EAS Journal of Anaesthesiology and Critical Care
Abbreviated Key Title: EAS J Anesthesiol Crit Care
ISSN: 2663-094X (Print) & ISSN: 2663-676X (Online)
Published By East African Scholars Publisher, Kenya

OPEN ACCESS

Volume-5 | Issue-2 | Mar-Apr-2023 | DOI: 10.36349/easjacc.2023.v05i02.002

Case Report

Drug Management of Direct Oral Anticoagulants for an Urgent Invasive Procedure: Contribution of Thoracic Ultrasound - Case Report

Moustapha Diedhiou[1*], N. Sarr[1], A. Dieye1, E.B.BA[2], A, F. G. Niang[1], S. M. Beye[1], ML Fall[1]

[1]Training and Research Unit in Health Sciences (UFRSS), Gaston Berger University, Saint Louis, Senegal
[2]Faculty of Medicine of Dakar, Cheikh Anta Diop University, Dakar 10700, Senegal

Article History
Received: 03.02.2023
Accepted: 07.03.2023
Published: 13.03.2023

Journal homepage:
https://www.easpublisher.com

Quick Response Code

Abstract: ***Introduction*:** Direct oral anticoagulants (DOA) are recent drugs prescribed for their anticoagulant properties. When an invasive procedure is planned for a patient under DOA, the challenge for the anaesthetist is to assess the risk of bleeding and thromboembolism secondary to the medication withdrawal. In certain situations, ultrasound, with its advantages of guidance and location, is an important tool that can reduce the peri-procedural bleeding risk. ***Method:*** We illustrate this problem with this clinical case. ***Observation*:** This is an 18-year-old female patient with a history of recent deep vein thrombosis treated with direct oral anticoagulants in an underlying pulmonary tuberculosis condition under treatment; received in the intensive care unit for management of respiratory distress due to a hydro-pneumothorax confirmed on pleuropulmonary ultrasound. Amain this urgent indication for thoracic drainage, the patient benefited from a decision by the referral team to withdraw the DOAs for 3 days, a relay with curative LMWH, an exsufflation of the pneumothorax and an evacuation puncture of the effusion under ultrasound guidance and location. Chest drainage was performed successfully and uneventfully after 3 days of DOA withdrawal. ***Conclusion*:** When an invasive procedure has to be performed in the emergency department or when the thromboembolic risk is very high, validated strategies for the peri-procedural management of DOAs have not been the subject of consensus. Our case-report highlighted the value of thoracic ultrasound in the intensive care unit, which facilitates the performance of minimally traumatic procedures in the emergency department. This tool allows to postpone a procedure of bleeding risk while promoting good drug management.

Keywords: Direct Oral Anticoagulants –invasive acts –chest ultrasound.

INTRODUCTION

Direct oral anticoagulants (DOAs) are recent drugs prescribed for their anticoagulant properties in the management of non-valvular atrial fibrillation, venous thrombosis, pulmonary embolism etc. They can be prescribed for preventive or therapeutic purposes. When an invasive procedure is planned for a patient under DOA, the challenge for the anaesthetist-intensive care physician is to assess the haemorrhagic risks associated with the procedure in an anticoagulated patient, as well as the thrombo-embolic risk secondary to their discontinuation, even if overlap with other molecules with a short half-life is considered. In certain situations, besides its advantages in terms of guidance and location, ultrasound is an important tool that makes it possible to reduce the peri-procedural haemorrhagic risk.

Method: We illustrate this problem with this clinical case.

CASE REPORT

We received in the intensive care unit of Saint Louis regional hospital of an 18-year-old female patient, referred from the medicine department for respiratory distress.

The patient has hospitalized 2 weeks ago in the medicine department for the management of pulmonary tuberculosis under treatment (RHZE 1cp/d) with an evolution marked by the discovery of a deep venous thrombosis reaching the left femoral vein confirmed by Doppler ultrasound of the lower limbs for which treatment with Rivaroxaban (Xarelto 15mg x 2 /d) was initiated. Two weeks later the patient presented with respiratory distress without signs of heart failure

***Corresponding Author:** Moustapha Diedhiou
Training and Research Unit in Health Sciences (UFRSS), Gaston Berger University, Saint Louis, Senegal

requiring admission to the ICU. The electrocardiogram and cardiac ultrasound showed no signs of acute pulmonary heart disease with a left ventricle with good systolic function and retained filling pressures. She benefited from conditioning (oxygen, half-seated position). The chest X-ray carried out in this backdrop identified a large hydro-pneumothorax on the left.

