Author’s response to reviews

Title: Glycemic control with a basal-bolus insulin protocol in hospitalized diabetic patients treated with glucocorticoids: a retrospective cohort study

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Version: 1 Date: 15 Mar 2018

Author’s response to reviews:

James Mockridge, PhD
Editor, BMC Endocrine Disorders

Dear Prof. Mockridge

BEND-D-18-00029: “Glycemic control with a basal-bolus insulin protocol in hospitalized diabetic patients treated with glucocorticoids: a retrospective cohort study”

Thank you for the comments suggested by the reviewers and the Editor. We have revised our manuscript accordingly.

In the following letter, we have responded to each comment point by point.

Technical comments:

1. Provide e-mail address of all authors.

Answer: Dr. Elena Chertok Shacham: e-mail: elena_ch@clalit.org.il,  Hila Kfir: hila_kf@clalit.org.il, Naama Swarthz: naama.stat@gmail.com, Dr. Avraham Ishay: ishay_av@clalit.org.il

2. We cited table 2 in the in the result paragraph of abstract. (Page 2; Line 16).
Reviewer 1:

Comment #1: Please clarify as part of the protocol is all long acting insulin given in the evening?

Answer: The long-acting insulins used in the study were insulin glargin (Lantus) and insulin detemir (Levemir) and were given in the evening.

Comment #2: Background 1st sentence is not a proper sentence—suggest add 'so' after (1,2,3); para 3...add 'a' before paucity

Answer: In 1st sentence of background section we added 'so' (Page 4; Line 3).

We added 'a' in the background section in line 19 before the word paucity, as required.

Comment #3: Results: 'diabetes' treatment rather than 'diabetic treatment'

Answer: Diabetic treatment was changed to diabetes treatment (Page 8; Line 3)

Comment #4: Discussion: BURT's not Bursts' study

Answer: We changed Burst's study to Burt's study in discussion paragraph (Page 12; line 13)

Comment #5: The high number of patients in both groups not receiving insulin as per protocol—need comment/discussion

Answer: We agree fully with the reviewer's remark and discuss this point in the discussion section in the, limitations of the study, paragraph. We added number of sentences addressing this point. It now reads: "In addition to the inherent limitations due to its retrospective design, the main limitation of our study is in the failure of our patients with diabetes on glucocorticoid treatment to achieve adequate glycemic control on the basal-bolus insulin protocol. A high proportion of patients in both groups were undertreated, according to the existing protocol. We attribute this to the inadequate insulin dosing adjustments done by junior doctors and nurses responsible for the treatment of each specific patient; thus, a substantial proportion of patients did not receive an appropriate insulin dose, essentially due to excessive caution taken to avoid hypoglycemia and inability to make appropriate fine tuning, especially of prandial dosing of insulin. On the other hand, the strength of our study lies in the collecting of data about real-world patient experience thus assisting in filling the knowledge gap between clinical trials and actual
clinical practice, by adding to the understanding of how best to incorporate new therapies into everyday clinical practice. We hope that our study will help to guide changes in protocols to achieve better glycemic control for inpatients receiving glucocorticoid treatment. Moreover, that this has the potential to improve the quality and delivery of medical care, reduce overall costs and improve outcomes."

We also add a paragraph in discussion section addressing the point of insufficient insulin adjustments. Now it's reads as: "In our study 61% of patients in the control group versus 36% in glucocorticoid treated group were adequately controlled during hospitalization. It's clear that in the control group the main reason for insufficient control was inappropriate dose adjustment, but in the steroid treatment group more adjustments were performed during hospitalization however less patients achieved appropriate blood glucose control.

Comment #6: wording: spelling glucocorticoid in Figure 2.

Comment #7: Figure 3: pls clarify: 'in the morning'...is this prior to breakfast. 'during mealtime'...what does that mean?

Answer: In the morning was changed to morning fasting state; meal time was changed to pre prandial (Figure 3, page 21)

Comment #8. Figure 4: very unclear; not treated with insulin etc needs clarification that this is referring to pre-admission diabetes management...indeed what is the heading for this figure? Did the findings of the study suggest that the prandial calculation was effective incl at each meal? would a higher ratio at lunch/afternoon work better? did the study help guide any changes to the protocol to better control the glycaemia?

Answer: Thank you for this suggestion. We include an additional text in table 4 explaining more clearly the calculation and distribution of insulin doses in our suggested protocol. (Page 22, Table 4). We add the heading of table 4. It now reads as: "suggested protocol for glucocorticoid treated patients". We changed the last paragraph in the discussion section and it now reads as: "This is in accordance with Burt's study (11) which found that blood glucose control was inadequate despite the higher insulin doses in glucocorticoid treated patients. Although we were not able to address this issue in this study we speculate that a different insulin protocol would be more effective in controlling glucocorticoid treated patients during hospitalization. The protocol we suggest includes less basal insulin and a higher ratio of prandial insulin at lunch and at supper (Figure 4)."
Comment #9: Table 1: Pls recheck the data in 'prior treatment'...should 'oral hypoglycaemic and insulin' be changed to 'oral hypoglycaemia and/or insulin given that the numbers suggest the oral hypoglycaemic only gp were included in the second gp.

Answer: We rechecked the data about prior treatment and indeed the first group included the patients treated with an oral hypoglycemic drug while the second group included patients treated with an oral hypoglycemic drug and insulin together.

Comment #9: Table 2: Shouldn't 'West Nail' Encephalitis be "West Nile' Encephalitis?

Answer: 'West Nail' Encephalitis was changed to West Nile Encephalitis?

We thank you and the referees for helping us generate a much-improved manuscript.

Yours Sincerely,

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