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Letter to the editor: Experience of medical professionals with Azoximer bromide as prophylactic treatment for COVID-19 patients in Chuvashia Republic, Russia

S.V. Efimov

Department of Infectious Diseases, Emergency Hospital, Moscow, Russia

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Dear editor,

In March 2020, the Emergency Health Care Hospital in Chuvashia Republic, Russia, was converted into a specialised COVID-19 hospital. Azoximer bromide, a high molecular weight synthetic immune modulator drug was chosen by a frontline team of 52 medical professionals at the Emergency Health Care Hospital, who agreed to self-administer azoximer bromide as a prophylactic treatment against COVID-19. During the dosing period, all 52 professionals, with one exception, remained symptom free and tested negative for COVID-19.

Like many European countries, Russia has been markedly affected by COVID-19. The first step in 'fighting' the epidemic was a nationwide lockdown, implemented on March 30, 2020. Most of the multidisciplinary hospitals were rapidly repurposed as dedicated COVID19 centres and health workers re-trained and deployed as infectious disease specialists. The outcome was the creation of a cohort of trained and dedicated staff readily available to support patients in intensive care units who needed mechanical ventilation.

Percutaneous tracheostomy under endoscopic control was generally adopted as standard practice. As well as minimizing complications associated with an endotracheal tube, the percutaneous tracheostomy is believed to have a lower potential for aerosol formation and thus posed a lower risk of viral exposure load on staff[1]. Nevertheless, any procedure undertaken in the care of patients carries the risk of aerosol formation and exposure of healthcare workers to infection. There is an ethical imperative to protect healthcare workers from exposure to coronavirus infection. Fortunately, this imperative is linked to a positive environment for the patient as healthcare personnel remains available to treat patients and healthcare facilities continue to function effectively.

In reviewing protective options for our colleagues, we were aware of azoximer bromide (Polyoxidonium®, PO), developed at the State Scientific Center of the Institute of Immunology of the Ministry of Health of the Russian Federation and available for clinical use since 1996. Azoximer bromide is a high molecular weight synthetic immune modulator drug, which is believed to increase an individual's resistance to local and general infection and is indicated for the treatment of viral infections[2]. *In vitro* studies have demonstrated the multiple effects of azoximer bromide, including increase of degranulation of natural killer lymphocytes, increase of T-cell proliferation, and expansion and maturation of dendritic cells with the expression of several co-stimulatory molecules[3]. Azoximer bromide penetrates the cell endosomal segment where it is associated with raised micromolecular concentrations of hydrogen peroxide, activation of some signal molecules and transcription factors, in particular Nuclear factor Kappa-B (NF-κB), as well as with detoxifying and antioxidant properties[2,4]. Azoximer bromide has shown to be generally well-tolerated in multiple infectious diseases of viral and bacterial aetiology[5,6].

Corresponding Author: Sergey Vitalyevich Efimov, MD; e-mail: eftat@mail.ru

Existing nonclinical and clinical data describing the action of azoximer bromide suggested that it might provide benefit when used prophylactically in areas at high risk of COVID-19 exposure[7,8].

In March 2020, our hospital (Emergency Hospital, Chuvashia Republic, Russia) was converted into a specialised COVID-19 hospital. Serving as the unit leading the medical response to the pandemic, the Department of Infectious Diseases expressed concern regarding its ability to protect its medical professionals from getting infected and thus, from maintaining the unit's operational functionality. Hence, the frontline team of 52 medical professionals in the Department of Infectious Diseases agreed to self-administer azoximer bromide (12 mg tablets) once a day during 5 months, while keeping a record of their experiences.

All 52 professionals started dosing with azoximer bromide on March 18, 2020 and maintained daily dosing until July 27, 2020, with the exception of a 10-day dosage break due to a shortage of tablets. Individuals were assessed daily for signs and symptoms of infection prior to starting their shifts and every 7 days for SAR-COV-2 infection by PCR test; no other health related examinations were conducted. Testing was also performed for levels of immunoglobin (Ig) G and IgM at the end of July when dosing with azoximer bromide was stopped. None of the medical professionals reported any tolerability issues. During the period of prophylactic dosing the medical team was exposed to over a thousand patients infected with COVID-19 during care delivery. Many of these patients experienced severe symptoms and were maintained on non-invasive, instead of invasive, ventilation.

All 52 professionals taking azoximer bromide remained symptom free and tested negative for COVID-19 during the 5-month dosing period with the exception of one of our colleagues who, during the 10-day dosage break, became infected with COVID-19 and subsequently died. Interestingly, during the same period, the department next to our in the hospital, which consisted of nearly 200 medical professionals who did not take azoximer bromide, reported ten positive COVID-19 cases and experienced one COVID-19-related death. As for the data on the number of cases and on mortality, no statistical processing for mortality was carried out. There was decrease in the number of cases of COVID-19 among medical personnel. Prophylactic administration of Polyoxidonium had no effect on mortality from COVID-19. Based on the available data using Fischer's exact test, the difference in the number of diseases (p=0.4687) and deaths (p = 0.3708) was not statistically significant. All medical professionals from ours and next to ours department used the same personal protective equipment (PPE).

Although the present observations are purely subjective in nature, it does raise the question of whether azoximer bromide could be used prophylactically to protect medical professionals in similar risk situations. Further work is clearly needed to address this question.

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