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[Efficacy of collagen infiltrations in the pelvic pain caused by episiotomy and caesarean scars. Pilot randomized clinical trial]

[Article in Spanish]

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Abstract

Background and aims: Pelvic pain is a frequently consulted symptom in pelvic floor rehabilitation units. The aim of this study was to evaluate the efficacy of collagen infiltrations in pain and the appearance of scars from perineal tears, episiotomies and caesarean sections.

Material and methods: Pilot randomized, controlled and single-blind clinical trial. Control group (CG) patients received conventional rehabilitation treatment. Additionally, those in the intervention group (IG) received 3-5 collagen infiltrations. The patients were evaluated at baseline and 6 weeks post-intervention. The main outcome was pain and it was evaluated with the Visual Analog Scale and McGill Pain Questionnaire. As secondary outcomes, the appearance of the scar was evaluated by Vancouver Scar Scale and the Patient Scar Assessment Scale. A sample of 15 women was analysed, 8 in the CG and 7 in the IG.

Results: The mean age was 33.1 years (SD 4.1). The intragroup analysis showed a significant decrease of the Visual Analog Scale punctuation and total McGill Pain Questionnaire score and the PRI-Emotional dimension of the McGill Pain Questionnaire. In the IG, a significant decrease was also observed in the PRI-Sensorial and PRI-Evaluative dimensions in comparison with baseline situation. In both groups, a significant improvement in the appearance of the scar was observed. In the intergroup analysis, a greater decrease in pain was observed in PRI-Sensorial subscale of the McGill Pain Questionnaire in the IG (-15.1 vs. -6; P=.040).

Conclusions: Collagen infiltrations may improve pain and the appearance of painful scars.

Keywords: Caesarean section; Cicatriz de cesárea; Collagen; Colágeno; Dolor pélvico; Episiotomy; Episiotomía; Infiltración; Infiltration; Pelvic pain; Rehabilitación; Rehabilitation.

Introduction

Pelvic pain (PP) is a frequent symptom of consultation in pelvic floor rehabilitation units after being treated in other services (Gynaecology, Urology, General Surgery and Digestology). It can affect more than 15% of women and only 30% of cases are attributable to gynaecological causes[1]. PP is a non-cyclic hypogastric pain that interferes with quality of life, being an important cause of discomfort, anxiety, increased visits to the doctor and surgery. It fundamentally affects women, in the absence of infectious and/or tumoral disease[2,3]. One of its causes is secondary to episiotomy or caesarean section scars. The incidence of postpartum PP due to episiotomy varies from 39% to 69%[4,5], remaining persistent in 6% to 10% at 12 months [5-7]. In caesarean sections, the frequency of immediate pain reaches 85-90% and persistent pain ranges between 8-22%[7,8]. There are different options in the therapeutic approach to painful scars: from silicone injections,

corticosteroids, subdermal procaine, immunomodulators, radiotherapy, laser therapy, cryotherapy, topical vitamin E, topical retinoid, colchicine, antihistamines or physiotherapy until surgery [9-11]. Physiotherapy treatments include ultrasound, transcutaneous nerve stimulation, as well as pelvic floor exercises and manual techniques. Massage of the scar, once the inflammatory phase has elapsed and complete repair of the dehiscence, improves flexibility and blood supply, and prevents possible adherence of the scar. [12-15]

There is little evidence of the efficacy of treatment with local infiltrations. Local collagen injections have recently been introduced. It is a health product based on purified type I collagen, together with ascorbic acid, magnesium gluconate, pyridoxine hydrochloride, riboflavin and thiamine hydrochloride. Type I collagen confers plasticity and flexibility in the final process of wound healing. The application of collagen in painful scars can confer these properties early and, therefore, reduce pain. There are different types of collagen infiltrations whose efficacy has been proven in disorders of the musculoskeletal system[16-18] such as myofascial pain syndrome[19,20] or atypical fascial neuralgia, and as a rejuvenating treatment[16]. However, its efficacy in the treatment of painful scars has not been evaluated. The aim of this study was to evaluate the efficacy of collagen injections on the pain and appearance of painful scars from perineal tears, and/or caesarean sections compared to conventional treatment with rehabilitation.

