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Journal of Clinical and Experimental Cardiology

Short Communication

Challenges and Strategies in Anticoagulation Management for DOAC-Treated Patients Undergoing Emergency Cardiac and Aortic Surgeries

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ABSTRACT

Effective anticoagulation management with heparin is critical during Cardiopulmonary Bypass (CPB) in emergency cardiac and aortic surgeries. However, in patients using Direct Oral Anticoagulants (DOACs), the administration of Andexanet alfa can induce heparin resistance, complicating management. This study aimed to investigate the mechanisms underlying heparin resistance induced by Andexanet alfa, as well as explore optimal hemostatic strategies for such patients during emergency cardiac and aortic surgeries.

Keywords: Andexanet alfa; Heparin resistance; Anticoagulation; Emergency surgery; Cardiopulmonary bypass

DESCRIPTION

Direct Oral Anticoagulants (DOACs) are widely used for cardiovascular diseases due to their predictable effects and ease of management [1]. Andexanet alfa , functions as a factor Xa analog, which reverses the effects of Xa inhibitors [2]. However, Andexanet alfa also binds to Unfractionated Heparin (UFH)-antithrombin complexes, leading to instances of heparin resistance, consequently complicating anticoagulation management during emergency surgeries [3-5].

UFH resistance occurs when normal heparin doses fail to achieve the expected anticoagulant effect. This phenomenon is particularly concerning in patients receiving DOACs when Andexanet alfa is administered. as studies suggest that Andexanet alfa nay partially inhibit heparin [6]. Furthermore, overcoming this resistance might necessitate higher heparin doses, which increases bleeding risk.

To prevent UFH resistance, avoiding Andexanet alfa during emergency surgeries involving Cardiopulmonary Bypass (CPB) is recommended. However, if Andexanet alfa has been administered preoperatively, alternative anticoagulation strategies may be necessary [4,5]. Research is ongoing to optimize the management of Andexanet alfa-induced UFH resistance, but a definitive solution has yet to be established.

Replenishing Antithrombin (AT) has shown promise as a viable solution by enhancing the effect of heparin, partially recovering the desired anticoagulant effect [3]. Nevertheless, this method may not be effective in all cases, requiring comprehensive individual patient assessments [4,5]. Additionally, Andexanet alfa risk of thrombotic complications [7,8]. Thus, close monitoring for thrombus formation is essential when using these drugs after CPB.

Four-Factor Prothrombin Complex Concentrate (4F-PCC), which is used in managing warfarin side effects and DOAC-associated bleeding, has been reported to be an effective alternative to Andexanet alfa. Furthermore, 4F-PPC does not induce UFH resistance after CPB, potentially allowing safe heparin use for subsequent procedures [9-14].

Another viable alternative is the use of CytoSorb® (CytoSorbents Corporation, Monmouth Junction, USA). This blood adsorber device reduces inflammatory mediator levels, mitigates excessive immune responses and cytotoxic effects, and enhances recovery potential. Additionally, it is CE-marked and capable of removing ticagrelor and rivaroxaban during CPB surgery. CytoSorb® is also effective for the *in vitro* removal of multiple DOACs and rapid reduction in plasma levels. In fact, patients undergoing cardiac surgery with CytoSorb following apixaban administration were reported to exhibit significantly reduced anti-factor Xa activity [15].

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Received: 30-Jul-2024, Manuscript No. JCEC-24-31723; **Editor assigned:** 01-Aug-2024, PreQC No. JCEC-24-31723 (PQ); **Reviewed:** 15-Aug-2024, QC No. JCEC-24-31723; **Revised:** 22-Aug-2024, Manuscript No. JCEC-24-31723 (R); **Published:** 29-Aug-2024, DOI:10.35248/2155-9880.24.15.901

Citation: Nagashima K (2024) Challenges and Strategies in Anticoagulation Management for DOAC-Treated Patients Undergoing Emergency Cardiac and Aortic Surgeries. J Clin Exp Cardiolog. 15:901.

CONCLUSION

Andexanet alfa-induced UFH resistance poses a significant challenge in anticoagulation management during cardiovascular surgery. potentially complicating anticoagulation management during emergency surgeries. While strategies such as AT supplementation or alternative anticoagulation methods are being considered, a definitive solution has yet to be established. Novel treatment options, such as 4F-PCC and CytoSorb®, show promise in managing DOAC-associated bleeding, especially in surgeries involving CPB.

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