Use of Rivaroxaban in Obese Patient With Pulmonary Thromboembolism.

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Case Report

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Abstract

Background. There are few clinical data about efficacy and safety of Direct Oral Anticoagulants (DOACs) for venous thromboembolism (VTE) in obese patients, especially those with a Body Mass Index (BMI) > 40 kg/m² or a weight more than 120 kg.

Case presentation. We discuss the case of a 41-years-old caucasian male affected by class III obesity, treated with Rivaroxaban at the dosage advised by the most recent guidelines for Pulmonary Embolism. Among DOACs, Rivaroxaban plasma concentration is not significantly influenced by elevated body weight. During follow-up, we noticed a greater control of symptoms and a progressive improvement in radiological and biochemical parameters and a good therapy compliance.

Conclusions. Despite the need for more data in this specific field, our experience suggests the possibility to use DOACs as an alternative to heparin, optimizing the adherence and the quality of life of these patients.

Introduction

In the last few years, there has been an increasing use of direct-acting oral anticoagulants (DOACs) for both prevention and treatment of venous thromboembolism (VTE) and stroke prophylaxis in NVAf (Non Valvular Atrial Fibrillation). The most recent guidelines recommend DOACs as first-line option over Warfarin (1, 2).

Although there is evidence about efficacy and safety of DOAC use in obese patients with NVAf, there are limited data for what concerns their employment in pulmonary embolism.

Moreover, there are not univocal evidences for what concerns pharmacokinetics and pharmacodynamics in the obese population, so that the International Society of Thrombosis and Haemostasis (ISTH) has suggested to avoid DOACs in these patients. (3).

Nevertheless, new data emerged supporting the use of DOACs in this specific setting.

Some old pharmacokinetics and pharmacodynamics studies showed that Rivaroxaban plasma concentration is not significantly influenced by elevated body weight (4, 5).

A more recent meta-analysis of five observational studies (6,580 patients) compared Warfarin and DOACs in terms of efficacy (VTE recurrence) and safety (major bleeding) in VTE treatment in obese patients (BMI > 40 kg/m² or weight > 120 kg); they found that DOACs were not inferior regarding the efficacy and safety compared to Warfarin (6). Similarly, a retrospective chart review performed in hospitalized patients with BMI > 40 kg/m² or weight > 120 kg (176 patients) that began Warfarin or Rivaroxaban as first-line therapy showed that there were no significative differences between the two groups, considering clinical failure (VTE recurrence, stroke incidence and mortality) and length of hospitalization. (7). In another important meta-analysis published in 2021 by Katel et al (8) DOACs

showed similar efficacy and safety in the prevention of recurrent VTE risk and major bleeding events in morbidly obese patients when compared to warfarin/LMWH.

Case Report

A 41-years-old caucasian male affected by class III obesity (weight 153 kg, BMI 42 kg/m²) came to the Emergency Room (ER) of our Hospital for a pain in his left leg from about 8 days, a dry cough, light dyspnea and low-grade fever. About a month earlier he was taken into care by orthopedists for a persistent knee pain, probably due to initial osteoarthritis, and seven days before accessing the ER he had performed an infiltration of hyaluronic acid in his left knee. He did not take any continuous therapy, but he occasionally took an NSAID or Paracetamol for leg pain. He denied any habit of smoking, and occasionally took on alcoholic drinks. He denied any family history of cardiovascular disease, thromboembolic accidents or sudden death.

At the first evaluation the patient was found slightly dyspnoic, in acute respiratory failure; the pulse was tachycardic (115 bpm) with normal and stable blood pressure values. Biochemical evaluation showed a great increase of D-dimer value (table 1-b). At the Doppler Ultrasound of the left lower limb vein, an extended floating thrombus of the left common femoral vein was found, also involving the superficial femoral vein, popliteal vein and the whole venous axis distally up to the tibio-peroneal vein. To confirm the strong suspicion of pulmonary embolism, a pulmonary CT-angio was performed, and it showed a bilateral diffuse embolism that involved the two main pulmonary arteries and almost all their branches. Nt-pro BNP was 1234 pg/ml and troponin t was 44 ng/l. There were no echocardiographic criteria of RV dysfunction. PESI score showed a high risk of 30-days mortality (class IV). Considering the severity of the case (intermediate-low early mortality risk for ESC guidelines (1) the patient was hospitalized to monitor vital signs.

