Case Report

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Clinical Improvement in COVID-19 After Use of Ivermectin: A Case Series

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ABSTRACT

Background: The Coronavirus disease 2019 (COVID-19) pandemic continues unabated worldwide, with a paucity of effective medications against the disease. Ivermectin has been shown to inhibit in-vitro replication of severe acute respiratory syndrome coronavirus 2 (SARS CoV-2), with several studies demonstrating clinical effectiveness. We report a case series of COVID-19 patients with rapid symptomatic improvement after commencing Ivermectin.

Case Presentation: Consecutive COVID-19 patients admitted in our facility between September and November 2020 received Ivermectin plus standard of care and followed up till clinical improvement or outcome (survived or died). Nine of our patients received Ivermectin plus standard of care during this period, with significant clinical improvement noted across all categories of patients, which was noted ≤3 days after commencement in 3(37.5%) and >3 days in 5(62.5%). Eight (88.9%) of our patients survived, with 1(11.1%) death.

Conclusion: There is an urgent need for local clinical trials to assess Ivermectin's effectiveness especially in resource poor areas.

KEYWORDS: COVID-19; SARS CoV-2; Ivermectin

INTRODUCTION

The coronavirus disease 19 (COVID-19) was first reported in Wuhan, China in December 2019 and has since spread across the world as a pandemic, resulting in millions of infections and hundreds of thousands of deaths [1]. It is a respiratory infection, which could also present with varied multi-systemic manifestation. At present there is no cure for COVID-19, although different medications have been tried with varying levels of efficacy.

Some of these are novel drugs while others are re-purposed drugs [2], with Azithromycin, Chloroquine, Hydroxychloroquine, as well as Ivermectin being some of the re-purposed drugs which have been used in our environment. Numerous studies have shown a shorter time to clinical improvement, reduced duration of hospital stay [3-5], mortality [6-8], as well as in time to viral clearance [7,8] in patients who have received Ivermectin.

There are also epidemiological reports of reductions in COVID-19 case counts, from some countries with widespread Ivermectin administration [9,10]. In all, there is a rapidly growing evidence base on the efficacy of Ivermectin, a broad-spectrum FDA-approved antiparasitic in COVID-19, which could be a potential game changer in bringing the pandemic under control, considering that the drug is cheap and widely available. This study describes clinical improvement observed in patients admitted for COVID-19 pneumonia in our facility who received Ivermectin and is important in that it further answers the question regarding the efficacy of Ivermectin in treatment of COVID-19 pneumonia, highlighting the need for large randomized controlled trials (RCT) in establishing its efficacy or otherwise.

MATERIALS AND METHODS

Study Design

A case series of COVID-19 patients who received Ivermectin at the Federal Medical Center, Abeokuta, Nigeria between September and November 2020. This period had the lowest confirmed COVID-19 case numbers across the country.

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Study Procedure

Consecutive confirmed adult cases of COVID-19 hospitalized during this period received standard of care [11] plus Ivermectin. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was diagnosed by reverse transcriptase Polymerase Chain Reaction (rt-PCR) of nasopharyngeal swabs obtained from each patient. Standard of care included antibiotics for super-imposed infections when present, intravenous fluids when required, as well as Oxygen when indicated and other supportive care. Ivermectin was given at a dose of 200mcg/kg daily for 3 days. All patients also received Tabs Azithromycin, Vitamin C and Zinc as part of the standards of care being administered in the country at the time. Survival was defined as clinical improvement with subsequent discharge from care or follow-up. Significant clinical improvement was defined as optimal resolution of patient's clinical symptoms, with improvement in physiological and laboratory parameters, as well as performance scores. Written informed consent was obtained from the patients or their legal representatives.

Data Collection

Sociodemographic and clinical details including physiological and laboratory parameters were obtained. Duration from onset of symptoms to commencement of Ivermectin, as well as duration from commencement to clinical improvement or outcome (died or survived) were also recorded from patient's case notes. This was then uploaded into an electronic spreadsheet.

Case Series/Results

As shown in Table 1, nine of the patients with confirmed COVID-19 who presented during this period received Ivermectin plus standard of care. Four (44.4%) were below the age of 45, 4(44.4%) between the ages of 45 and 65, and 1(11.1%) above 65 years, with a mean age of 42 years. There were 3(33.3%) males and 6(66.6%) females. Fever (88.9% *vs* 11.1%), cough (77.8% *vs* 22.2%), malaise (88.9% *vs* 11.1%) and breathlessness (55.5% *vs* 45.5%) were the commonest presenting complaints, with 5(55.5%) of our patients having other additional complaints apart from these.

Table 1: Ivermectin patient's data.

