

Multicentre, open label study to evaluate the efficacy and tolerability of a gel (Elastolabo®) for the reduction of the incidence of perineal traumas during labour and related complications in the postpartum period

Summary

The perineal massage is a particular massage technique, widely documented in literature, that allows to prepare the perineal tissues for delivery, increasing elasticity and reducing resistance during distension. The purpose of this multicentre, open-label study, was to evaluate the efficacy and tolerability of Elastolabo® in the reduction of the incidence of perineal traumas during labour and of related complications in the postpartum period. The ingredients of the formulation have a specific elastic, soothing and lubricating action that allows the improvement of elasticity and the extensibility of the perineal skin and muscles in pregnant women, when combined with a perineal massage, potentially reducing the risk of perineal traumas during delivery and of related complications during the postpartum period. The primary end point was the reduction in the percentage of episiotomies/lacerations during labour, following Elastolabo® application. 118 primiparae (aged 18 to 35 years) were enrolled and, of these, 95 were evaluable for the primary endpoint. Elastolabo® was administered at the dosage of 1 application per day, starting from the 32nd week of pregnancy until delivery. Three examinations were scheduled: day 0, after 28 days, and before delivery. Elastolabo® was able to increase significantly ($p < 0.001$) the perineal tissue extensibility and elasticity and was effective in the prevention of episiotomies, decreasing statistically the episiotomies incidence rate in comparison to epidemiological data recorded in the northern and central Italy ($p < 0.01$). Elastolabo® was judged positively by the investigators and the participating women in terms of efficacy, tolerability and acceptability.

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Introduction

Episiotomy is a surgical incision of the vulvar ring, carried on with special rounded off and blunted scissors that is performed in order to facilitate the delivery of the baby and to avoid perineal lacerations. The incision includes three to five external stitches on the skin as well as internal ones for the deeper layers: vaginal mucosa and muscles¹. Over the past 20 years, evidence supporting the restrictive use of episiotomy has been discussed. International acceptance of this approach to perineal management can be seen in policy statements and clinical practice recommendations issued by many prominent public health and professional bodies. The World Health Organization recommends that episiotomy be used only for select indications². Perineal traumas are a frequent complication of delivery³. This is a very serious problem affecting millions of women undergoing a regular vaginal delivery all over the world¹.

During pregnancy, there are changes in the genital anatomophysiology that prepare the structures of the delivery canal. Tissues become gradually softer and more elastic. Perineal muscles, on the other hand, are not as “prepared” as other tissues and tend to sustain most of the damage during delivery. Recently, the acquisition of better knowledge in the anatomical, physiological and pathological areas regarding the pelvic floor, has shown that subclinical damages associated with the delivery, can have debilitating consequences. They, in fact, cause long- and short-term maternal morbidity, lacerations, urinal and faecal incontinence, infections, dyspareunia, persistent perineal pain and have a negative impact on the quality of life, self-esteem and sexuality of new mothers^{4,6}. Up to 50% of women that give birth suffer damage to the pelvic support structures, 10-20% of which need medical treatment for the symptoms^{1,7,8}. Episiotomy is performed on a routine basis in up to 40-80% of deliveries, especially if the women are primiparae, with the aim to reduce lacerations¹. Of those women that have perineal tears about 2/3 have second degree tears and 1/3 first degree tears. Third degree tears have been reported in 3-4% of women^{17,18}. The perineal massage is a particular massage technique, widely documented in literature, that allows to prepare the perineal tissues for delivery, increasing elasticity and reducing resistance during distension. The method, being absolutely natural, has no contraindications or side effects. The massage is performed daily, starting usually from the beginning of the eighth month until the moment of delivery⁹⁻¹³. The Authors concluded that perineal massage during pregnancy, is an effective approach to increase the possibilities of a delivery with the perineum intact, with a protective effect against the number of spontaneous lacerations, particularly in women at their first vaginal delivery. A study published in *Lancet* reports that 80% of women in a group sample, would repeat the perineal massage in future pregnancies and 90% stated that they would suggest it to other pregnant women¹⁴. Elastolabo® is a class IIa medical product, composed mainly of Elastocel® (lysine carboxymethyl cysteinate), paraffin, sweet almond-oil. Due to the elastic, soothing and lubricating characteristics of its constituents, Elastolabo® increases the elasticity of muscles and tissues of the pelvic floor during perineal massage and potentially reduces the risk of perineal traumas during delivery and relating complications during the postpartum period.