The examination on admission to the intensive care unit found a conscious patient, hemodynamically stable. Looking at the respiratory patterns, SpO2 was 82% under oxygen (high concentration mask at 12 l/min) with clinical signs of respiratory distress. A gasometry performed was in favour of severe hypoxia with slight respiratory acidosis with a PH of 7.32, PO2= 45 mm hg, PaCO2= 48mmhg.

Amain this context, the patient was given optiflow oxygen therapy with a flow rate of 60l/min and a FiO2 of 100%, which increased the Sp02 to 93%. The decision to evacuate the hydro-pneumothorax was taken by the team as a matter of urgency. Regarding the risk of bleeding that may result from an invasive procedure such as drainage, we decided to proceed with a puncture of the effusion and exsufflation of the pneumothorax under ultrasound guidance. The thoracic ultrasound was performed using a high-frequency linear probe placed on the left mid-clavicular line anteriorly and opposite the second and third left intercostal spaces and on the middle axillary line opposite to the fifth and sixth intercostal spaces.

In the left anterior section, the ultrasound results showed an absence of a distinct pleural line with a bar-code image on time-lapse (TM) and an anterior lung point opposite the fourth left intercostal space (Figure 1). On the left basal sections, the ultrasound showed a pleural detachment with a sinusoidal aspect of the pleura in TM mode highlighting a hypoechoic image in favour of a pleural effusion (Figure 2). In addition, the biology revealed a prothrombin time of 100%, an INR of 1. The blood count showed a platelet rate of 192,000 elements/mm, a haemoglobin rate of 10 g/dl, white blood cells of 7,200 elements/mm3, a serum creatinine level of 08mg/dl with a clearance according to Cockcroft's formula of 35 ml/min, liver enzymes (ASAT, ALAT) measured as part of the therapeutic assessment of tuberculosis had returned normal. The anti-Xa activity was not measured because it was not available in our context. The decision was therefore made to proceed with insufflation of the pneumothorax with the help of the ultrasound location. An echo-guided pleural puncture was also performed and outlined 450 ml of citrine yellow fluid and samples were taken for cytobacteriological and biochemical purposes. A follow-up pleural ultrasound showed a disappearance of the anterior bar-code appearance and significant regression of the pleural effusion. A few hours later, we noted an improvement in SPO2 to 98% and the process of weaning from oxygen therapy was initiated.

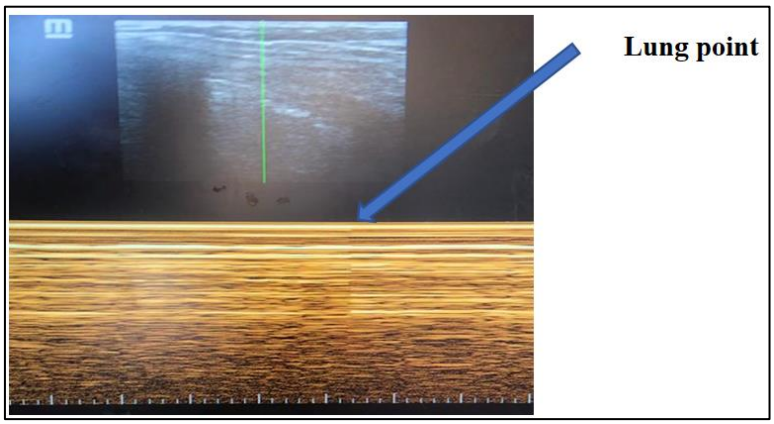

Figure 1: Pleural ultrasound showing a bar-code appearance

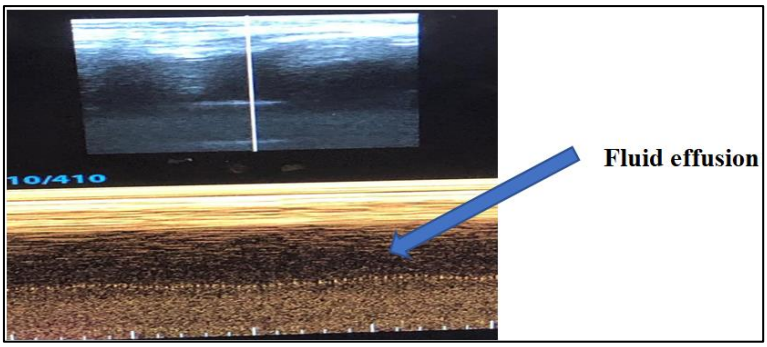

Figure 2: Pleural ultrasound showing a sinusoidal appearance of the visceral pleura

After respiratory stability, we performed a thoracic angioscan, which came back in favour of a pleural effusion of small to medium abundance on the left, and a pneumothorax of small abundance on the left.

