

January 20, 2017

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 31230-Revised manuscript.doc).

Title: CT-guided catheter drainage with urokinase and ozone in management of empyema

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Name of Journal: World Journal of Radiology

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We thank five reviewers for their positive comments. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in World Journal of Radiology.

The revised manuscript incorporated suggestions of the editor and reviewers, as follows:

1 Text format has been updated according to the editor's specifications. We have made a improvement on the structure of

the text, including the additional statement of academic norms, and modified references superscript. In particular, we added the "Comments" section after the Discussion.

2 Revision has been made according to the suggestions of the reviewers. Revised and added sentences have been highlighted in red in the revised text.

Reviewers 03010522, 00233953, 00503175 and 00289471 suggested minor language polishing, and reviewer 00289467 suggested a great deal of language polishing. We asked an English-mother language colleague to correct grammar errors and refine the text. Then we asked professional institutions to embellish the article and got a language certificate. We believe that English language is now suitable for publication.

(1) Reviewer 00503175 *"The only needed is minor revision about language"*

Response: We have been checked the grammar mistakes and refined the language.

(2) Reviewer 03010522 *"The authors poorly justified selection of applied ozone dose. In my opinion, the work of therapy are*

underrepresented in the literature. Required some correction of the text of the article in connection with the presence of a number of failed expressions and stylistic designs. ”.

Response: We select 10.0-20.0 ml ozone dose based on the existing literature and our own clinical experience and the dose varies from the size of the empyema cavity.

Although the reports of ozone in treatment of empyema is not much. In our study, urokinase and ozone are proved to be a useful adjunct in the management of empyema. These work could attract more clinicians pay more attention to it. Our work has some practical significance.

We have modified the structure of the article and polished the words.

(3)Reviewer 00233953 *”The authors should explain why some patient were treated with urokinase and ozone. How decided and why. Does this introduce a bias?”*

Response: In our clinical work, part of the patient's treatment effect is not satisfactory. To improve the treatment effect, we choose urokinase and ozone in the management of empyema. We have

explicit inclusion and exclusion criteria, so there is no bias in this study.

(4) Reviewer 00289467 *"However, in my opinion there are two limits that strongly weaken the value of the study. First, the authors administered intrapleural urokinase 50000 UI once just for one day: in all the most recent papers published on this topic urokinase was administered for at least three days, so it is likely that fibrinolytic treatment has been underdosed in this paper. Second, and most important, if group II (urokinase alone, 24 successful treatments and 8 failures) and group III (urokinase + ozone, 36 successful treatments and 5 failures) are directly compared with chi-square test excluding the group treated with only pleural drainage, there is no difference between the two groups ($p=0.267$): it follows that it is hard to conclude that urokinase plus ozone is more effective than urokinase alone. The authors should deeply change their discussion and conclusions accordingly"*

Response: In our study, 50,000 units of urokinase diluted in 20.0 ml normal saline was injected into the pleural space via the pigtail catheter per day. It not just one day and it could be appropriately adjusted according to the follow-up imaging.

We are sorry for making some mistakes in sorting out the form data, which is not updated earlier experimental data. With the

increasing number of cases, we increased the sample size and perform statistical analysis on data. The success rate of treatment was statistically significant. And we have corrected and updated the data which is shown in table 2 and text.

(5)Reviewer 00289471 *“Methods are not clear: how patients were selected? how the authors decided to treat with any of the three methods? I suppose that the more complicated cases were treated more aggressively. why diabetic patients were not treated? they were excluded from the study or were not treated at all? There were differences in the size of catheters used in the different groups? Pneumothorax does not seem to be in compliance though that the patients had a drainage.”*

Response:

The selection of therapeutic methods of patients is randomly selected.

The wound healing speed of diabetic patients are slow comparing to the normal persons. So we excluded diabetic patients from the study in order to reduce the bias.

The choice of the catheter depended on the viscosity of the initial aspirate. And most of the patients are with 10F drainage tube, some patients use relatively small tubes if the viscosity of abscess

is not thick.

Some patients had complications of pneumothorax. Some gases more or less entered the chest during the processes, especially when dilated the skin. After catheter implantation and connection drainage bottle in patients with empyema, the gas would be drained out. So we have no statistics of pneumothorax.

Finally, we wish to thank the Editor and the Reviewers for their comments that helped us to improve the value of our paper.

Sincerely yours,

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