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Pouchitis: An Empirically Treated Disease in the Era of Evidence-based Medicine

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Commentary on:
Nikfar *et al.* (2010). A review and meta-analysis of the efficacy of antibiotics and probiotics in management of pouchitis. Int. J. Pharmacol., 6(6): 826-835.

Proctocolectomy with Ileal Pouch-Anal Anastamosis (IPAA) is the preferred surgical approach for ulcerative colitis. Unlike proctocolectomy with permanent ileostomy, IPAA preserves intestinal-anal continuity and spares patient from anxiety and inconvenience of ileostomy care. However, this surgical method is commonly complicated with inflammation of the ileal pouch.

There are no universal clinical, endoscopic or pathologic diagnostic criteria for pouchitis which has lead to a large variation in the prevalence rates reported in the literature (7-95%) (Lohmuller *et al*., 1990; Shepherd *et al*., 1993). In our centre, we diagnose pouchitis after exclusion of other relevant pathologies (i.e., Crohn's disease, bacterial, parasitic and viral infections) and upon the presence of a constellation of clinical, endoscopic and pathologic findings compatible with non-specific inflammation of ileal reservoir. While acute pouchitis usually responds to a short course of antibiotics, chronic pouchitis (symptoms longer than four weeks) remains elusive to treat.

Nikfar *et al.* (2010) recently conducted a meticulous meta-analysis on the efficacy of probiotics and antibiotics in management of pouchitis. Probiotics significantly improved the symptoms of pouchitis; however, as authors stipulate, these results should be interpreted with extreme caution for the following reasons:

(1) Possibility of publication bias as shown in on the funnel plot; (2) Heterogeneity in the design of the studies in terms of quality, duration of follow-up (16-60 weeks), probiotic of use and the dosing and (3) Lack on blinding in the largest trial Gosselink *et al.* (2004) and the trial with the highest absolute risk reduction (i.e., 100%) (Shen *et al*., 2005). When only the VSL#3 trials with a dose of 6 g/day are included in the meta-analysis, more homogenous results were achieved but publication bias remains. In contrast to the included studies, Pronio *et al.* (2008) in an open-label randomized study have shown that VSL#3 is not superior to "no treatment" for prevention of pouchitis. Therefore, a definite recommendation for the use of probiotics cannot be made and further large blinded randomized trials are needed to explain the current discrepancies among VSL#3 trials.

As authors well illustrate, evidence on the efficacy of antibiotics in pouchitis is scarce and inadequate. However, whether by right or not, antibiotics have become the "standard medical management" for pouchitis. While further elucidation of the role of antibiotics in pouchitis is critical, conducting controlled trials on a de facto standard therapy is exceptionally hard specially in the recruitment phase (Elahi *et al*., 2008, 2009).

Based on the current available data, my recommendations for treatment of chronic pouchitis are compatible with Pardi and Sandborn (2006). In our centre we initially use ciprofloxacin with a better tolerability, side effect profile and possibly effectiveness comparing to metronidazole. Upon non-response, we use further medical therapy in the following order: metronidazole, 5-aminosalicylates, budesonide and immunosuppressants. If pouchitis remains refractory to these treatments, biologic therapy or surgical revision should be considered. However, as Nikfar *et al.* (2010) clearly demonstrate, further studies are required to optimize future therapeutic recommendations.

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