19th October 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 14011-review.doc).

Title: PERFACT Procedure: A new concept to treat highly complex anal fistulas

Author: Pankaj Garg, Mahak Garg

Name of Journal: *World Journal of Gastroenterology*

ESPS-Columns scope note- Prospective study

ESPS Manuscript NO: 14011

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated
2 Revision has been made according to the suggestions of the reviewer. The italic portions in the answers have been incorporated in the revised manuscript.

Reviewer's suggestion-This is an interesting description of a novel method of anal fistula closure, including a cauterization of the internal opening, curretage of the fistula tract, and mechanical debridement of the tract 4 times a day (usually performed by a patient's relative). Comments:

1) **As you state in your manuscript, cauterization of the internal opening alone was not successful. I think that the intensified mechanical cleaning of the fistula tract is the key to fistula healing. Did you combine your intensified fistula cleaning program with other operations, like mucosal advancement flap? One might speculate that this would again lead to lower recurrence rates.**

   Ans- This is a wonderful suggestion. But we have not tried the intensified mechanical cleaning of the fistula tract with mucosal advancement flap. The speculation is justified that it might improve the results of the advancement flap procedure. *However, there are certain patients in whom the internal opening is enlarged/ widened due to previous surgical interventions (like tightening setons). In these patients, proximal superficial cauterization fails or takes much longer to heal. In this subgroup, advancement flap plus the intensified mechanical cleaning of the fistula tract could be a better option.*
   The suggestion is very good and has been incorporated in the manuscript.

2) **Another argument that cauterization is not the crucial step in your PERFACT procedure: cases in which the internal opening could not be identified had the same healing rate. Did you employ the intensive cleaning procedure without**

cauterization of the internal opening? Perhaps this would reach the same healing rates.

Ans- The cauterization of the internal opening (or the probable site of the internal opening) was a crucial step and was done in all the cases. We believe that in cases where we failed to accurately trace the internal opening, the internal opening was still present. The tortuousness of the fistula tract, compression of the tract while passing through the sphincter complex or temporary occlusion of the internal opening could be few probable reasons for not identifying the internal opening. Therefore in such cases, with the help of the MRI scan, the internal opening was localized and the area cauterized. We strongly felt that if the area all round the internal opening was not cauterized, the fistula wouldn't get cured.

Thanks a lot for mentioning this point. In the manuscript, this point has been mentioned and now has been highlighted further.

"*Perfact procedure was effectively carried even in fistula where no definite internal opening could be localized intraoperatively. Failure to identify the internal opening during the operation perhaps happens because of the temporary closure of the internal opening due to debris or the oblique course of the collapsible tract through the sphincters. As per literature, this can happen in upto 15-20% of cases[8]. In our series, this happened in 15.7% (8/44) cases (Table-1). This procedure worked quite successfully in 87.5% (7/8) of such cases in our series (Figure-5) (Table-2). As the MRI was done preoperatively in every case, it helped to fairly localize the tracts in the majority of cases and gave a reasonable idea where the tract was coursing towards the rectum. This information along with the intraoperative examination findings (induration of the sphincter complex in the region of internal opening) helped to determine the site of internal opening. At that place, the superficial cauterization was done even if the internal opening was not identified. In two patients, the MRI picture was creating doubt that the tracts could be going both anteriorly and posteriorly and hence superficial cauterization was done at both the places(Figure-5). Superficial cauterization was a safe step to do. Though it created a wound, but it was not associated with any risk of incontinence as the wound was quite superficial. Therefore in case of confusion/ doubt, the superficial cauterization can be done at two places as well.*"

3) You should comment on your follow-up time which does not allow to rule out late recurrences. As shown for mucosal advancement flaps, a substantial number of recurrences occures up to three years after fistula surgery.

Ans- This is a very valid point and is of high importance. *The study is waiting its long term follow up (>3 years) results.* We have now included this in the shortcomings of the procedure.

4) Please discuss the potential role of PERFACT opposed to mucosal advancement flap, anal Fistula plug, OTSC proctology, and others.

Ans- Comparison with other existing procedures is very much needed. Thanks for pointing this out. We have included this in the revised manuscript.

Perfact procedure adds a potentially useful treatment option in our armamentarium against

complex fistula-in-ano. This procedure compliments the mucosal advancement flap, anal fistula plug, OTSC proctology, LIFT, VAAFT and glue procedures. It is simple, associated with least morbidity and minimal risk of incontinence. Compared to mucosal advancement flap, the Perfact procedure is technically less demanding. Unlike anal fistula plug, Laser-FiLaC and OTSC proctology procedure[9, 10], Perfact procedure can be done as a definitive procedure in the fistula patients presenting with acute abscess or collection. Unlike other existing procedures, Perfact procedure can be done in the patients where the internal opening cannot be definitely localized. Lastly, compared to fistulotomy and cutting tightening seton, Perfact procedure is associated with a minimal risk of incontinence.

5) Please explain how you developed the present PERFACT procedure. What were your observations that let you perform it like this? Did you have good results by intensified fistula cleaning after other types of fistula surgery?

Ans- The concept of Perfact procedure was devised as a result of persistent endeavors to permanently close/ heal the internal opening. We took clue from the chronic non healing wounds in other parts of the body, where freshening the wound and keeping it clean stimulated the growth of the granulation tissue. We hypothesized that if we created a raw wound all around the internal opening and kept it clean, this would stimulate the growth of healthy granulation tissue which in turn would facilitate the closure of the internal opening. Once this is achieved, then regular cleaning of the fistula tracts would lead to complete closure of the fistula-in-ano. However, if there was some accumulation of fluid/pus in the tracts, then it could reopen the healed internal opening. Hence regular cleaning of the tracts was also an integral part of the procedure.
Simple suture closure of the internal opening usually fails to close the internal opening and heal the fistula. So we thought that the regular entry of bacteria through the internal opening and the stagnation in the tracts, both facilitate each other. Therefore both the problems need to be tackled together if the fistula has to be cured.
We have incorporated intensified cleaning in our postoperative care after fistulotomy and this has led to the improvement in the outcome results.

6)The compliance / adherence of your patients seems to be excellent; I can imagine difficulties to persuade patients of fistula cleaning four times a day.

Ans- We appreciate your insight and clinical acumen. It was indeed a challenging task and perhaps the most difficult part of the procedure. This was helped by a proper detailed preoperative counseling session where the whole concept was explained to the patient and the relatives. Along with this, regularly motivating the patient also helped. Thirdly, the patients of complex fistula-in-ano were usually suffering for a prolonged period and were desperate for cure. In our series, 77% were recurrent fistulas. Therefore, they willingly accepted to get the dressings done four times a day to get rid of this dreaded disease.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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