

Permacol™ collagen paste injection for the treatment of complex anal fistula: 1-year follow-up

B. Fabiani¹ · C. Menconi¹ · J. Martellucci² · I. Giani¹ · G. Toniolo¹ · G. Naldini¹

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Abstract

Background Optimal surgical treatment for anal fistula should result in healing of the fistula track and preserve anal continence. The aim of this study was to evaluate Permacol™ collagen paste (Covidien plc, Gosport, Hampshire, UK) injection for the treatment of complex anal fistulas, reporting feasibility, safety, outcome and functional results.

Methods Between May 2013 and December 2014, 21 consecutive patients underwent Permacol paste injection for complex anal fistula at our institutions. All patients underwent fistulectomy and seton placement 6–8 weeks before Permacol™ paste injection. Follow-up duration was 12 months.

Results Eighteen patients (85.7%) had a high transsphincteric anal fistula, and three female patients (14.3%) had an anterior transsphincteric fistula. Fistulas were recurrent in three patients (14.3%). Seven patients (33%) had a fistula with multiple tracts. After a follow-up of 12 months, ten patients were considered healed (overall success rate 47.6%). The mean preoperative FISI score was 0.33 ± 0.57 and 0.61 ± 1.02 after 12 months.

Conclusions Permacol™ paste injection was safe and effective in some patients with complex anal fistula without compromising continence.

Keywords Anal fistula · Permacol · Fistula treatment · Seton · Biomaterial · Porcine dermal collagen matrix

Introduction

Optimal surgical treatment for anal fistula should result in healing of the fistula track and preservation of anal continence. For simple and low fistulas, conventional surgical approaches as fistulotomy, fistulectomy and cutting seton have achieved good results with low recurrence rates and minimal impact on continence. Several surgical alternatives have been proposed to treat complex and high transsphincteric fistulas since traditional surgery in these cases is associated with a high risk of anal incontinence. Many authors have proposed the use of biomaterials such as fibrin glue, fistula plugs and stem cells to increase fistula healing and reduce negative functional sequelae. Although early studies about fibrin glue reported good results with a success rate ranging from 64 to 85% [1–3], subsequent studies did not confirm these results, reporting a success rate less than 33% [4–6]. The same phenomenon occurred with the fistula plug: the first reported success rates of 87–92% [7, 8] are in sharp contrast with the latest reports of 14–29% [9–11]. Initially promising results with expanded adipose-derived stem cells (eADSC) were reported, with a success rate of 71% [12], but unfortunately at 1 and 3 years of follow-up, respectively, the success rate fell to 62 and 33%, respectively [13]. Recently, the injection of a collagen matrix was introduced as a new biomaterial to treat complex anal fistulas [14–16].

Permacol™ collagen paste (Covidien plc, Gosport, Hampshire, UK) consists of an acellular cross-linked porcine dermal collagen matrix milled and suspended in saline, that is injected into the fistula track.

✉ J. Martellucci
jamjac64@hotmail.com

¹ Proctological and Perineal Surgical Unit, Department of Gastroenterology, Cisanello University Hospital, Pisa, Italy

² General, Emergency and Minimally Invasive Surgery, Careggi University Hospital, largo Brambilla 3, 50134 Florence, Italy

The aim of this study was to evaluate Permacol™ injection for the treatment of complex anal fistulas, reporting safety, outcome and functional results.

Materials and methods

Between May 2013 and December 2014, 21 consecutive patients underwent Permacol™ paste injection for complex anal fistula, defined according to American Society of Colon and Rectal Surgeons guidelines [17]. All patients underwent clinical examination, endoscopic ultrasonography (Bruehl and Kjaer 10-MHz 3-D rotating probe) and/or magnetic resonance imaging before surgery. Continence was evaluated before and after surgery, using the validated Fecal Incontinence Severity Index (FISI) [18]. All patients took an enema the evening before surgery. All operations were performed under spinal or general anesthesia with patients in the lithotomy position. Previously all patients had undergone preliminary surgical treatment consisting of drainage and/or fistulectomy with positioning of a draining silicone seton that was maintained for a period of 6–8 weeks to allow adequate drainage of the septic material. When the tract was considered too long and an external orifice was present far from the anus, fistulectomy was performed with the aim of rendering the tract more linear and shorter (ideally 2–5 cm between internal and external orifice). Fistulectomy extended up to the external part of external sphincter. Drainage was performed in the absence of an external orifice. A draining seton was always placed. Prophylaxis consisted of a single preoperative administration of cefazolin 2 g. After seton removal, a gentle debridement of the fistula track was performed. The scar tissue was removed from the internal orifice, and about 1 cm of mucosa around the internal orifice was detached so that a side-to-side mucosal suture could be placed. The closure of the internal opening was performed with a “Z” vicryl 0 suture on the smooth muscle covered by a side-to-side mucosal suture. The choice of a lateral suture was made in order to prevent tension and dehiscence. Then, liquid porcine dermal matrix (Permacol™ paste) was injected through the external opening into the fistula track, and the external opening was sutured in order to prevent early leakage of the biomaterial. The paste was injected until the tract was completely filled. The fistula track was measured by evaluating the length of the seton that had been in the fistula, after seton removal.