Considering the evidences in literature for Rivaroxaban's good pharmacodynamics properties even in obese patients, and the evidence of efficacy and safety in patient with NVAf (2), we administered Rivaroxaban 15 mg twice daily for the first 21 days and then 20 mg once a day. After the first three days of Rivaroxaban, its plasmatic downstream concentration was found to be within the therapeutic range (table 1-b). During hospitalization there was an improvement of respiratory exchanges, measured on sequential blood gas analysis (table 1-a), and the patient was gradually weaned from oxygen therapy. We did not find any known bleeding or adverse reaction. Furthermore, we observed a progressive improvement of the left lower limb symptoms. After about 13 days from the first administration of Rivaroxaban, we observed a significant drop of serum D-dimer concentration; the second dosage of plasmatic Rivaroxaban was in range (table 1-b).

Table 1. Trend of blood gas and biochemical parameters of patients during the follow-up.

a

	day 1	day 3	day 4	day 8	day 11	day 13
pH	7.43	7.45	7.46	7.40	7.42	7.42
pCO ₂ (mmHg)	35	36	36	36	39	39
P/F	152	174	192	219	321	309
HCO ₃ ⁻ (mmol/L)	23	25	26	22	27	25

b

	T ₀	day 3	day 13	3 months
BP (mmHg)	125/80	140/80	145/85	130/80
HR (bpm)	115	85	75	70
Hb (g/dL)	14.9	13.5	13.2	14.7
Plts (unit/mm ³)	174000	250000	231000	227000
S-creat (mg/dL)	1.00	0.85	0.84	0.83
ALT (U/L)	28	35	-	21
CRP (mg/L)	64	42	5	-
P-Rivaroxaban (ng/mL)	-	52*	68*	-
D-dimer (mcg/L)	> 10000	-	3079	186

*therapeutic range: P-Rivaroxaban [6–87 ng/ml]

Before discharge we performed another lower limb venous Doppler Ultrasound that showed resolution of the common femoral vein thrombosis and a reduction in the superficial femoral vein one.

At the 3-months follow-up visit there was no evidence of VTE recurrence at the ultrasound check or major bleeding (Fig. 1).

The patient's clinical status and biochemical evaluations were in the normal range with a reduction of D-dimer plasmatic levels, and a Doppler ultrasound demonstrated a further reduction in the extension of the thrombus. The patient guaranteed a good therapy compliance. We advised him to continue rivaroxaban for a total of six months.

At the 6-month follow-up, the patient was in excellent condition, he had lost 6 kg of weight following the diet and there were no signs of thromboembolism. The drug was then discontinued.

Discussion

Even if there are growing evidences of the effectiveness and safety of rivaroxaban in obese population affected by non-valvular atrial fibrillation (9–11), there are still no strong indications for the choice of DOACs in obese patients with venous thromboembolism.

In this case, we treated our acute patient with rivaroxaban at a dosage of 15 mg twice daily for the first 21 days, and then 20 mg once daily, according to the ESC guidelines for the treatment of pulmonary embolism (1). We monitored the efficacy and safety of therapy during hospitalization and 6 months later. The use of DOACs has already been consolidated in overweight and obese subjects with NVAf (9–11), but the availability of plasma dosage of drug level can optimize the management of these patients.

Despite the presence of a third-grade obesity, plasmatic dosage of rivaroxaban was always in therapeutic range, confirming the low influence of body weight in the effective plasmatic level of the drug (11). We observed a good response in terms of safety, without any major bleeding or adverse event reported, and efficacy, in terms of reduction of D-dimer plasmatic levels, improvement of the respiratory function and ultrasound thrombus size.

Conclusions

We believe that our experience could reinforce the use of DOACs, and Rivaroxaban in particular, as an alternative to heparins in obese patients, with the aid of the possibility of plasma dosage of the drug, thus optimizing the adherence and the quality of life., and despite the need for more data in the treatment of VTE, we believe that the extension of their employment even in this specific field could be considered safe and efficacious.

Declaration Section

- Ethical Approval and Consent to participate

Informed written consent was obtained from the patient.

- Consent for publication

Not applicable

- Availability of supporting data

We confirmed the availability of supporting data

- Competing interests

The authors have no competing interests as defined by BMC, or other interests that might be perceived to influence the results and/or discussion reported in this paper

- Funding

Not applicable

- Authors' contributions

CR, CE FA and DMS collected the data, SA, CM and GD analyzed the results, DCL, CR and GD contributed the writing of the manuscript.

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Not applicable

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Figures

Evolution of the thrombotic lesion of popliteal vein at baseline and after the treatment

Figure 1

Legend not included with this version.