In addition to the benefits of sweet almond oil and vitamin E as established in standard massage products Elastolabo® also contains carboxymethylcysteine (Elastocel®) which has an effect on both the extensibility phase and on the phase of elastic return of the tissues.

The technical and safety data on file, have shown that the product, under the anticipated conditions of the intended use, presents no risks to the users. It is characterized, in fact, by a very low oral and cutaneous toxicity and, under regular conditions of use; it should not be hazardous to health. The product has also been known to have a capacity for self-preservation thank to its mainly lipidic composition that does not offer an ideal culture medium for proliferation of microorganisms.

Subjects and Methods

One hundred-eighteen (118) primiparae pregnant women, aged 18 to 35 years, with regular pregnancy, were enrolled after providing written informed consent. The study was an open-label, single-arm, multicentre GCP trial, which was aimed at assessing the efficacy and tolerability of Elastolabo® (a vaginal gel containing Elastocel® (lysine carboxymethyl cysteinate), sweet almond-oil, citric acid, ascorbyl palmitate, tocopherol, lecithin, white soft paraffin, hydrogenated castor oil, vaselin, manufactured by Sinerga s.r.l., via Pitagora 11, 20016 – Pero – Milano – Italia).

The perineal massage is a particular massage technique, widely documented in literature, that allows the perineal tissues to prepare for delivery, increasing elasticity and reducing resistance during distension, resulting in the reduction of the number of episiotomies, during labour in women, at their first pregnancy and with a normal course of pregnancy, compared with epidemiological data coming from Istituto Superiore di Sanità^{15,16}. The main exclusion criteria were: genital and/or fetal abnormalities, presence of vulvovaginal infections and any vaginal medications administered 15 days before the enrolment. The application period lasted from the 32nd week (beginning of the 8th month) of pregnancy to labour, for a total of about 8 weeks.

Assessment of efficacy and safety were performed at baseline (day 0), after day 28 (visit 1) and at delivery (visit 2). A diary was filled in daily by the subjects until the end of the application. The follow-up period duration was 4 weeks.

Before any application, using a special ruler, the subjects had to apply, on a thigh, two stripes of

gel 7 cm (seven) in length that were the equivalent of 4g of gel followed by a perineal massage, performed throughout the trial every day for 10 minutes, moistening the area with the product under study, performing circular movements with the thumb on *labia minora* and on *labia majora* and on the perineal area in order to increase blood circulation and perineal sensitivity. The massage was continued by the patient inserting the thumbs or fingers, 2 to 3 cm into the vagina and stretching the vagina down, gently, towards the anus. Massage continued using a “U-shaped” movement around the inside of the patients vagina stretching the tissue upwards and outwards.

The primary end point was the reduction in the percentage of episiotomies/lacerations during labour, following medical product application compared with epidemiological data recorded in northern and central Italy. Episiotomies and the degree of the vaginal tears were judged according to Royal College of Obstetricians and Gynaecologists (RCOG) (first degree tear: injury to perineal skin only; second degree tear: involvement of the perineal muscles only; third degree tear: injury to the perineum, involving partial or complete disruption of the anal sphincter complex (external [EAS] and internal [IAS]); fourth degree tear: involvement of anal sphincter and rectal mucosa)¹ Secondary efficacy/tolerability criteria were: gynaecological examination, extensibility of perineal

tissues, elasticity of perineal tissues, investigator's judgement of efficacy, investigator's judgement of tolerability, patients' judgement of acceptability and related complications in the postpartum period.