Socio-Demographics					Mean
Age (years)	<45 4(44.4%)	45-65 4(44.4%)	>65 1(11.1%)		42
Gender	Male 3(33.3%)	Female 6(66.6%)			
Presenting Complaints	Yes	No	Duration <5 days 7(77.8%)	>5 days 2(22.2%)	
Fever	8(88.9%)	1(11.1%)			
Cough	7(77.8%)	2(22.2%)			
Breathlessness	5(55.5%)	4(45.5%)			
Malaise	8(88.8%)	1(11.1%)			
Other	5(55.5%)	4(45.5%)			
Co-morbidity	Yes	No			
HTN	5(55.5%)	4(45.5%)			
DM	1(11.1%)	8(88.9%)			
Obesity	2(22.2%)	7(77.8%)			
COVID Category	Freq (%)				
Mild	2(22.2%)				
Moderate	3(33.3%)				
Severe	2(22.2%)				
Critical	2(22.2%)				
Intervention received	Yes	No			
Ivermectin	9(100%)	0(0%)			
SOC	9(100%)	0(0%)			
Day from onset of symptoms to commencing Ivermectin	<3 days 1(11.1%)	≥3 days 8(88.9%)			4.8 days
Days from Ivermectin to clinical improvement	≤3 days 3(37.5%)	>3 days 5(62.5%)			5 days
Labs	Normal	Abnormal			
FBC	7(77.8%)	2(22.2%)			
e/u/cr	7(77.8%)	2(22.2%)			
CXR					
Outcome	Survived 8(88.9%)	Died 1(11.1%)			
Duration of hospitalization	≤7 days 8(88.9%)	>7 days 1(11.1%)			4.9 days

Hypertension 5(55.5%) was the commonest co-morbidity, followed by obesity 2(22.2%) and Diabetes 1(11.1%). Two (22.2%) had mild disease, with 3(33.3%) having moderate disease, 2(22.2%) severe disease, and 2(22.2%) critical disease. All patients received Ivermectin plus standard of care as appropriate, with Ivermectin being commenced less than three days from symptom onset in 1(11.1%) and three or more days from symptom onset in 8(88.9%); mean duration of commencement was 4.8 days. Significant clinical improvement was noted three days or less after commencing Ivermectin in 3(37.5%) and greater than three days in 5(62.5%), with a mean duration of 5 days to clinical improvement. The full blood count and electrolytes were both normal in 7(77.8%) and abnormal in 2(22.2%) of patients. Chest X-ray wasn't uniformly done. Eight (88.9%) patients were hospitalized for less than or equal to seven days, while 1(11.9%) was hospitalized for greater than seven days; mean duration of hospitalization was 4.9 days. Eight (88.9%) of our patients survived, while 1(11.1%) death was recorded in one of the critical cases.

DISCUSSION

Ivermectin is a FDA-approved broad spectrum anti-parasitic drug commonly used in many conditions including Onchocerciasis, Loasis, Strongyloidiasis [12], with the drug also possessing broad spectrum anti-viral activity with effectiveness demonstrated against Dengue virus, Zika, Yellow fever, and West Nile virus amongst others [13-15]. Ivermectin has been said to play its anti-viral role through a nuclear transport inhibitory activity [16,17]. Recently, Caly [18] demonstrated that Ivermectin potently inhibits replication of SARS CoV-2 *in vitro*, with a notable reduction in SARS-CoV-2 RNA levels by 5,000-fold after incubating SARS-CoV-2 infected Vero/hSLAM cells with a single dose of Ivermectin for 48 hours.

They postulated that this effect of Ivermectin was possibly through its inhibition of IMPα/β1-mediated nuclear import of viral proteins, like it did for other RNA viruses. The effective dose, however was about 50 to 100-fold the peak plasma concentration of the dose used for parasitic diseases; levels that might not be feasible in humans. Despite this, as demonstrated in this case series, several studies have reported rapid and significant clinical improvement [3-5], including reduced mortality [6-8] in COVID-19 patients treated with Ivermectin either alone or in combination with other medications e.g. Doxycycline; one study comprising 100 patients reporting both symptomatic improvement as well positive viral clearance after a single dose of Ivermectin and Tabs Doxycycline 100mg daily for 10 days [19], while several other clinical trials are underway.

Epidemiological reports from countries with routine mass Ivermectin administration for the control of parasitic diseases (mostly from Africa) also show reduced COVID-19 case numbers compared to countries without [9,10]. In our patients, Ivermectin appeared to have positive effects across categories, from mild to critically ill patients, with the response being more rapid than our previous line of care where just standard of care and Azithromycin was used. Significant improvement was noted in more than a third of patients less than three days after commencing Ivermectin, and there is a possibility of having even better outcomes the earlier the drug is commenced. While the rapid clinical improvement seen in our patients after receiving Ivermectin might seem anecdotal, when taken in light of several other reports demonstrating similar clinical improvement, highlights the urgent need for well-designed large scale possibly multi-center clinical trials to objectively assess the effectiveness of Ivermectin in treatment of COVID-19 in our environment [19].

CONCLUSION

As the world-wide push to find medications effective against SARS CoV-2 frantically continues, a cheap and readily available drug like Ivermectin could serve as a major game-changer in this fight, especially in resource poor areas like ours that might not have access to more expensive novel anti-virals, leading to an urgent need for local clinical trials to evaluate its efficacy.

DECLARATION

Ethics approval and consent to participate – Our institution does not require ethical approval for case reports, but written informed consent was obtained from each participant or their legally approved representative.

Consent for publication – consent for publication was obtained from each patient or their legally approved representative.

AVAILABILITY OF DATA AND MATERIALS

All data generated or analysed during this study are included in this published article and its supplementary information files.

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