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Rivaroxaban Consumption Outcome in SARS-CoV-2 Pneumonia

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Abstract

Background: SARS-COV-2 is one of prothrombotic illness, and this raise mortality and morbidity. Rivaroxaban is one of antithrombotic agent helpful in reducing SARS-COV-2 morbidity and mortality. The study aimed to assess the effectiveness of early administration of Rivaroxaban in reducing SARS-COV-2 mortality.

Method: A cross-sectional observational study was done among 200 Iraqi cases with SARS-COV-2. The cases attended a private outpatient clinic at a period from June 2020 to July 2022. All cases received Rx (20mg one by one). The data included age, gender, smoking tobacco, comorbidities, treatment with Rx, any complication and bleeding occurrence.

Results: The mean age of (50.2 ± 18.6 years). The proportion of 44% within the age group (40-55) years. Females were prevalent (120, 60% of cases). Smokers were 139 cases (69.6%). Cases with comorbidity were 150 (75%). Of most study cases, 160 (80%) had moderate SARS-COV-2. D-dimer was elevated in 145 (72.5%). Hospitalized cases were 44 (22%). Cases required ICU admission were 28 (14%). Eleven cases were died. Clinical bleeding documented in 25 cases.

Conclusion: Rx 20 mg 1×1 as early management in moderate and severe SARS-COV-2 cases cans potentially protecting from thrombotic squeal. Follow-up of patients received Rx is mandatory. The administration should follow international guideline in prevent thromboembolic phenomena.

Keywords: Rivaroxaban, SARS-COV-2, anticoagulants, viral diseases, pneumonia

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Introduction

Many theories developed to explore the reasons of coagulation abnormalities in SARS-COV-2. Authors thought that endothelial vascular injuries seen in SARS-COV-2 tied with coagulo-pathic ways lead to thrombotic complications (arterial, venous thromboembolic, and in-situ arterial microthrombi) [1]. In addition, thrombosis, DIC, and storm of cytokines has been connected with bad SARS-COV-2 severity and prognosis [2].

Previously, about 25% of SARS-COV-2 cases admitted to the ICU are expected to develop thrombotic outcomes [3-5]. The SARS-COV-2 life-threatening thrombotic events are microvascular thrombosis (which cause diffuse lung damage) [6]. The major reasons of mortality are progressive hypoxemic respiratory failure and ARDS (which occur because of the invasion viruses into lung alveoli by activated via the storm cytokines of lead to activation of thrombosis and which led to microvascular and macrovascular thrombosis with diffuse lung injuries) [7].

The previous review suggested that prophylactic anticoagulants were safe and effective for hospitalised cases with SARS-COV-2 [8]. Anticoagulants and antithrombotic treatment were beneficial in reducing SARS-COV-2 morbidity and mortality [9, 10]. Rx is an oral selective factor X-a inhibitor with high bioavailability ranging (from 80-100%) for the 10 mg tablet irrespective of food intake and for the 15- and 20 mg tablets when taken with food [11].

There was a decrease in the consumption of rivaroxaban, with an increase in apixaban’s share in the structure of DOAC consumption during the coronavirus pandemic. Obtained data indicate that in 2021 the apixaban consumption in the Russian Federation corresponded to the recommended DDD in the national guidelines, which indicates the most correct use of apixaban according to Russian GPGs [12].

SARS-CoV-2 infection may predispose patients to thrombotic disease. Patients with SARS-COV-2 pneumonia who are receiving non-vitamin K antagonists or direct oral anticoagulants for chronic disease are usually switched to heparin treatment during hospitalization. However, information about the most appropriate antithrombotic therapy after the acute infection phase is lacking. This case highlights the risk of thrombotic complications after COVID-19 infection, raises some concern about their underlying mechanisms, and supports the use of effective anti-thrombotic therapy [13].

Authors did not demonstrate an impact of rivaroxaban on disease progression in high-risk adults

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with mild COVID-19. There remains a critical public health gap in identifying scalable effective therapies for high-risk people in the outpatient setting to prevent COVID-19 progression [14].

The study aimed to evaluate the effectiveness of early administration of Rx in SARS-COV-2.

Methods

A cross-sectional observational study was done among 200 Iraqi cases with SARS-COV-2. The cases attended a private outpatient clinic at a period from June 2020 to July 2022. All cases received Rx (20mg one by one).

Inclusion criteria

- Age > 18 yrs.
- PCR for SARS-COV-2 positive.

Exclusion criteria

- Chronic diseases.
- CVA.
- GIT ulcers.
- Pregnancy.
- Cases with haemophilia.

The data included age, gender, smoking tobacco, comorbidities, treatment with Rx, any complication and bleeding occurrence.

Statistics

Data were analysed by SPSS (Statistical Package for Social Sciences, ver-26). Variables are described as mean and SD, numbers and percentages. The Fisher exact test were used. $P < 0.05$ was considered as significance.

Results

The mean age of (50.2 ± 18.6 years). The proportion of 44% within the age group (40-55) years. Females were prevalent (120, 60% of cases). Smokers were 139 cases (69.6%). Cases with comorbidity were 150 (75%). As shown in Table 1.

