Efficacy of porcine dermal collagen (Permacol™) injection for passive faecal incontinence in a dedicated Colorectal Unit at the Wits Donald Gordon Medical Centre

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Background: Passive faecal incontinence (FI) due to a defect of the internal anal sphincter is a distressing condition and can be difficult to manage medically and surgically. The use of a trans-anally injected bulking agent to improve continence has been published internationally with contradictory results.
Objectives: To describe the results obtained with use of Permacol™ in a private practice setting in South Africa.
Methods: Patients with passive FI due to confirmed internal anal sphincter deficits that had been treated with Permacol™ injections were followed up. They were asked to complete the Wexner faecal incontinence scores and Rockwood QoL scores for both their pre- and post-treatment continence state.
Results: Of the 14 patients who completed the questionnaires, most were women with a mean (SD) age of 56.4 (13.4) years. The majority of the patients had a history of a predisposing event. They reported a significant improvement in both the Wexner scores ($p < 0.0005$) and the Rockwood QoL ($p=0.004$), including all subsections. The Wexner scores and the Rockwood scores were significantly correlated post-procedure ($r= -0.6186$; $p=0.0183$). There were no significant correlations between change in scores and time after procedure.
Conclusion: Trans-anal submucosal Permacol™ injections produced a significant improvement in both faecal continence and quality of life scores in patients with passive faecal incontinence for up to two years.
Keywords: incontinence, bulking agents

S Afr J Surg 2017;55(2)

Introduction

Faecal incontinence (FI) results from an alteration in the mechanism that normally maintains continence.[1] While the internal and external sphincters both play a role, most of the resting anal pressure is provided by the internal anal sphincter (IAS). A localized defect in the IAS or loss of the anal cushions, most often caused by iatrogenic injury, birth trauma or age-related factors, may present with passive FI resulting in the leakage of liquid and gas.[2] Passive FI due to an abnormality of the IAS cannot be repaired primarily with surgery, thus an alternative treatment is required. Non-surgical management includes changes in diet, use of constipating agents and the most efficacious, biofeedback.[3] Surgical options include the use of bulking agents or, in extreme cases, the creation of an ostomy.

Bulking agents were initially prescribed for the treatment of urinary incontinence; the first report of the use of such agents for FI was in 1993 using a PTFE paste.[4] The results were promising and this brought about the search for improved agents and alternative implant techniques to improve the side-effect and risk profiles. A Cochrane review in 2013 found five eligible trials, most of which reported a short term effect.[5] Overall there was insufficient evidence to recommend bulking agents in the treatment of FI.

More recently the use of a variety of bulking agents has been published: Bulkamid™ and Permacol™ [6-8] have been tested most frequently. Improvements in continence were noted, lasting from 6 weeks post-procedure[6] to 36 months.[7] Various scores have been used to measure the change in function and quality of life, however there is no universally accepted score which has been validated.[9,10] In South Africa, medical

funders are not willing to pay for the procedure owing to lack of evidence of efficacy.

The Colorectal Unit (CRU) at Wits Donald Gordon Medical Centre (WDGMC) has been using Permacol™ as a bulking agent for passive FI for the last five years. The clinical impression is that patient satisfaction has been good. The aim of this study was to quantify perceived changes in symptoms and quality of life in patients who have had Permacol™ injections for passive FI.

Methods

The study design included a retrospective record review for clinical data as well as a prospective arm for collection of symptoms pre and post procedure.

The files of all patients who had undergone Permacol™ injections for passive FI during 2012 and 2013 in the CRU were accessed retrospectively. All had had a colonoscopy and endo-anal ultrasound (EAUS) as part of their work up. Only patients with an intact external sphincter and in whom other possible causes of FI had been excluded were included in the study. Patients were then contacted telephonically and asked if they would consider participating in the study. Only after informed consent was obtained were data including age, gender and predisposing causes extracted from the patient files. The study was approved by the Human Research Ethics Committee of the University of the Witwatersrand (M140221).

