

PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Paediatrics Open. The paper was subsequently accepted for publication at BMJ Paediatrics Open.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Efficacy of an interventional educational program in mitigating post-traumatic stress in parents who have witnessed a febrile seizure: a pilot before-and-after study
AUTHORS	Frasconi, Flora; Dreyfus, Isabelle; Chaix, Yves; Tison-Chambellan, Camille

VERSION 1 - REVIEW

REVIEWER	Borggraefe, I. Comprehensive Epilepsy Program for Children Department of Pediatric Neurology, Developmental Medicine and Social Pediatrics Dr. von Hauner`s Children`s Hospital University of Munich Germany Competing interests: none
REVIEW RETURNED	17-Jul-2017

GENERAL COMMENTS	In this project, Frascari et al. report on the result of an interventional educational program for parents who have witnessed a simple febrile seizure.- I have only a few comments. -due to the small sample size, I suggest to call this study a pilot study -please mention that the differences of the intergroup analysis is statistically significant within the result part in the abstract -please give a detailed list of in- and exclusion criteria within the "methods" part
-------------------------	--

REVIEWER	Claret-Teruel, Gemma Hospital Sant Joan de Déu, Barcelona (Spain) Competing interests: No
REVIEW RETURNED	17-Jul-2017

GENERAL COMMENTS	I have found this article very interesting. Febrile seizure is a common illness in childhood. I think that interventions to reduce stress in parents that have witnessed an episode are a great initiative. I have minor comments: - Table 1 could be better done: there are two empty lines, if there are 0 patients it's not necessary 0%, homme/femme (male/female), SD has to be explained at the bottom...
-------------------------	---

	<ul style="list-style-type: none"> - In Figure 3 I cannot see where is the sign “**p<0.01” in the figure. - Table 2 is difficult to read <p>And major comments:</p> <ul style="list-style-type: none"> - As you say in limitations, there are a small number of patients included and there are all from one center. Although there is a statistically significant difference between group 1 and 2, only 7 parents decreased his score under 33 in group 1 (4 in group 2). Those are small numbers. - Also mentioned in limitations, voluntary participation also it's important, as a selections bias.
--	---

VERSION 1 – AUTHOR RESPONSE

Reviewer 1:

“In this project, Frascari et al. report on the result of an interventional educational program for parents who have witnessed a simple febrile seizure. - I have only a few comments:

-Due to the small sample size, I suggest calling this study a pilot study”

We agree with the reviewer that 50 patients do not constitute a large series. We followed the reviewer’s suggestion and amended the title of the manuscript. The new title is “Efficacy of an interventional educational program in mitigating post-traumatic stress in parents that have witnessed a febrile seizure: a pilot before-and-after study”. We also revised the abstract on page 3, paragraph “design”, as well as the section “Study design and Participants” on page 5, paragraph 1, line 2.

“Please mention that the differences of the intergroup analysis are statistically significant within the result part in the abstract”

Thank you for this comment. We amended the abstract, on page 3, paragraph “results” with the significant intergroup comparison. We also mentioned the intergroup analysis in the results, in section 3 entitled: “Evolution of IES-R score, and effect of the workshops”, as well as in Figure 3.

“Please give a detailed list of in and exclusion criteria within the "methods" part”

We added important details regarding the in- and exclusion criteria in the “Study design and Participants” section:

“Inclusion criteria were (1) mothers or fathers ≥ 18 years old, who had witnessed their child’s first episode of simple febrile seizure, (2) only one parent per family could be included. Exclusion criteria were as follow: (1) grand-parents or other relatives of the child, (2) second episode of simple febrile seizure, (3) complex febrile seizures or non-febrile seizures, and (4) parental psychiatric past medical history.”

Reviewer 2:

"I have found this article very interesting. Febrile seizure is a common illness in childhood. I think that interventions to reduce stress in parents that have witnessed an episode are a great initiative. I have minor comments:

- Table 1 could be better done: there are two empty lines, if there are 0 patients it's not necessary 0%, homme/femme (male/female), SD has to be explained at the bottom..."

Thank you for this constructive comment. We improved table 1 according to all your suggestions. We also decided to delete the site of enrollment in the table 1. However, to have a nice view of the 2 participating centers at patient enrollment, we added a supplementary table.

*"In Figure 3, I cannot see where is the sign $***p<0.01$ in the figure."*

The reviewer is right, there is no sign $***p<0.01$ in Figure 3, hence the irrelevant information has been deleted from the Figure legend.

"Table 2 is difficult to read."

Thank you for giving us this feedback. We worked on the formatting of Table 2 and have greatly improved the readability.

"And major comments:

- As you say in limitations, there are a small number of patients included and there are all from one center. Although there is a statistically significant difference between group 1 and 2, only 7 parents decreased his score under 33 in group 1 (4 in group 2). Those are small numbers."