There were no signs of pulmonary embolism. The next day, the patient was eupneic with a saturation of 97% on room air.

Regarding drug management, the decision was to stop Xarelto for 3 days and to start LMWH 0.6ml/10kg/12h. On the third day, the last injection of LMWH was skipped and the patient underwent a pleural ultrasound which revealed a pleural effusion of moderate size for which thoracic drainage with a 28 G chest drain was carried out which brought back 350 ml immediately and 800 ml over 24 hours. Xarelto 15mg X 2 / day was reintroduced 06 hours after drainage in the absence of bleeding complications.

The evolution during her hospitalization in the intensive care unit was favourable and the patient was transferred back to the medical department with a drain in place on an anti-reflux valve. During her stay in medicine, the drain was removed after 3 weeks based on unremarkable evolution and a satisfactory pleural ultrasound control. One month later, the patient was declared discharged under Xarelto cp 15 mg/day and antituberculosis treatment. The patient and her family were informed of the hygienic and dietary preventive measures and the isolation measures against tuberculosis and a team from the health district were called in for follow-up at home.

DISCUSSION

The indications for the new direct oral anticoagulants (DOAs), direct anti-Xa or anti-IIa, have progressively broadened: Initially used in "prophylactic" doses for the prevention of deep vein thrombosis (DVT), these new molecules are now prescribed in "curative" doses for the treatment of DVT or pulmonary embolism, for the long-term prevention of venous thromboembolism disease (VTE), or for the prevention of stroke and systemic embolism in non-valvular atrial fibrillation (AF) [1]. Rivaroxaban (Xarelto), dabigatran (Pradaxa) and apixaban (Eliquis) are likely to replace AVKs in many indications. Each year, approximately 10% of patients receiving antithrombotic treatment undergo surgery or an invasive procedure requiring the discontinuation of this treatment. In the case of an elective (anticipated) invasive procedure, the practitioner will have to decide on a preoperative strategy for stopping the DOAs, a strategy made difficult by the different molecules, their different pharmacokinetic properties and the various dosage regimens. Furthermore, the absence of an antidote to suppress the anticoagulant effect of DOAs and the lack of a simple biological test that is rapidly accessible to all to measure the anticoagulant effect of DOAs encourages caution. Similarly to any anticoagulant treatment, DOAs increase the risk of bleeding, particularly in the case of invasive procedures [2]. There is no validated therapeutic range, and the safe threshold concentration below which there is no excess bleeding risk is not known with certainty. Therefore, in patients who may have decreased clearance of DOA, especially in cases of kidney injury, it is not possible to verify, by simple assay, that the concentration of DOA before the invasive procedure is indeed minimal and that the risk of bleeding induced by DOA is nil. Even if the practitioner had this assay, the threshold concentration allowing the invasive procedure to be performed safelý is not known for each DOA [1].

Based on pharmacokinetic modelling, some authors propose a drug concentration of 30 ng/ml or less as a safety threshold for dabigatran and rivaroxaban [3]. This threshold value does not apply to apixaban. The inter-individual pharmacokinetic variability of DOAs is large, influenced by renal and hepatobiliary function, age, sex, weight, and drug interactions so it is difficult to calculate the residual concentration of the DOA after short treatment discontinuation [4]. Recommendations on the need to stop the DOA, whether or not to switch to LMWH (low molecular weight heparin) and when to restart the DOA depend on the molecule but especially on the assessment of the bleeding risk of the procedure or surgery. The attitude is also influenced by the urgency of the surgical act or procedure. In our case, we were faced with the need to perform an urgent invasive procedure with moderate bleeding risk. Overall, for good peri-procedural management of DOAs, three situations must be considered, clearly defined by the learned societies: low-risk bleeding procedures, high-risk bleeding procedures (including moderate-risk bleeding procedures and major-risk bleeding procedures) and emergency procedures.

