CORRESPONDENCE

Direct Oral Anticoagulants in Emergency Trauma Admissions—Perioperative Management, and Handling Hemorrhage

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perioperative management, and handling hemorrhage. Dtsch Arztebl Int 2016; 113: 575–82.

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Conflict of interest statement
The author declares that no conflict of interest exists.

Laboratory Monitoring Needs to Be Improved

One of the problems in dealing with direct oral coagulants (DOACs) is the fact that specific laboratory parameters for detecting these drugs are not commonly used. However, many labs feature a test that reacts highly sensitively to factor Xa inhibitors—namely, measuring the antithrombin concentration. For this parameter, the testing systems that are mostly used nowadays actually do measure the anti-Factor Xa effect, which antithrombin does have, too (1). Using this method will give antithrombin values that are too high, under the influence of factor Xa inhibitors. In this case, the combination of lowered Quick value and seemingly raised antithrombin is a reliable indicator of a factor Xa inhibitor.

It is also possible to calibrate a reagent used for measuring antithrombin with a factor Xa inhibitor. A major obstacle in this setting is the compulsory, laborious in-house validation if a reagent is used outside its licensed application scope.

Usually the measurement of the anti-factor Xa activity is required to be calibrated to the medication actually used. In routine laboratory diagnostics, however, it is a well-known fact that the results are largely interchangeable. A high concentration of rivaroxaban corresponds to a high concentration of edoxaban or apixaban and also a high concentration of low molecular weight heparin.

Laboratories would have to go to great lengths in order to provide in parallel the measurement of anti-factor Xa activity for rivaroxaban, apixaban, edoxaban, and low molecular weight heparin. It would therefore be pragmatic and a significant progress in treating such emergencies to agree on a generally calibrated anti-factor Xa activity. Moreover, there is a vast potential for error if, for example, a patient is taking rivaroxaban but erroneously, anti-factor Xa activity for edoxaban is ordered and appears on the laboratory report.

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Intracranial Hemorrhage

In their article on the importance of direct oral anticoagulants in emergency trauma admissions (1), the authors pay particular attention to traumatic intracranial hemorrhages, as half of all patients with (severe) trauma have traumatic brain injury (TBI).

Indeed, traumatic brain injury presents a particular challenge in the emergency setting—mild TBI is one of the most common presentations in emergency departments, and severe TBI is the most common injury-related cause of death in persons under the age of 45 (2). Furthermore, the number of older patients receiving direct oral anticoagulants who suffer from TBI is increasing, evolving the importance of therapeutic recommendations regarding antithrombotic drugs.

Owing to the character of a review article, the authors were able to provide only limited therapeutic recommendations regarding intracranial hemorrhages following TBI in patients receiving direct oral anticoagulants. Complementary we would like to indicate recent evidence-based guideline recommendations from US associations in terms of reversing antithrombotic treatment in the setting of intracranial hemorrhage (3). The transparent guidelines are based on the most recent scientific evidence and daily usefulness; they can therefore help health care professionals in the acute setting to avoid unnecessary risks, use limited resources of blood and plasma products at the same time reasonably, and ensure quality of treatment overall.

In addition to direct oral coagulants the guideline (3) also considers oral vitamin K antagonists, direct thrombin inhibitors, unfractionated heparin, low-molecular weight heparin, pentasaccharides, thrombolytics, and thrombocyte function inhibitors.

For the factor Xa inhibitor antidote andexanet, which was touched on in the article and is undergoing clinical tests, initial results from phase IV studies have become available in the meantime (4).

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In Reply:

We thank Ostendorf as well as Leidel and Kanz for their interest in our published article (1). Ostendorf addresses one of the main problems in dealing with the new direct oral anticoagulants (DOACs), and in this context he makes a good suggestion. The number of anticoagulants for clinical and outpatient use has increased enormously over the years, and this situation really triggers a desire for more practicable laboratory monitoring, with comparable results and units. Even though a treatment center may usefully restrict the number of anticoagulants to merely a few, in the emergency setting—with potentially resulting interventional or surgical healthcare provision strategies—the confrontation with any number of these substances cannot be ruled out. This problem has, however, remained unresolved for decades in the diagnostic evaluation of coagulation physiology that is used to monitor anticoagulation. Partial thromboplastin time (PTT) reagents are known to react differently to the same amount of unfractionated heparin. The multitude of anticoagulants has been continually increasing since the introduction of low molecular weight heparins and DOACs. A consensus about comparable inhibition units for factor Xa or thrombin has never been reached. What is needed is

a consensus between treating physicians, manufacturers, and regulatory bodies. Ostendorf rightly asks for communication on generally calibrated inhibitor units; which is pragmatic and practical, and on the other hand a clear step ahead for emergency treatment. Such a consensus is, however, not in sight. Whether such universal units can then be scientifically ensured is currently not clear. For this reason, what is required in addition to a rough estimate by using global tests is the substance specific calibration for the individual DOACs, including measuring the individual plasma concentration.

We thank Leidel and Kanz for their valuable contribution in pointing out the recently published, evidence-based guideline from the US Neurocritical Care Society and the US Society of Critical Care Medicine (2). This refers to the reversal of antithrombotic agents exclusively in intracranial hemorrhages, which was not dealt with in detail because of the review character of our article. In addition to DOACs, the guideline also includes all other classes of substances and is therefore very well worth reading. The publication of the initial phase IV studies of the factor Xa inhibitor andexanet, which was cited by our colleagues, was not yet available to us at the time of writing our article. Further studies of antidote development, including specific substances vis-à-vis DOACs are likely to be published in the near future.

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On behalf of the authors

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