Table 1: Demographic characteristics of the study sample

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Variables		Mean ± SD /No. (%)
Age (years) / range		**50.2 ±18.6 years (18 - 68)**
Gender	**Female**	120 (60)
	Male	80 (40)
Smoking History		139 (69.9%)
Comorbidity (DM, HT, IHD)		**75%**

Of most study cases, 160 (80%) had moderate SARS-COV-2. D-dimer was elevated in 145 (72.5%). Hospitalized cases were 44 (22%). Cases required ICU admission were 28 (14%). Eleven cases were died. Clinical bleeding documented in 25 cases. (Table 2**)**

Table 2: SARS-COV-2 clinical characters

Variable		No. (%)
COVID- 19 severity	Moderate	160 (80)
	Severe	40 (20)
D-dimer level	Elevated > 500 ng/ml	145 (72.5)
	Normal ≤ 500 ng/ml	55 (27.5)
Hospitalization		44 (22)
ICU admission		28 (14)
Outcome	Live	189 (94.5)
	Died	11 (5.5)
Clinical bleeding		25 (12.5)

Discussion

Rx is utilized to droping arterial and venous thrombotic sequel risk when the drug indicated [15-17]. Previously, many authors found that Rx used as prolonged prophylaxis lead to reduced thrombotic events, especially those admitted for severe respiratory illness [18].

We enrolled severe illness adults who presented with mild disease during the first week of their

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illness to intervene, as the disease is thought to transition from the active viral replication phase to the inflammatory phase, and before disease progressed [19]. Rivaroxaban does not possess direct antiviral or antiinflammatory properties but it may mitigate the consequences of SARS-CoV-2 replication and inflammation. We posited that rivaroxaban could prevent COVID-19–associated VTE and microthrombi in the lungs and other organs that have been theorized to cause COVID-19 symptoms and progression. This could potentially explain the observation that more participants achieved asymptomatic status. It appears that the observed differences between groups occurred after day 14 of the study and in participants who had longer time from onset of symptoms to randomization. We postulate that the persistence of symptoms after the second week of illness may be the result of microthrombi against which rivaroxaban is exerting a positive effect. It is possible that administration of rivaroxaban during mild disease and within the first 2 weeks of illness was too early, as a major shift to a proinflammatory and coagulopathy state occurs when disease transitions from mild to moderate [20]. We did not collect blood for biomarkers such as D-dimer in this community-based study. However, such examination should be considered in future studies to aid in potentially identifying a population that would most benefit from prophylactic anticoagulant. The daily dose of 10 mg rivaroxaban for 21 days may have been insufficient. The selection was based on the indication for VTE prophylaxis in acutely ill patients (10 mg daily for 31–39 days after hospital discharge) and a safety profile suitable for remote monitoring in our study. Fatigue, cough, anosmia, and ageusia appeared less frequently in the rivaroxaban group at day 28. Whether rivaroxaban could benefit long-term COVID-19 symptoms is unknown and should be further investigated.

A study by Capell et al. [21] concluded that factor Xa has a potential role in the pathogenesis of coronavirus morbidity and mortality. Moreover, out cases and hospitalised SARS-COV-2 cases could benefit from early prophylaxis with Rx to prevent severe SARS-COV-2 progression.

It established that cases with SARS-COV-2 pneumonia show abnormal coagulation tests were associated with a fatal outcome [21]. Preliminary reports on using anticoagulants like therapeutic heparin in moderate SARS-COV-2 to reduce SARS-COV-2 mortality and morbidity suggest improved outcomes [23]. Experts' guidelines included prophylactic low-dose anticoagulants for adults admitted with moderate and severe SARS-COV-2 but not the critically ill to reduce SARS-COV-2 mortality [24]. Moreover, in a retrospective cohort study, up to half of venous thrombotic complications in hospitalized SARS-COV-2 cases were diagnosed within the first 24

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hours of admission [25]. An importance of early use of anticoagulants for SARS-COV-2 treatment, a prospective randomized open-label trial was conducted from 14 centres in Brazil to test the efficacy and safety of using Rx [26]. This study aimed to evaluate the safety and efficacy of Rx 10 mg once daily for 35 ± 4 days versus no intervention after hospital discharge in COVID-19 patients who were at increased risk for VTE and have received standard parenteral VTE prophylaxis during hospitalization. The composite efficacy endpoint is a combination of symptomatic VTE, VTE-related death, VTE detected by bilateral lower limbs venous duplex scan and computed tomography pulmonary angiogram on day 35 ± 4 posthospital discharge and symptomatic arterial thromboembolism (myocardial infarction, nonhemorrhagic stroke, major adverse limb events, and cardiovascular death) up to day 35 ± 4 posthospital discharge. The key safety outcome is the incidence of major bleeding according to ISTH criteria. The MICHELLE trial is expected to provide high-quality evidence around the role of extended thromboprophylaxis in COVID-19 and will help guide medical decisions in clinical practice .

Conclusion

Rx 20 mg 1×1 as early management in moderate and severe SARS-COV-2 cases cans potentially protecting from thrombotic squeal. Follow-up of patients received Rx is mandatory. The administration should follow international guideline in prevent thromboembolic phenomena.

Disclosure

None

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