

Manuscript NO.: 60779, Case Report

Response to Reviewers

Dear Mr. Ma,

Thank you for giving us the opportunity to submit a revised draft of the manuscript “*Intramuscular hematoma in rhabdomyolysis patients treated with low-molecular-weight heparin: two case reports*” for publication in the *World Journal of Clinical Cases*. We appreciate the time and effort that you and the reviewers dedicated to providing feedback on our manuscript and are grateful for the insightful comments on our paper that led to valuable improvements. We have incorporated most of the suggestions made by the reviewers. Those changes are highlighted within the manuscript. Please see below, in blue, our point-by-point responses to the reviewers’ comments and concerns. All page numbers refer to the revised manuscript file with tracked changes.

Reviewers' Comments to the Authors: Reviewer 1

1. While paper is understandable, it requires editing to improve English, as there some stylistic and grammatical mistakes. e.g ‘as it an increased use of anticoagulants? ’ in the section of introduction.

Author response: We apologize for the inconvenience that the stylistic and grammar mistakes imparted on your review. This is a common problem for authors in nonnative-English-speaking countries. To ensure that the English quality of the manuscript meets the publishing requirements, we sent the revised manuscript to American Journal Experts for language editing.

2. The title is not specific, and it is better to describe as ‘Intramuscular hematoma in rhabdomyolysis patients treated with low molecular weight heparin: two case reports’

Author response: Thank you for pointing this out. We agree with your suggestion because the proposed title more accurately describes the report.

3. Most patients with rhabdomyolysis can be cured by discontinuation of fibrates or in combination with hydration, alkalization and diuresis. Heparin sodium is excreted through the kidney, so the risk of bleeding is increased in patients with renal insufficiency. The level of creatinine for case 1 was 192 $\mu\text{mol/L}$, why CRRT and subsequent heparinized anticoagulation was performed?

Author response: 1) We agree with your viewpoint that “Most patients with rhabdomyolysis can be cured by routine treatment.” The difference is that our 2 cases of rhabdomyolysis were both caused by heat stroke. This can cause the release of large amounts of muscle cell contents (such as myoglobin, creatine kinase, and small-molecule substances) into extracellular fluid and blood. Therefore, we used CRRT to eliminate these metabolites, carry out effective liquid management, and correct acid-base imbalance. In addition, case 1 had persistent high fever, and the adoption of CRRT quickly and effectively controlled the core body temperature of the patient. The fact that these patients recovered quickly also demonstrates the effectiveness and safety of CRRT treatment. 2) The primary objectives of CRRT with anticoagulation are to reduce the membrane contact response and maintain the integrity of the filter function and the effectiveness of vascular access. The ideal anticoagulant should have antithrombotic activity, fewer bleeding complications, mild adverse reactions, low cost, short half-life, and other advantages and should have the corresponding antagonist; in addition, it should be easy to monitor the anticoagulant effect. There are a variety of anticoagulants. Currently, the most commonly used anticoagulants clinically suitable for CRRT are unfractionated heparin and sodium citrate. The choice of anticoagulant should be determined according to the actual situation of each patient. Patients with renal insufficiency may have increased bleeding risk due to the accumulation of heparin in the body, but renal insufficiency is not a contraindication. The risk is predictable and controllable, for example, by reducing the dosage of heparin and continuously monitoring APTT. Before using CRRT, we did not find any obvious bleeding risk except renal insufficiency. Therefore, unfractionated heparin was selected for CRRT, and APTT was monitored continuously. In our postanalysis, we overlooked the possibility that rhabdomyolysis could lead to muscle bleeding. At this time, we believe that sodium citrate antifixation is more reasonable. This has also informed our future clinical work in which we will evaluate the patient's condition more comprehensively and carefully.

4. The coagulation function after bleeding was not monitored, and the secondary coagulation dysfunction can not be ruled out completely.

Author response: Thank you for your rigorous review. In this paper, we did not thoroughly explain the coagulation function of patients after bleeding; it is simply mentioned that no obvious bleeding tendency was found: *“At this time, we excluded digestive system diseases leading to blood loss through stomach content and fecal occult blood examinations, and no obvious pleural or peritoneal effusion was found with bedside ultrasound examination...Subsequently, the levels of hemoglobin continued to decrease, and no obvious bleeding sites were found.”* In fact, for critically ill patients hospitalized in the ICU, we usually review blood tests, coagulation function, biochemistry, and other related examinations at least every 24 hours. When conditions require, examination frequency even reaches once every 8 hours. Our description may be too concise and not clear to readers, so we considered adopting your suggestion and added "No coagulation dysfunction was found."

We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in *WJCC*.

We look forward to hearing from you at your earliest convenience.

Sincerely,

Shiyang Yuan