Material and methods

Design

Randomized, controlled, single-blind pilot clinical trial of patients with PP secondary to painful scars or caesarean sections. The protocol was approved by the Clinical Research Ethics Committee of the Fundació Unió Catalana d'Hospitals (code CEI17/73) and registered in clinical-trials.gov (NCT04112888). The study was conducted in accordance with current legal and regulatory requirements and following international ethical guidelines for research involving human beings. The results have been reported in accordance with the CONSORT 2010 statement.[21]

Study subjects

The study sample was obtained from patients referred between the months of April 2017 and May 2018 to the Pelvic Floor Rehabilitation consultation of our center, due to PP secondary to painful scars from both episiotomy and caesarean section. Women between 18 and 45 years old with a history of caesarean section or episiotomy delivery, with pain in the scar, who agreed to participate in the study and signed the informed consent were included. Women with PP due to other causes, mental or cognitive disorders, pregnancy, pacemaker carriers, treatment with oral anticoagulants, local infections, presence of episiotomy granuloma, total or partial denervation of the pelvic floor, and neurological diseases were excluded.

Randomization

Random assignment to the group control (CG) or intervention group (IG) was performed at the baseline visit. A list of 8 blocks with 2 patients per block was generated using a random sequence generation software (http://www.randomization.com). This process was the responsibility of the Unitat de Recerca i Innovació.

Study groups

The CG patients received conventional treatment of 8 individual rehabilitation sessions of 45 min. Two weekly sessions were scheduled for 4 weeks. The techniques of massage therapy, muscle stretching, fascia work were performed by the same physiotherapist specialized in pelvic floor. Scar massage therapy is a massage that consists of moving the tissues in all directions. Longitudinal and circular movements were made to release the tension, horizontal and vertical zigzag movements forming an «S», small pinches lifting the skin around the scar and, finally, rolling. Myofascial work consists of the relaxation of the fasciae to treat soft tissues that have suffered trauma, such as a scar. Work was done at the level of deep planes by means of

crossed hands/fingers or by placing one hand on top of the lesion and the other at the level of the sacrum, seeking restriction and causing sliding to improve mobility. Iliac psoas, piriformis, gluteal and hamstring stretches were performed. IG patients received the same rehabilitation treatment as CG patients. Additionally, IG patients received 3 (in case of episiotomy) to 5 (in case of caesarean section) injections of MD-Tissue® collagen into the scar once a week. Infiltrations of 2 ml (one vial) of collagen were performed in the episiotomy scars and 4 ml (2 vials) in the caesarean scars. Based on clinical criteria, it was decided to perform 3 to 5 infiltrations, which is the minimum number of infiltrations in order to be able to objectify clinical responses, performing more infiltrations and larger volumes in caesarean sections as they are larger. The rehabilitation doctor performed the intradermal infiltration using the tunnelling technique.

Procedure

The baseline assessment was carried out by the rehabilitation doctor. The demographic and clinical information of the patient (age, pathological and gynaecological-obstetric history) was collected, a basic examination of the pelvic floor was performed, evaluating the capacity for voluntary vaginal contraction (modified Oxford scale) and the areas to be infiltrated were located. For the subjective assessment of pain, the visual analogue scale (VAS)[22] and the McGill Pain Questionnaire (MPQ, «McGill pain questionnaire»[23]) validated in Spanish by Lázaro *et al.*[24] were used. To assess the appearance of the scar, the rehabilitation physician used the Vancouver Scar Scale (VSS) and the patient used the Patient Component of the Patient Scar Assessment Scale (PSAS) of the Patient and Observer Objective Assessment Scale.[25,26] An initial photograph of the scar was taken. Patients were reassessed 6 weeks postoperatively by a midwife blinded to group assignment. Information was collected through the VAS, the MPQ, the VSS and the PSAS, adding the subjective perception of scar improvement using the clinician's (CGI-I) and patient's (PGI-I) global impression scales.[27,28] A new photograph of the scar was taken to compare it with the baseline. Initially, 30 patients were evaluated for eligibility, of which 14 (46.7%) were excluded. Of the remaining 16, 8 were assigned to the CG and 8 to the IG. One patient moved from home before the post-intervention visit, so finally 8 in the CG and 7 in the IG were analysed (Fig. 1).