- Yes, in group 1 all parents were from site 1. As the reviewer noticed, this limitation is mentioned in the discussion section. The workshops were geographically located on site 1 and far from site 2 (about 40 minutes driving); we think this could have dissuaded parents from group 2 to register to the workshops, but for different reasons (time, space) we were unable to organize workshops on site 2 for this pilot study. We amended the discussion section, 2nd paragraph, 3rd stated limitation, with this rationale.

- We also agree that the absolute numbers of participating parents we reported is small. However, we think that our results still deserve consideration because after the workshop, 7 out of 15 parents decreased their score under 12, which represents almost half of the parents (47%). Without any intervention, only 4 parents out of 33 decreased their score under 12 which represents a very small portion of the parents (11%). These results are statistically significant.

"- Also mentioned in limitations, voluntary participation also it's important, as a selections bias."

We agree that self-selection of parents to intervention or control is very important. We could have recruited parents with different characteristics (e.g. different psychologic profiles). This limitation is addressed in the section “discussion”. The self-selection did not alter the comparability amongst the 2 groups in terms of demographic characteristics and IES-R1, comparability that we verified before running the statistic tests. We think that our results deserve to be published because (1) they show that more than 75% of parents are highly stressed after seeing their child’s first simple febrile seizure, and to the extent of our knowledge this hasn’t been published elsewhere before, and (2) we fully described our workshops in the paper as we anticipate them to be expanded and developed in other leading pediatric centers.

VERSION 2 – REVIEW

REVIEWER	Phillips, Bob CRD, University of York, UK Competing interests: None
REVIEW RETURNED	08-Sep-2017

GENERAL COMMENTS	<p>Introduction - would be far better opening with content of para 2 not para 1</p> <p>Study design - final para - spelling - tone not tonus. Can you explain if patients parents were involved in the creation of the programme and the research, and if not, justify the absence of PPI?</p> <p>Stats analysis - words: groups were 'assessed' rather than 'verified', child age not kid age, would suggest the use of 'continuous' and 'categorical' rather than quantitative and qualitative to describe variable .. not because the latter is wrong .. just the former has a wider understanding</p> <p>I think an ANOVA or multiple regression analysis would be a more correct method to assess for the effect of group-selection over time in evaluating the T2-T1 PTSD scores within this study. With the simple analysis as stands, the conclusions may be statistically incorrect and so cannot fairly comment on the rest of the results.</p> <p>Results - the English abbreviation is 95%CI (rather than IC95%)</p> <p>Final Discussion para - the importance of this study is overstated - if it is show to be the same on a more effective stats analysis. This is good data to provide enthusiasm to develop such a programme going forwards and to trial it - not to roll it out across all centres</p>
-------------------------	--

VERSION 2 – AUTHOR RESPONSE

Reviewer 1:

“Introduction - would be far better opening with content of para 2 not para 1”

We agree with the reviewer that opening with content of paragraph 2 is more relevant. We followed the reviewer’s suggestion and amended the introduction of the manuscript, on page 4. We updated the order of the reference in this section as well.

“Study design - final para - spelling - tone not tonus. Can you explain if patients parents were involved in the creation of the programme and the research, and if not, justify the absence of PPI?”

Thank you for these comments.

- We spelled the word “tone” properly at the end of “study design” (line 21 of the paragraph) as well as in “statistical analysis” (line 4 of the paragraph).

- Although we do believe in the role of public and patients in improving the quality of health research, patients’ parents were not involved in the creation of our research, per se. However, the creation of the workshops was motivated by the results of two previous studies (these studies are referred in the main text of the manuscript as references 25 and 26):

Tison-Chambellan C, Fine A, Cances C, et al. [Anthropological approach to current parental perceptions of children's seizures]. *Arch Pediatr*. 2013;20(10):1075-1082.

Chambellan-Tison C, Fine A, Cances C, et al. [Seizures and epilepsy: popular thinking and beliefs from antiquity to the 19th century]. *Arch Pediatr*. 2010;17(9):1259-1263.

In these studies, we gathered parental mental representations regarding the word “seizure”. We also gathered parental emotional response to their child’s first seizure (stress, fear, feeling helpless, lack of knowledge especially for the post-ictal state, not knowing how to help their child...). For the purpose of these studies we chatted extensively with 38 parents (28 interviews total: 16 mothers alone, 2 fathers alone, 10 couples). One typical interview was 30 minutes long on average (20-60 minutes). A total of 16 hours of interviews were analysed using an anthropological approach.

We feel that this research is close to the patients, and we are deeply committed to broadening the scope of our patient and public involvement activity in our further studies.