The extensibility of perineal tissues and elastic return of perineal tissues were evaluated by the investigator at baseline, after 28 day and at delivery using a validated Visual Analogue Scale (VAS). The VAS was represented by a notched 10-cm long line. An extremity (0) indicated the complete absence of extensibility of the tissues (or the complete absence of elastic return of the tissues), while the other extremity (10) represented the maximum extensibility of the tissues (or the maximum elastic return of the tissues). The distance measured in millimetres, starting from the extremity that indicated absence (zero) of the clinical parameter, represented the measure of the particular modality to quantify.

The VAS Scale score was tested by the analysis of the variance (ANOVA) for repeated measures. For the other study variables, appropriate parametric and non-parametric tests were used. The statistical significance level was prearranged at 5% ($\alpha=0.05$). All statistical tests were two-tailed.

Results

A total of 118 pregnant women fulfilling the inclusion-exclusion criteria, were included in the trial. The demographic characteristics are summarized in Table 1.

Only one patient presented an abnormality during vulva inspection at baseline, whereas the others gynaecological parameters were normal. Table 2 reports the baseline VAS scoring refer-

Table 1. Baseline demographic characteristics of the intention to treat population (N = 118).

Characteristics	
Age (years)	
N	118
Mean (SD)	30.0 (3.54)
Median	30.8
Min, Max	20.1 - 35.4
Height (cm)	
N	118
Mean (SD)	165.8 (5.84)
Median	166.5
Min, Max	150.0 - 185.0
Weight (Kg)	
N	118
Mean (SD)	69.4 (9.84)
Median	67.0
Min, Max	48.5 - 104.8

Table 2. Baseline VAS Scoring.

Perineal tissue extensibility	
N	118
Mean (SD)	4.9 (1.13)
Median	5.0
Min, Max	2.0 - 8.9
Perineal tissue elasticity	
N	118
Mean (SD)	4.9 (1.09)
Median	5.0
Min, Max	2.0 - 9.0

Table 3. Efficacy analysis: number (%) of episiotomies and vaginal tears.

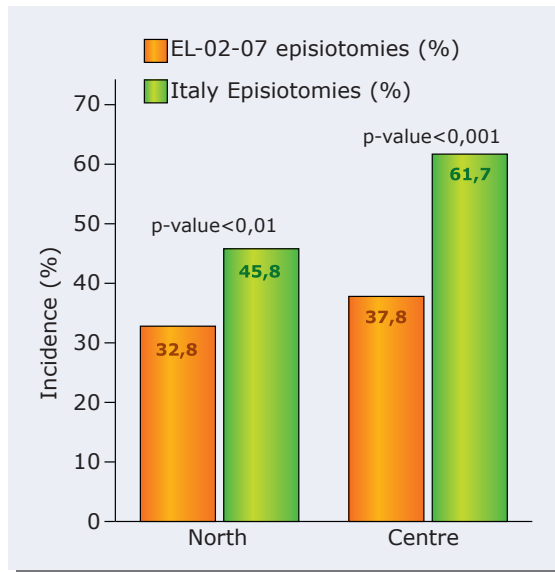
	n	%
Episiotomies	33	34.7
Absence of vaginal tears	14	14.7
Vaginal tears:	48	50.5
I degree	32	33.7
II degree	16	16.8
III degree	0	0.0
IV degree	0	0.0

ring to the extensibility and elasticity of the perineal tissue valued by the investigator.

Table 3 summarizes the data of Elastolabo® gel efficacy. Out of 118 women enrolled in the study, 95 (80.5%) were evaluable for the primary endpoint on ITT population, defined as all women, who performed at least one massage and had a vaginal delivery. The calculation was performed on 95 (80.5%) women since 22 (18.6%) underwent cesarean section and one (0.9%) was withdrawn from the study due to lack of compliance. The table shows the number of episiotomies, vaginal tears, grouped by degree.