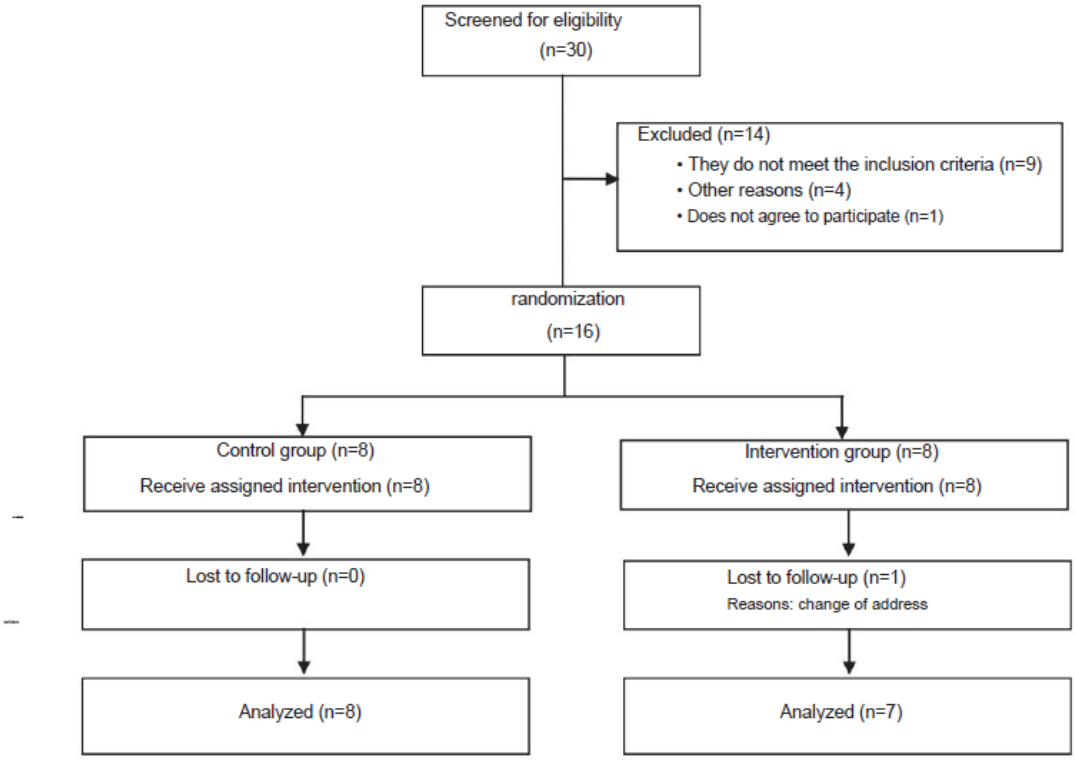

Figure 1 Flow chart.