Low-risk bleeding procedures are those that cause infrequent, low-intensity or easily controlled bleeding and can be performed in patients with therapeutic levels of anticoagulation. These procedures can be performed under DOA [5]. According to the recommendations of the SFAR (French Society of Anaesthesia and Intensive Care) in 2016, the following attitudes should be applied regardless of the patient's treatment regimen [5]:

- If the patient takes a DOA twice a day, they should take their treatment in the morning of the day before the operation and skip 2 doses before the procedure.
- If the patient is taking a one-dose DOA in the morning, they take their treatment the day before the procedure and skip one dose before the procedure.

- If the patient is taking a one-shot DOA in the evening, then they take their treatment the day before the procedure and skip 1 dose before the procedure. It is not advisable to repeat the treatment with LMWH, nor to measure the anticoagulant activity, and it is recommended that the treatment be resumed at the usual time and at least 6 hours after the end of the invasive procedure if there is no bleeding event [5].

High-risk invasive procedures are defined as those that cannot reasonably be performed in the presence of anticoagulants [6]. For these procedures, the proposed high-risk bleeding regimen applies indiscriminately to rivaroxaban, apixaban, and edoxaban due to the great similarities in the pharmacokinetics of these drugs. Thus, and considering the partial renal elimination of these drugs, a last dose at d-3 before the procedure is proposed for clearances greater than 30 ml/min. Given the predominantly renal elimination of dabigatran, a different stopping time is proposed according to the creatinine clearance (CrCl) calculated according to the Cockcroft and Gault formula: last dose at d-4 if CrCl ≥ 50 ml/min and last dose at d-5 if CrCl between 30 and 50 ml/min. This assumes that recent creatinine levels are available. This should be available as it is regularly monitored by the referring physician in charge of the patient [7]. For procedures with a high risk of bleeding, it is not appropriate to use LMWH and coagulation monitoring is not necessary [7].

With the proposed preoperative regimens, there is no need for preoperative heparin (UFH or LMWH) therapy, except in exceptional cases of very high thrombotic risk, which should be managed by a multidisciplinary referral team. In these situations, DOAs and heparins should not be administered simultaneously [5]. Apart from exceptional circumstances, or for clinical research purposes (registries), there is no need for standard haemostasis assays or tests to check residual concentration for elective procedures when the recommended stopping times are respected and accumulation or prolonged elimination is not suspected [5].

The urgent nature of the invasive procedure does not allow the DOA treatment to be stopped several days before. The time of the last intake of the DOA, the molecule, and its dosage (dose and the number of daily intakes) must be documented. It is important to assess kidney function (creatinine clearance according to Cockcroft), which allows the assessment of drug elimination. For dabigatran, when measured concentrations are removed, haemodialysis would allow faster elimination of the drug [1].

For patients treated in the early phase of deep vein thrombosis or pulmonary embolism, rivaroxaban doses are 15 mg x 2 for 3 weeks, apixaban doses are 10 mg x 2 for 10 days. During this period, when the need to schedule surgery is a rare event and should be avoided, the standard drug management regimen proposed above does not apply [5]. A personalized strategy should be discussed by a multidisciplinary referral team. In patients who are to undergo a procedure with a high bleeding risk and a particularly high thrombotic risk, an alternative strategy may be considered by a multidisciplinary referral team [5]. This exceptional situation described in the literature was found in our patient who had a high thromboembolic risk and an urgent indication for a procedure with a moderate bleeding risk (chest drainage). Indeed, the main concern in the early management of deep vein thrombosis is its progression to pulmonary embolism [8]. Our patient had a high probability of developing pulmonary embolism according to the simplified Wells score [8]. The attitude of our referral team was therefore to consider the high thromboembolic risk in the face of the impossibility of placing a venous filter in our context.

The decision was to stop rivaroxaban by the recommendations for 3 days, and a relay with HPBM at a curative dose was instituted as soon as the creatinine clearance of our patient was normal. Given the high risk of bleeding associated with the urgent indication to perform thoracic drainage, the decision was to proceed urgently to the evacuation of the pleural effusion and to perform the exsufflation of the pneumothorax under ultrasound guidance. This attitude made it possible to postpone thoracic drainage considered an act with moderate haemorrhagic risk. These procedures were carried out with complete safety thanks to ultrasound detection and guidance and allowed the transformation of an urgent invasive procedure into an elective invasive procedure allowing better drug management. After stopping rivaroxaban for 3 days, the recommendations should be respected by performing the drainage procedure after skipping the last dose of LMWH. The resumption of rivaroxaban at H6 in the absence of a bleeding situation was carried out without incident. Our attitude is supported by the findings of Jasper M. Smit *et al*., who reported that lung ultrasound is a suitable diagnostic modality for patients in intensive care units to detect consolidations, interstitial syndrome and pleural perfusion [9]. Pulmonary ultrasound allows visual medicine to be practised in a field where everything must be done quickly and accurately, particularly in intensive care emergencies [10]. Also, if puncture procedures with a risk of haemorrhage are planned, the use of ultrasound guidance in addition to the diagnosis can reduce the complications.