The incidence of episiotomies in this study population was compared with statistical data on woman living in northern and central Italy. Both in northern (32.8% vs. 45.8, $p < 0.01$) and central Italy (37.8% vs. 61.8%, $p < 0.001$), the rate of episiotomies in women, using Elastolabo® gel

Figure 1. Incidence of episiotomies in Elasto-Labo gel study population in comparison with women living in northern and central Italy.



before labour was significantly reduced (Figure 1). Of those women that had a perineal tear the majority (66.7%) had a first-degree tear and only 33.3% had a second-degree tear. No woman had third- or fourth-degree tears.

The Perineal Tissues Extensibility and the Perineal Tissues Elasticity improved throughout the massage period with both measures showing statistically significant improvement ($p < 0.001$) from baseline at delivery after 8 weeks of daily application (Figure 2).

Figure 2. Perineal Tissues Extensibility (VAS scale) (A) and Perineal Tissues Elasticity (VAS scale) (B) by study visit (ITT; N=118).

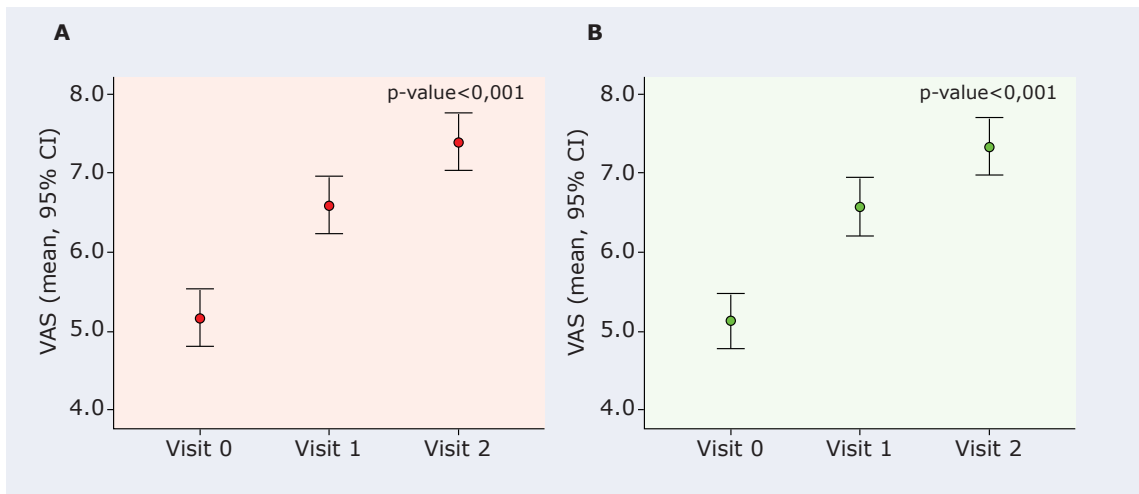
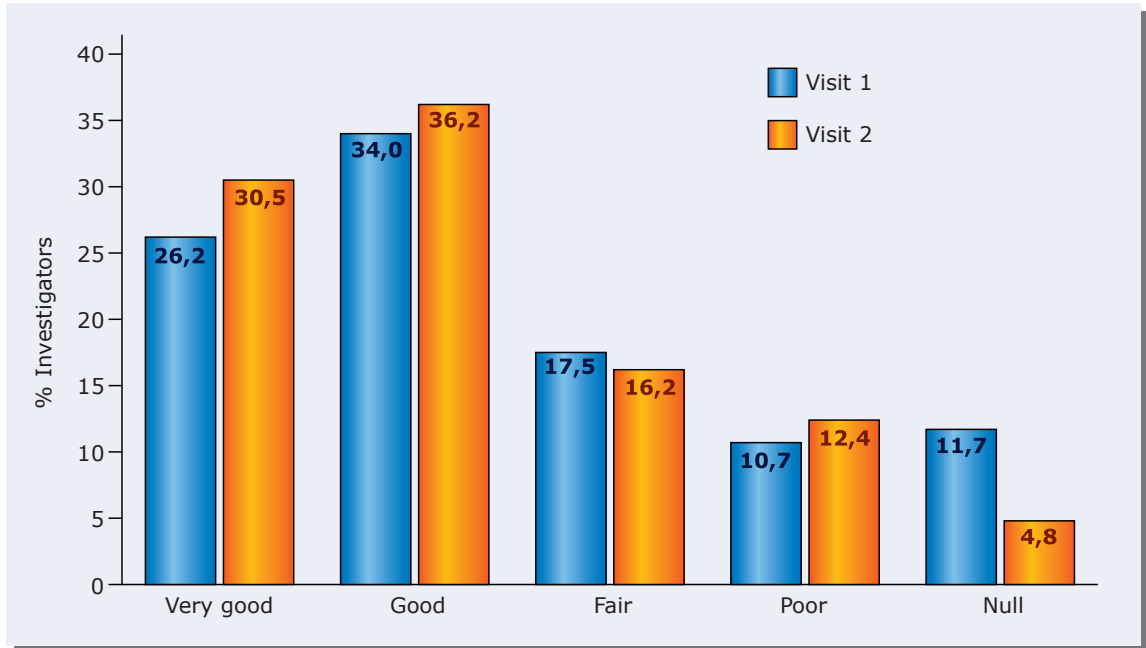