Primary and Secondary Dependent Variables

The primary dependent variable was pelvic scar pain according to VAS and MPQ. The VAS makes it possible to measure the intensity of pain, which is described by a 10-cm horizontal line whose ends are the extreme expressions of pain. Score from 0-10. The MPQ is made up of 64 descriptors distributed in 19 subclasses (12 sensory, 3 miscellaneous-sensory, 3 emotional and an evaluative). Each of the descriptive terms is assigned a number or range that allows a score to be obtained according to the words chosen, thus obtaining the Pain Rating Index (PRI). Likewise, it allows assessing qualitative and quantitative characteristics of the pain experience by dividing the global results into three subscales: PRI-Sensory (12 subclasses), PRI-Emotional (3 subclasses) and PRI-Appreciative (1 subclass). As secondary dependent variables the appearance of the scar and the CGI-I and PGI-I were evaluated. VSS and PSAS were used to assess the appearance of the scar. The VSS evaluates 4 characteristics of the scar, such as pigmentation, vascularity, flexibility and height. The score range is between 0 and 10; the higher the score, the worse the healing. The PSAS allows to evaluate, on a numerical measure and subjectively, the symptoms related to pain, itching, colour, stiffness, thickness and relief. Each of the 6 questions has a value from 1 to 10, with a score of 10 being the worst scar imaginable or the worst feeling, and a score of 1 being normal skin. For the assessment of the global improvement after the intervention, the PGI-I scale was used, which describes the patient's perception of improvement between the categories of: much better, much better, a little better, no change, a slightly worse, much worse and much worse. The CGI-I describes the perception of improvement by the physician responsible for the treatment between the categories of: much better, better, no change, worse and much worse.

Statistical analysis

Continuous variables are summarized with the mean and standard deviation. Categorical variables are expressed in absolute value and relative frequencies. For the analysis of homogeneity of the baseline characteristics of both groups, the Student's t test was used to compare means with a normal distribution, and the Mann-Whitney U test for variables with a non-normal distribution. Fisher's exact test or Monte

Carlo's exact method was used for the comparison of proportions. For the efficacy analysis, the difference between the value obtained in the post-intervention assessment (6 weeks) and the baseline value of the main and secondary dependent variables was calculated for each one of the groups, together with its 95% confidence interval. Student's t test was used to compare the difference in means with normal distribution and the Mann-Whitney U test for variables with non-normal distribution. Cohen's d was calculated as a measure of effect size. A value ≤ 0.2 is considered a small effect, a d around 0.5 as a moderate effect and a d ≥ 0.8 as a large effect. For the comparison of the impression scales of global improvement post-intervention between the CG and IG used the exact Montecarlo method. The level of statistical significance used was 5% bilateral ($p < 0.05$). Data was analysed using IBM®SPSS®Statistics for Windows version 25 (IBM Corp, Armonk, New York, USA) and R® version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics (Table 1) were similar in both groups, with a mean age of 33.1 (SD 4 ,1). The proportion of caesarean sections was higher in the CG than in the IG (50.0 vs. 28.6%; $p = 0.608$). The subjective perception of baseline pain according to the VAS was higher in the CG than in the IG (7.5 vs. 5.7; $p = 0.021$). Table 2 shows the differences in the means between the post-intervention assessment and the baseline for each one of the groups. In the intragroup analysis, a significant decrease in pain (VAS, MPQ, PRI-Emotional) and a significant improvement in wound healing (VSS) were observed in both groups. In the IG, a significant decrease was also observed in the PRI-Sensory and the PRI-Value. In the intergroup analysis, a statistically significant difference was observed in the PRI-Sensory subscale ($p = 0.040$). The decrease in the PRI-Sensory score was higher in the IG compared to the CG: −15.1 (−22.2 to −8.1) vs. −6 (−12.6 to 0.6). No significant differences were observed in the rest of the scales. However, despite the fact that a significant decrease in pain was observed in both groups according to the overall score obtained on the MPQ, this was higher in the IG (Cohen's $d = −1.02$). The decrease in the MPQ score in the IG was −17.4 (−25 to −9.9) vs. −8.4 (−16.3 to −0.4) of the CG. Table 3 shows the PGI-I and the CGI-I after the intervention according to the study group. The proportion of patients who scored much or very much better was lower in the CG than in the IG (50.0 vs. 71.5%; $p = 0.814$). The clinician rated 87.7% of the patients in the CG and 100% of those in the IG as much or very much better ($p = 1.000$). None of the patients presented complications or adverse reactions due to infiltrations.