Patients were evaluated at 7 days and at 1, 3, 6 and 12 months after surgery. Postoperative pain was measured with a visual analog scale [VAS range 1 (least)–10 (most)]. Success was defined as the closure of the external opening and the absence of drainage from the fistula, confirmed on

clinical evaluation, that suggested the fistula track was closed. Surgical complications, including continence disorders, were also evaluated.

Statistical analysis

The data were collected in a prospective database expressly created, and Microsoft Excel and SPSS 16.0 (Statistical Package for Social Sciences, Chicago, IL, USA) was used for the statistical analysis. Continuous data were expressed as the median and range. FISI and VAS values are presented as mean and standard deviation (SD). Two-side *p* values of <0.05 were considered statistically significant.

Results

Of a total of 21 patients (13 males) with a median age of 48 years (range 22–72 years), 18 patients (85.7%) had a high transsphincteric anal fistula, one of which was related to Crohn’s disease, and three female patients (14.3%) had an anterior transsphincteric fistula. Three patients (14.3%) had a recurrent fistula. Seven patients (33.3%) had a fistula with multiple tracks. All patients underwent fistulectomy and seton positioning 6–8 weeks before the Permacol™ paste procedure. The mean (\pm SD) preoperative FISI score was 0.33 ± 0.57 . Median operative time of the Permacol™ procedure was 30 min (range 20–40 min). Median fistula tract length was 31 mm (range 9–77 mm). No intraoperative complications occurred. During the first week after surgery, the overall mean VAS score was 0.62 ± 0.97 . No patient experienced severe pain (expressed as a VAS score >7) during the first week after surgery. Median hospital stay after surgery was 1 day (range 1–2 days). At 3 months, an abscess was reported in one patient (4.8%) and in six patients (28.6%) an external opening with secretions was still present. One of these (4.8%) had a premature opening (within 30 days after surgery) of the external orifice with a partial leakage of the biomaterial. The abscess was immediately drained, and the six patients with drainage from the external opening underwent reoperation within 6 months for failure to heal. Of the remaining patients with a closed external orifice at 3 and 6 months after surgery, four had a recurrence 12 months after surgery (Table 1). At 12 months, ten patients (one of whom had Crohn’s disease) had a closed external orifice, so that the success rate was 47.6%. No correlation was found between fistula healing and fistula tract length. At 12 months, the FISI score was 0.61 ± 1.02 without any significant difference from the preoperative value (*p* = 0.27). No patients reported a worsening in their continence status.

Table 1 Clinical results at 3, 6 and 12 months after surgery

Patient Id	3 months	6 months	12 months
PI01BD	Abscess/drained		
PI02BA	EO not closed	Reoperation	
PI03SA	EO closed	EO closed	EO closed
PI04BA	EO closed	EO closed	EO closed
PI05GE	EO closed	EO closed	Recurrence
PI06SM	EO not closed	Reoperation	
PI07MG	EO closed	EO closed	EO closed
PI08SR	EO closed	EO closed	EO closed
PI09MF	EO closed	EO closed	EO closed
PI10GS	EO closed	EO closed	EO closed
PI11PS	EO closed	EO closed	EO closed
PI12AC	EO not closed	Reoperation	
PI13TP	EO not closed	Reoperation	
PI14SM	EO closed	EO closed	Recurrence
PI15AG	EO closed	EO closed	Recurrence
PI16PA	EO not closed	Reoperation	
PI17MM	EO closed	EO closed	EO closed
PI18GG	EO closed	EO closed	EO closed
PI19GG	EO not closed	Reoperation	
PI20RS	EO closed	EO closed	Recurrence
PI21GL	EO closed	EO closed	EO closed