“Stats analysis - words: groups were 'assessed' rather than 'verified', child age not kid age, would suggest the use of 'continuous' and 'categorical' rather than quantitative and qualitative to describe variable .. not because the latter is wrong .. just the former has a wider understanding ”

The reviewer is right, and we made the following changes in “Statistical Analysis”:

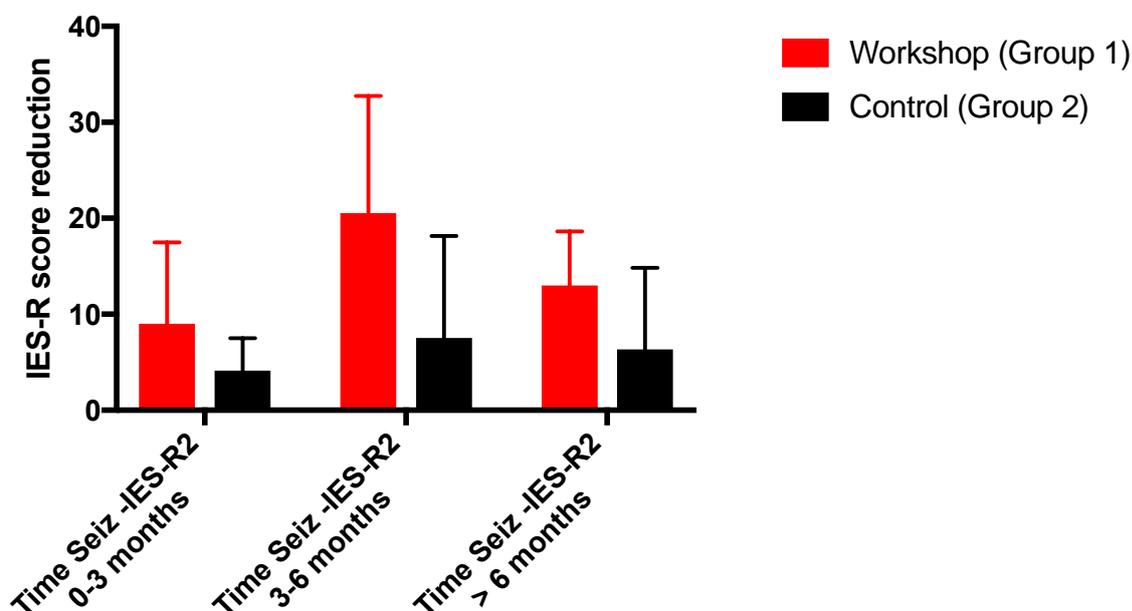
- We changed “the comparability of the two groups was verified” by “(...) was assessed” (line 4).
- We changed “kid age” by “child age” (line 5).
- We used 'continuous' and 'categorical' rather than “quantitative” and “qualitative” to describe variable (line 7).

“I think an ANOVA or multiple regression analysis would be a more correct method to assess for the effect of group-selection over time in evaluating the T2-T1 PTSD scores within this study. With the simple analysis as stands, the conclusions may be statistically incorrect and so cannot fairly comment on the rest of the results.”

Thank you for this constructive comment. A conventional two-way analysis of variance was used to assess for the effect of group-selection over time in evaluating the IES-R1-IES-R2 score reduction.

The analysis yielded a significant effect for the workshops attendance such that the average reduction of score was significantly higher for parents who attended a workshop than for the controls (p=0.0398). The effect of time was non-significant p=0.1468. This statistical analysis was performed using GraphPad Prism 6.0.

ANOVA table	SS (Type III)	DF	MS	F (DFn, DFd)	P value
Interaction	115	2	57.52	F (2, 44) = 0.6664	P=0.5187
Time	346.1	2	173	F (2, 44) = 2.005	P=0.1468
Workshop	387.4	1	387.4	F (1, 44) = 4.488	P=0.0398
Residual	3798	44	86.31		



“Results - the English abbreviation is 95%CI (rather than IC95%).”

Yes, we changed to 95%CI in the following sections:

- Section “results”, paragraph “Prevalence of post-traumatic stress symptoms”, line 12 and 13.
- Section “results”, paragraph “Evolution of IES-R score, and effect of the workshops”, line 5 and 6.
- In the Abstract, line 19 and 20.
- In Table 1.
- In Table 3.

- In Table 4.

“Final Discussion para - the importance of this study is overstated - if it is show to be the same on a more effective stats analysis. This is good data to provide enthusiasm to develop such a programme going forwards and to trial it - not to roll it out across all centres.”

A two-way analysis of variance yielded a significant effect for the workshops attendance ($p=0.04$), such that the average reduction of score was significantly higher for parents who attended a workshop than for the controls. The effect of time was non-significant ($p=0.1468$).

Nonetheless, we slightly changed the last sentence of the conclusion by “Our results provide a path forward for the development of multidisciplinary workshops on simple febrile seizure in leading pediatric centers.”

VERSION 3 – REVIEW

REVIEWER	Phillips, Bob CRD, University of York Competing interests: None
REVIEW RETURNED	03-Oct-2017

GENERAL COMMENTS	This revision appears to have developed te analysis further and demonstrates a probable effect ($p=0.04$) of being a person who elected to attend a group; the absence of PPI still needs to be explained.
-------------------------	--

VERSION 3 – AUTHOR RESPONSE

Reviewer 1:

“This revision appears to have developed the analysis further and demonstrates a probable effect ($p=0.04$) of being a person who elected to attend a group; the absence of PPI still needs to be explained”

Yes we added the following sentence to our manuscript: “Parents were not involved in the design of this research, but it builds on previous qualitative research exploring the experiences and beliefs of the parents”.