Table 1 Baseline characteristics

	Control n = 8	Intervention n = 7	p
Age (years), ¨mean (SD)	34,5 (3,7)	31,4 (4,1)	0,152
Primiparous, n (%)			
No	7 (87,5) 1	7 (100,0) 0	1,000
Yes	(12,5)	(0,0)	
Birth rate, n (%)			
Vaginal	4 (50,0) 4	5 (71,4) 2	0,608
Caesarean section	(50,0)	(28,6)	
Instrumental, n (%)			
No	1 (25,0) 3	2 (40,0) 3	1,000
Yes	(75,0)	(60,0)	
Oxforda, n (%)			
0 a 2	2 (50,0) 2	3 (60,0) 2	1,000
3 a 5	(50,0)	(40,0)	
Pain in relationships, n (%)			
No	4 (50,0) 4	2 (28,6) 4	0,608
Yes	(50,0) 0	(57,1)	
not relations	(0,0)	1 (14,3)	
Pelvic pain, mean (SD)			
EVA	7,5 (0,9)	5,7 (1,4)	**0,021**
McGill Pain Questionnaire	28,9 (8,0)	31,1 (4,8)	0,525
PRI-Sensorial	23,6 (8,3)	26,1 (2,5)	0,456
PRI-Emotional	2,5 (1,7) 2,8	2,7 (2,1) 2,3	0,867
PRI-Valuation	(1,2)	(0,5)	0,463
Lesion appearance, mean (SD)			
Vancouver Scar Scale	5,5 (1,9)	4,6 (1,9)	0,356
Patient Scar Assessment Scale	34,8 (9,9)	25,4 (11,2)	0,109

The data highlighted in bold corresponds to a statistically significant difference.
SD: standard deviation; VAS: visual analog scale; PRI: *Pain Rating Index*. a In case of vaginal delivery.

Discussion a significant decrease in the global assessment of the pain of the pelvic scars and an improvement in the healing of the lesion. The decrease in pelvic scar pain in the PRI-Sensory subscale was significantly greater in the IG patients.

Pain intensity scales are capable of determining changes in the same patient over time, but they have little ability to compare between subjects[29]. The VAS of pain is not very sensitive in the assessment and description of pain, the MPQ being more specific in this case in the evaluation of improvement in pain. The use of more specific scales/questionnaires can help us in the assessment of patients with any type of pain[30] The PP of perineal tear scars, episiotomies and/or caesarean sections is a frequently underdiagnosed and undertreated condition. A greater awareness of health professionals is required so that they ask about and assess the pain

Table 2 Primary and secondary dependent variables at baseline and post-intervention

	Basal, media (DE)		Post-intervention, mean (SD)		Differences between postintervention and baseline [95% CI]a		p[b]	*d* of Cohen
	Control n = 8	Intervention n = 7	Control n = 8	Intervention n = 7	Control n = 8	Intervention n = 7		
EVA	7,5 (0,9)	5,7 (1,4)	4,0 (3,1)	2,1 (2,4)	−3,5 [−6,3 a −0,7]	−3,6 [−6,3 a −0,9]	0,966	−0,02
McGill Pain Questionnaire	28,9 (8,0)	31,1 (4,8)	20,5 (15,4)	13,7 (8,9)	−8,4 [−16,3 a −0,4]	−17,4 [−25 a −9,9]	0,071	−1,02
PRI-Sensorial	23,6 (8,3)	26,1 (2,5)	17,6 (13,8)	11,0 (7,7)	−6 [−12,6 a 0,6]	−15,1 [−22,2 a −8,1]	0,040	−1,18
PRI-Emotional	2,5 (1,7)	2,7 (2,1)	1,1 (1,0)	1,1 (1,3)	−1,4 [−2,7 a −0,04]	−1,6 [−3,1 a −0,1]	0,817	−0,12
PRI-Valuation	2,8 (1,2)	2,3 (0,5)	1,8 (0,9)	1,6 (0,5)	−1 [−2,3 a 0,3]	−0,7 [−1,2 a −0,3]	1,000	0,25
Vancouver Scar Scale	5,5 (1,9)	4,6 (1,9)	3,4 (2,9)	1,7 (2,0)	−2,1 [−4 a −0,2]	−2,9 [−4,7 a −1,1]	0,613	−0,34
Patient Scar Assessment Scale	34,8 (9,9)	25,4 (11,2)	23,1 (18,3)	13,1 (16,1)	−11,6 [−25,4 a 2,2]	−12,3 [−26,6 a 2]	0,938	−0,04