EO external opening

Discussion

The goals of the treatment of anal fistula include healing of the fistula track and maintaining continence. The risk of postoperative incontinence and recurrence is significantly increased in patients with complex anal fistulas [19, 20]. Anal fistula should be considered complex if the primary track involves the upper two-thirds of the external sphincter, is anterior in a female patient, is recurrent, has multiple tracks or has a history associated with fecal incontinence, radiotherapy or Crohn's disease [17]. Traditional surgical approaches, including fistulotomy or cutting seton, are associated with high risk of incontinence in complex fistulas. Fistulotomy, the complete opening of the fistula track between the external and the internal opening, has resulted in success rates of up to 100%, but impairs continence in 20–82% of cases [21, 22]. Cutting seton is associated with high healing rates, but fecal incontinence has been reported in a significant percentage of patients [23]. For this reason, sphincter-preserving techniques such as ligation of the intersphincteric fistula tract (LIFT) and transanal advancement flap repair (TAFR) were developed. Both procedures had widely variable success rates, ranging from 47 to 100% [24, 25] and 40 to 88% [26, 27], respectively; moreover, advancement flap is associated with incontinence rates of up to 28% [26, 27]. A

combination of the two techniques has been reported, but it does not seem to improve outcomes [28]. So, biomaterials such as fibrin glue, fistula plugs and stem cells have been proposed to increase fistula healing and reduce incontinence rates [1–3, 7, 8, 12]. Unfortunately, the encouraging early results have not been replicated and did not seem to persist at follow-up in subsequent studies [4–6, 9–11, 13]. A recent systematic review and meta-analysis confirmed that none of the sphincter-preserving techniques proposed seems to be superior to the others [29].

PermacolTM paste is an acellular cross-linked porcine dermal collagen matrix milled and suspended in saline. Chemical cross-linking seems to provide resistance to premature enzymatic degradation in the face of bacterial contamination, while facilitating fibroblast migration into the fistula track and tissue regeneration [30]. Furthermore, the consistency of this micronized collagen suspension can conform to the shape of the fistula and also fill any secondary tracts, unlike solid biomaterials, reducing the risk of early extrusion and recurrence. Sileri et al. [16] showed that collagen matrix injection combined with flap repair for the treatment of complex fistulas is safe and effective. They reported a success rate of 75% and overall surgical complications in 21% (5/24) of patients treated with a mean follow-up of 14 months. However, the commercial product PermacolTM paste was only used in a recently published prospective multicentre study, in which a decline in the benefits of PermacolTM paste at long-term follow-up was reported with a fistula healing rate of 54% at 12 months after surgery [31]. In that study, patients with intersphincteric and transsphincteric fistula were included. The authors hypothesized several reasons for failure, including residual undetected sepsis and abscess formation, implant extrusion or non-optimal biological features of the implanted material.

In the present study, the overall success rate was 47.6% at 12 months, but only complex anal fistulas were included. The main problem in treating anal fistula is the high risk of recurrence and it is not clear whether this is due to a failure of internal orifice closure or a failure of fistula track healing. For this reason, we acted on both factors. The internal opening was closed with a double layer of sutures, and fistula track was at first treated with fistulectomy including the external sphincter. Moreover, the external opening was closed to prevent extrusion of material. As proposed by Sileri et al. [16], a draining seton was then positioned and maintained for 6–8 weeks in order to drain residual septic material and to make the fistula track fibrotic and regular. In a second step, the fistula track was closed with PermacolTM paste. Some authors have hypothesized that fistulectomy and draining seton are not strictly necessary in the presence of a regular and chronic fistula track. However, this assumption should be clearly

demonstrated in further studies even if Stamos et al. [32] have already reported that in patients treated with plug implantation without previous use of a draining seton the healing rate (73%) is significantly higher than in patients treated with a draining seton before plug implantation (43%). The study exclusion criteria included an active infection, a fistula with multiple tracks and Crohn's disease. A partial and early leakage of the biomaterial occurred in one patient (4.8%) who experienced fistula recurrence within 3 months after surgery. It confirmed that the early extrusion of the paste is one of the causes of fistula recurrence as shown by Sileri et al. [16]. In their study, extrusion was observed in six patients (25%) and all of them experienced recurrence. In the present study, no intraoperative complications occurred and no patient experienced severe pain during the first week. Moreover, there was no significant correlation between fistula tract length and fistula healing.

As expected, no significant differences were observed in FISI scores before and after surgery, confirming that Permacol™ paste injection did not have negative impact on function. The treatment apparently does not compromise normal continence like the other surgical sphincter-saving techniques that use injection of biomaterials [16, 32]. In particular, it has been reported that the lower incidence of continence disorders with Permacol™ paste than with the advancement flap technique [33] is due to the making of a smaller flap with a side-to-side suture after a lateral mucosal dissection.

Conclusions

Our results do not suggest that the use of Permacol™ paste is superior to other sphincter-saving methods for the treatment of complex fistulas. To date, very few studies have been conducted on the role of Permacol™ paste in the treatment of anal fistula, and more are needed to establish which patients are ideal candidates for Permacol™ paste injection and to explain treatment failures.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all participants included in the study.

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