM: Diabetes mellitus, [c]HTN: Hypertension, [d]CCRT: Concurrent chemoradiation therapy

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