Data highlighted in bold correspond to statistically significant differences.
SD: standard deviation; VAS: visual analog scale; 95% CI: 95% confidence interval; PRI: *Pain Rating Index*.
a Difference of intragroup means together with their 95% confidence interval.
[b] p of the contrast of the intergroup mean difference.

Table 3 Impression scales of global improvement of postoperative patient / clinician

	Control n = 8	Intervention n = 7	p
PGI I			
Much better	2 (25,0)	2 (28,6)	0,814
Better	2 (25,0)	3 (42,9)	
A bit better	4 (50,0)	2 (28,6)	
CGI-I			
Better	3 (37,5)	3 (42,9)	1,000
Better	4 (50,0)	4 (57,1)	
No change	1 (12,5)	0 (0,0)	

CGI-I: Clinician's Global Impression of Improvement Scale; PGI-I: impression scale of global improvement of the patient.

caused by these scars in women who have recently given birth, since a delay in diagnosis can cause a chronification of this pain and the consequent central sensitization, dificultivating the treatment and reducing the effectiveness of actions at the local level. This pilot study has shown a greater reduction in pelvic scar pain in temporal-spatial terms (PRI-Sensory subscale) in the IG. A large effect is also observed in the global MPQ score in favour of the IG, although the difference is not statistically significant, possibly due to the lack of statistical power as it is a pilot study with a small sample of patients. This small sample is clearly a limitation of the study, as well as the fact that it was not possible to carry out a blinded study. The fact that the intervention was not masked, and that the patient was aware of the group to which she was assigned could have led to a problem of social desirability in her responses so that they were seen as favourable by the health professional. As a pilot study, it was decided to compare with the Rehabilitation treatment commonly used without carrying out an infiltration with saline solution as a placebo or compared with other infiltrated treatments (glucocorticoids, local anaesthetics), thus being able to be carried out in future lines of research. The results obtained point to a new line of treatment for the approach of these scars and an unknown use of type I collagen. To date, there is no previous evidence of the use of collagen in painful scars, but more studies are required to establish the line of treatment in which the use of collagen can be placed. Double-blind comparative studies with placebo in which physiological saline is infiltrated, and comparative studies with other types of interventions such as infiltrations with substances such as glucocorticoids or local anaesthetics, are required. In addition, specific studies are required to determine the amount of collagen and the number of infiltrations that would be most appropriate for each type of scar, the effect depending on the time of evolution of the scar. Likewise, it is necessary to know the long-term efficacy of collagen infiltrations in the evolution of the appearance of scars in case repetition of these infiltrations is necessary.

Conclusions

Collagen infiltrations could improve PP in painful scars and their appearance in comparison with conventional rehabilitation treatment. Further studies are required to establish its efficacy and cost-effectiveness and its role in the routine treatment of painful scars.

Conflict of interest

The investigators of this study did not receive any type of financial compensation for conducting the study. The Oyasama laboratory provided the MD-Tissue® collagen vials used free of charge.

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