Permacol™ injection procedure

Once diagnosed with passive FI, all patients were counselled on the available treatment options including Permacol™ injections. Patients were informed that if they chose the Permacol™ injections, they would be responsible for payment for the procedure as it was not covered by the medical aid. No sponsorship of either product or of a monetary nature was accepted from the manufacturers and distributors of Permacol™ for the procedure. Patients who chose Permacol™ injection were treated in theatre under general anaesthesia in the lithotomy position. Prophylactic antibiotics were given then a rectal examination was performed to confirm the position of the sphincters, the intersphincteric groove and any local sphincteric defect. Occasionally a repeat EAUS had to be performed to confirm clinical findings.

Permacol™ is pre-packaged in a 2.5 ml syringe; the syringe is connected to a second empty 2.5ml syringe. Prior to injection, the Permacol™ was transferred between the two syringes 20 times to make it more pliable and easier to inject. Once the sphincter complex was localised, the syringe needle was inserted into the submucosal plane trans-anally, superficial to the internal sphincter in the upper third of the anal canal. This was done under tactile guidance on the surgeon's index finger as described by Hussain[8] and repeated by others since then.[3,7] For patients with a diffuse sphincter lesion the first injection was positioned posteriorly (6 o'clock). From the first injection site three other sites were selected and injected to create one injection in each quadrant of the sphincter at 90° to each other. In cases with a discrete sphincter lesion, one vial of Permacol™ was injected on each side of the defect followed by the other two vials into the other thirds of the circumference. A full syringe of 2.5 ml of Permacol™ was injected at each site.

After injection, the patients were checked for bleeding and discharged from hospital the same day.

Follow-up study

All Permacol™ patients identified during the period 2012-2013 who agreed to participate were asked to complete a Wexner[11] and Rockwood FI QoL questionnaire[12] based on their recall of their pre-procedure incontinence and their current symptoms.

The Wexner score measures how frequently grades of incontinence occur. The lower the score, the better the continence. Five endpoints of incontinence, namely, incontinence to solid, liquid, and gas, lifestyle modification as well as pad usage are measured on frequencies ranging from never to always (more than once a day).

The Rockwood FI QoL score has 29 questions divided into four subscales measuring: lifestyle (10 questions), coping and behaviour (9 questions), depression and self-perception (7 questions) and embarrassment (3 questions). Higher scores indicate better continence and, for this study, a total score as well as an average score for each subsection was calculated.

Data was then entered into a specially designed REDCap™ database.

Data analysis

Descriptive analysis was conducted using means and standard deviations (or medians and ranges for highly skewed data) for numerical data including subsections of the Rockwood QoL and percentages for categorical data. The comparison between pre- and post-procedure for both scales was done using the Wilcoxon matched-pairs signed-rank test. Spearman tests for non-parametric data were used for all correlations. Results were considered significant at a P value < 0.05.
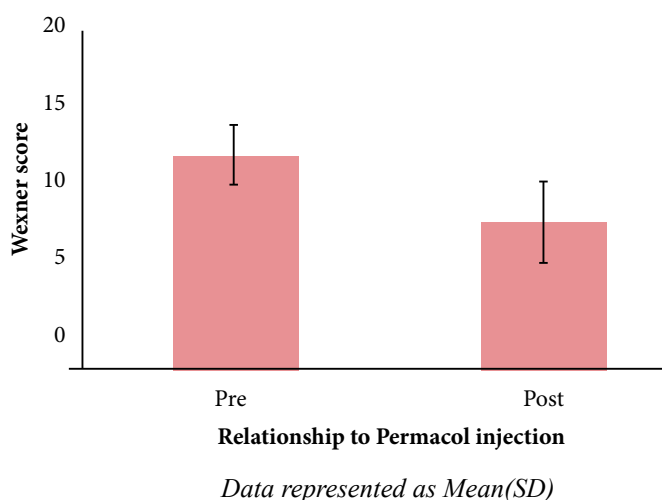
Results

Permacol™ injections for passive FI had been performed on 36 patients during the stipulated time period. All were contacted but only 16 agreed to complete the questionnaires and in the end only 14 completed the full data set. The mean age of the patients was 56.4 (13.5) years and 12 were female. The mean (SD) interval between injection and our review was 13.8 (6.9) months with a range of 2.9–26.9 months. There were few co-morbidities: one patient had a history of diabetes and two were hypertensive.