CONCLUSION

Peri-procedural drug management for procedures with high or moderate bleeding risk is well codified. However, when the procedure is invasive and must be performed urgently or when the

thromboembolic risk is very high, validated strategies have not been the subject of consensus. Our case report has highlighted the interest in thoracic ultrasound in the intensive care unit, which facilitates the performance of minimally traumatic procedures in the emergency department. For thoracic drainage under DOA, this tool can help postpone invasive procedures for better drug management.

Competing Interest: The authors declare no competing interest.

REFERENCES

1. Schnyder-Joris, C., Bonhomme, F., Bonvini, R., & Fontana, P. (2013). Gestion péri-interventionnelle des nouveaux agents antiplaquettaires. *Revue médicale suisse*, *9*(372), 326-330.
2. Tendera, M., Syzdół, M., & Parma, Z. (2012). ARISTOTLE RE-LYs on the ROCKET. What's new in stroke prevention in patients with atrial fibrillation?. *Cardiology journal*, *19*(1), 4-10.
3. Pernod, G., Albaladejo, P., Godier, A., Samama, C. M., Susen, S., Gruel, Y., ... & Sié, P. (2013, October). Prise en charge des complications hémorragiques graves et de la chirurgie en urgence chez les patients recevant un anticoagulant oral anti-IIa ou anti-Xa direct. Propositions du Groupe d'intérêt en Hémostase Périopératoire (GIHP)-mars 2013. In *Annales françaises d'anesthésie et de réanimation* (Vol. 32, No. 10, pp. 691-700). Elsevier Masson.
4. Mueck, W., Schwers, S., & Stampfuss, J. (2013). Rivaroxaban and other novel oral anticoagulants: pharmacokinetics in healthy subjects, specific patient populations and relevance of coagulation monitoring. *Thrombosis journal*, *11*(1), 1-17.
5. Albaladejo, P., Bonhomme, F., Blais, N., Collet, J. P., Faraoni, D., Fontana, P., ... & Susen, S. (2016). Gestion des anticoagulants oraux directs pour la chirurgie et les actes invasifs programmés: propositions réactualisées du Groupe d'intérêt en hémostase périopératoire (GIHP)–septembre 2015. *Anesthésie & Réanimation*, *2*(6), 414-420.
6. Garcia, D., Alexander, J. H., Wallentin, L., Wojdyla, D. M., Thomas, L., Hanna, M., ... & Lopes, R. D. (2014). Management and clinical outcomes in patients treated with apixaban vs warfarin undergoing procedures. *Blood, The Journal of the American Society of Hematology*, *124*(25), 3692-3698.
7. Heidbuchel, H., Verhamme, P., Alings, M., Antz, M., Diener, H. C., Hacke, W., ... & Savelieva, I. (2015). Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation. *Ep Europace*, *17*(10), 1467-1507.
8. Sanchez, O., Benhamou, Y., Bertoletti, L., Constant, J., Couturaud, F., Delluc, A., ... & Sevestre, M. A. (2019). Recommandations de bonne pratique pour la prise en charge de la maladie veineuse thromboembolique chez l'adulte. Version courte. *Revue des maladies respiratoires*, *36*(2), 249-283.
9. Smit, J. M., Haaksma, M. E., Winkler, M. H., Heldeweg, M. L., Arts, L., Lust, E. J., ... & Tuinman, P. R. (2021). Lung ultrasound in a tertiary intensive care unit population: a diagnostic accuracy study. *Critical Care*, *25*(1), 1-9.
10. Lichtenstein, D. (2008). Échographie pulmonaire en réanimation et aux urgences. *Réanimation*, 17(8), 722-730.

Cite this article: Moustapha Diedhiou, N. Sarr, A. Dieye, E.B.BA, A, F. G. Niang, S. M. Beye, ML Fall (2023). Drug Management of Direct Oral Anticoagulants for an Urgent Invasive Procedure: Contribution of Thoracic Ultrasound - Case Report. *EAS J Anesthesiol Crit Care*, *5*(2), 23-27.