Reviewer 1

Comment:

Interesting and well designed study that has a definitive conclusion to the pathophysiology of the investigated subject. Minor syntactical and spelling correction are needed, mainly regarding the spacing between words.

Answer:

Authors thank the reviewers for positive comments. The revised article is reviewed by language editor and corrected.

Reviewer 2

Comment:

Although the study failed to identify significant association between autonomic function and AP-FGIDs, the hypothesis is good and worthy investigation since there has been evidence of the link in adult population. I have several comments for the authors to consider:

1. How did you recruit your control children? from community or school ? more details are needed. sINCE the control population can be large, did you use the random technique to screen children?

Answer:

We advertise the request for healthy children within the age group of patients through volunteers and health workers in the community (same geographical areas of patients). Those who volunteered with parental consent were screened for

diseases, including gastrointestinal disorders using history, examination and basic investigations mentioned in the article. After screening, age, sex and BMI compatible group healthy children were recruited as controls from the community in the same geographical areas of patients to get maximum compatible control group. Random recruitment was not possible since patients are from the community with large number of possible controls and there was no method to identify all possible subjects that could be included in the study.

More details of recruitment of controls were included in the revised manuscript.

2. In statistical analysis, did you still use t test when data are non-normal? remember that the assumption for t test is normal data. suggest to cite a reference for the statistical description (Ann Transl Med. 2016 Mar;4(5):91. doi: 10.21037/atm.2016.02.11.).

Answer:
The article is revised and non-parametric test were used for comparison of motility and autonomic parameters instead of t test.

3. Since you have matched age and gender for the two groups, the age should be exactly the same, but the result showed conflicting results (7.9 vs. 8.6 years).

Answer:

Since there are 100 children with abdominal pain and 50 controls, we have used age and sex comparable control group, not a matched group. The manuscript is corrected as accordingly.

4. Fig 1 provides a good theoretical framework for the study, but the study is simply an observational study (case-control) that cannot help to identify causal relationship between these items. thus, I suggest to remove the figure. other advanced models such as structrul equation model may be helpful in this situation.

Answer:

Figure 1 is based on available evidence from previous studies. More details are included in the revised manuscript to support the theory suggested in the Figure 1. The authors prefer to keep the Figure 1 in this manuscript.

5. One reason for the non-significant results may be due to limited sample size and the authors have not performed sample size calulation prior to study.

Answer:

Sample size calculation for this study was done before starting the study and minimum sample needed was 26 in a group. Therefore, 100 patients and 50 controls recruited are adequate sample size for this study.

Therefore, we believe the lack of difference we observed in cardiovascular autonomic function is more likely to be a true difference and unlikely to be due to small sample size.

Details of sample size calculation is as follows.

Sample size calculation

There were no previous studies to assess autonomic function in children with AP-FGIDs by Ewing's test. Therefore, we calculated the sample size using on the 30:15 ratio taken from an Indian study done on obese children aged 5-10 years [1]. The similarity with the race and age group was considered for selecting values from the Indian study.

Sample size for this study was calculated by the following formula

$$n = \frac{f(a,\beta) \times 2 \times SD^2}{(d)^2}$$

n- Patients per group, 90% power, Significance = 0.05

- The clinically meaningful difference we wish to detect is d = 0.1

- SD = .11

90% power and 0.05 significance $f(a, \beta)$ =10. 5

$$n=\frac{f(a,\beta) \times 2 \times SD^2}{(d)^2}$$

$= \frac{10.5 \times (2 \times 0.11^2)}{0.1^2} = \frac{0.2441}{0.01}$

$= 25.41$

Therefore, autonomic functions were assessed in 100 patients and age, sex compatible 50 healthy children recruited as the control group.

1. Bedi, M., S. Khullar, and V. Varshney, *Assessment of autonomic function activity in obese children.* Vascular Disease Prevention, 2009. **6**: p. 139-141.