Reviewer’s report

Title: Significant predictive factors of the severity and outcomes of the first attack of acute angioedema in children

Version: 0 Date: 29 Sep 2019

Reviewer: Anette Bygum

Reviewer's report:

Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.

This is a highly relevant study, however with retrospective data, reporting acute angioedema in children presenting in the ED. Relevant comorbidities and medications were noticed. Due to the retrospective design, the authors should be very careful on their conclusion as a cause-relationship cannot be extrapolated from their data. Figure 1 includes details about medication and food and this should be further discussed in the text. Seemingly atopic dermatitis is included as an allergic history, but atopic is not necessarily allergy. Please observe if known asthma is a confounder to be hospitalized (POU or hospital admission).

The size of the study (406 children) was appropriate.

Specific comments:

P4
line 8: You mention that allergic angioedema is the most common type - I'm not sure. Please document your statement with original literature.
line 21: You should include original studies related to the subject instead of reference 6
line 21-28: You write about the most common anatomical areas involved - it is not clear which kind of angioedema you describe here (idiopathic - drug-induced - ACEI-induced?), please make this clear and be aware of your references.
line 28: You use the word hives - every other places in the article you mention urticaria - is this on purpose?
line 34: You use a reference describing threat of asphyxiation to document swelling of the intestinal tract?
line 40:.............which leads to suffocation, hypotension and even respiratory failure. Please look at this sentence and also the sentence on lines 40-50 which is not totally clear to me.

P7
line 31: Food or medications were suspected to be the possible etiologies when patients or family members stated that they suffered from skin symptoms after eating a particular food or taking a
particular medication. You need to discuss this statement, as the patient/family history is no proof. In relation to food, you can do allergen-specific IgE, SPT and provocation. For some medications, it is also possible to verify such a suspicion.

P13
line 1 (and Table 1): contact materials?

P15
line 34-37: Angioedema frequently presents with skin lesions, mainly wheals. Please rephrase this sentence.
lines 5056: You write that co-occurrence of angioedema with urticaria indicates a more severe clinical presentation - please document this also with references. For me it seems to be the opposite, as bradykinin-mediated angioedema (hereditary angioedema, ACEi angioedema and other drug-induced angiodema) is the most severe and usually does not present with urticaria. It may be different in children, please discuss and document with your data.
Figure 2: How do you define Inhalants? (inhalation allergens?) and Contact materials. You may skip some of the figures.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable
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If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I have been involved in research and educational activities with the following companies producing medications for hereditary angioedema:
CSL Behring

Shire now part of Takeda
Biocryst
SOBI
Viropharma

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