Of the 12 women, 10 (83%) had a previous predisposing event: 50% had a previous difficult normal vaginal delivery

(including episiotomy, vaginal tear or prolonged labour), 50% had a previous hysterectomy and 42% had previous proctological surgery including four procedures for haemorrhoidectomy. Three participants had more than one high risk event. On rectal examination, 29% of patients had normal anal tone, 50% had low tone and 29% had a poor anal squeeze response. On ultrasound, 64% had a discrete defect of the IAS. In all cases, the EAS was intact. Two patients had received a previous Permacol™ injection.

There was a significant improvement in the Wexner score post-procedure (12.5 pre-injection, 7.9 post-injection; p=0.0005, Wilcoxon rank sign test, Figure 2). However, there was no correlation between the change in Wexner score (r=0.0008; p=0.999) or final Wexner score (r=-0.120; p=0.6828) and time since injection.

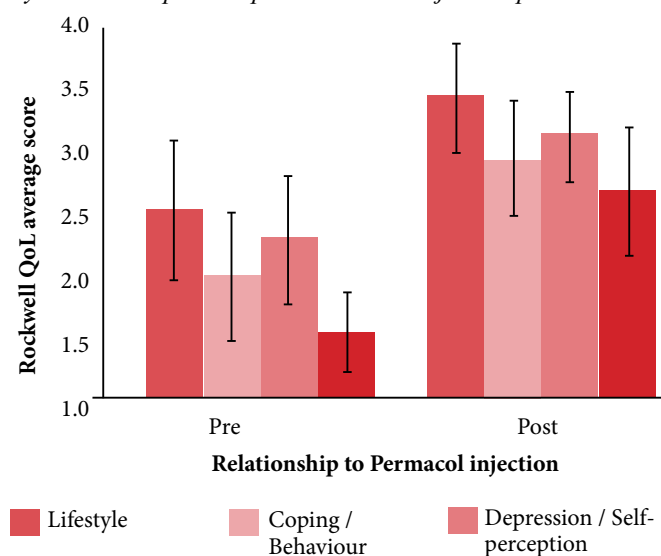*Figure 1. Changes in Wexner Score before and after Permacol injection*

Data represented as Mean(SD)

The mean (SD) change in the Rockwood FI QoL total score was 27 (25) with a range of -4 to 78. The total mean (SD) score before the procedure (64.3 (23.7)) was significantly lower compared to the follow-up score (90.1 (19.8); p=0.004; Wilcoxon rank sign test). All post-procedure sub-scores were significantly higher than pre-procedure scores (lifestyle p=0.001, coping/behaviour p=0.002, depression/self-perception p=0.002 and embarrassment p=0.0005, all Wilcoxon rank sign test; Figure 2). There was no correlation between change in scores and follow-up time (r=0.0665, p=0.813) or between final scores and follow-up time (r=0.194, p=0.506 Spearman's correlation).

The Wexner and Rockwood QoL scores were negatively correlated because clinical improvement gives a lower Wexner and a higher Rockall score. Although the pre-injection scores on both questionnaires (r=-0.5294; p=0.0516) were not significantly correlated, the scores post-procedure were significantly correlated (r=-0.6186; p=0.0183; Spearman's correlation).

Figure 2. Rockwood Faecal incontinence quality of life scores by subsection pre and post-Permacol injection procedure

Discussion

In this small retrospective pilot study of mainly middle-aged women with passive FI most, as would be expected, had a predisposing event. With a follow-up ranging from three months to more than two years there was a significant improvement in both Wexner and Rockwood Quality of life scores after trans-anal injection of Permacol™. There was also significant improvement in all components of the Rockwood QoL score but no correlation between the length of follow-up and the improvement after Permacol™ injection, i.e. we did not find any obvious fall-off in efficacy. Post-procedure, there was a significant correlation between the two scores.

The main limitation of this study is the small numbers. The sample sizes of previously published trials of Permacol™ injection for faecal incontinence range from 100 patients[7] to ten patients.[6] Despite our low sample size the significant differences obtained in follow-up are worth reporting. Another limitation is the reliance on memory for change in function and quality of life which may not be accurate enough. Participants might have deliberately selected an improvement in scores owing to failed recall or desire to please or failed to remember accurately, particularly those with a longer follow-up period. There might also have been a bias created in the sample as less than half of the patients who had the injection responded to the appeal to measure the quality of life. A second source of bias in the sample was that only those patients who could afford to pay for the procedure themselves could be included as this procedure is not subsidised by the medical aids and not available in the state sector. The injections were done by two different surgeons who had discussed and standardized the procedure but there were too few patients to compare the surgeons' outcomes individually.

Epidemiological information would suggest that between 7–15% of adults are affected by FI [2] although there are no figures for South Africa. The most common cause of FI is childbirth trauma, so most FI patients are women. This is confirmed in this study as well as other studies reporting on the

use of bulking agents to treat passive faecal incontinence.[6-8,13]

In other studies various questionnaires were used to measure FI and QoL. There are ongoing debates as to the pros and cons of each questionnaire,[9,12] however, no single score, measurement or questionnaire has been validated. We chose to use the Wexner and Rockwood QoL questionnaires as they had been used previously [8,13] and shown improvements post-injection of Permacol™ [7,8] for up to six months. Some studies, however, allowed multiple injections which enhanced the positive outcomes.[7] Others showed no improvements post-injection but had included patients with both internal and external sphincter defects[14] or only used three points of injection.[6] There was also no connection between improvement in continence and improvement in quality of life.[13] Ours is the first study to use both questionnaires together showing that an improvement in the function of the anal sphincter correlates with an improvement in quality of life. This may be due to careful selection of patients and a standardized technique using four points of injection.

There is no validated method of injection or validated bulking agent. We chose to use the technique, trans-anal injection, and a substance, Permacol™, that had been used most recently and frequently. While NASHA Dx is now being used in Sweden, and has been found to be efficacious,[15] it was unavailable to us due to its price. Permacol™ seems to have a better risk profile as it is physiologically inert, easy to inject with a very low sepsis rate[8]] but its cost in South Africa (R8000 for four vials – > $600 at current exchange rates) has led to a reluctance of medical funders to pay for the procedure without data as to its effectiveness. It is unclear whether this procedure produces a cost saving for the medical funders.

The lack of a relationship between improvement and time to follow-up in our patients is interesting. Other studies have shown a decreased effectiveness of the procedure with return to the previous state sometimes as early as six weeks[6] and 12 months.[7] Deterioration over time should have produced a negative correlation between improvement and time in this study. The longest reported follow-up was 7 years and improvement of function was not maintained.[16] It was not possible to stratify time to loss of continence post-procedure or any relationship between improvement and possible deterioration over time in this study due to the small sample size and variable time of follow-up.

This study has shown that an injection of Permacol™ in patients with passive FI caused by a defect in the internal anal sphincter significantly improved the continence and quality of life. A prospective study is necessary to counter the limitations of the small sample size and the inherent problems of late recall of previous function. Selecting specific time points of follow-up and longer follow-up would answer the question of longevity of the procedure. A cost analysis versus conservative treatment also needs to be done.

Acknowledgements

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