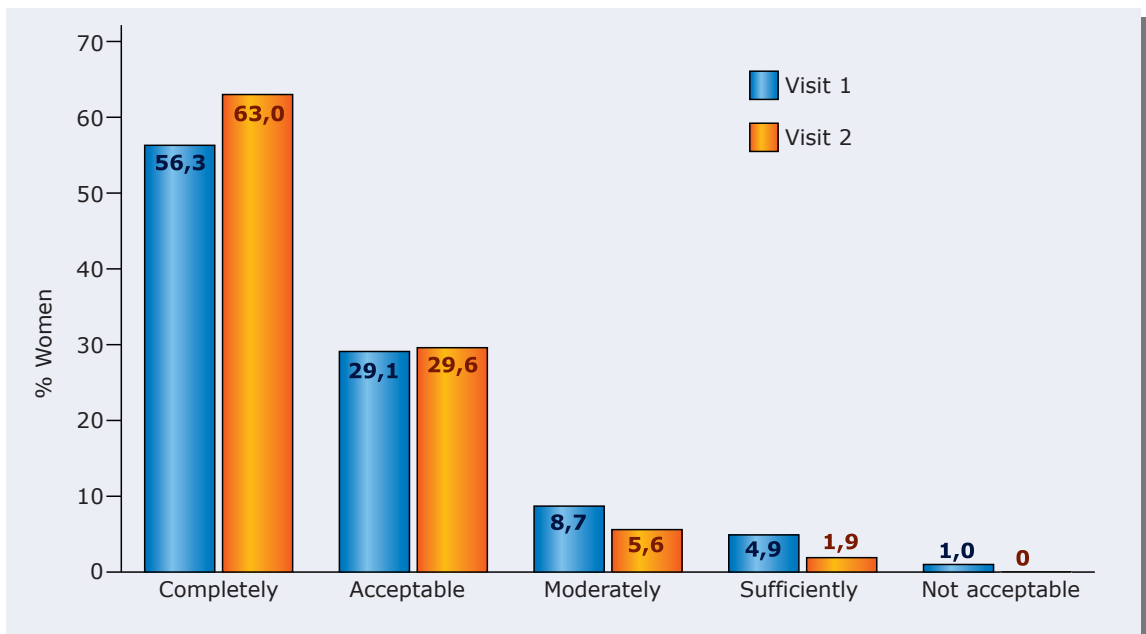
Figure 3. Efficacy according to investigators' judgements (ITT; N=118); Visit 1 vs Visit 2.



Elastolabo® gel was judged positively by the investigators and by patients in terms of efficacy, tolerability and acceptability. According to the investigators' judgements regarding efficacy at Visit 1, the treatment was considered "good" or "very good" in 60.2% of cases. These percentages showed a slight further increase at Visit 2 (66.7%) which did not reach statistical significance (Figure 3).

At visit 1, nearly 50% of patients expressed an opinion of "very good" regarding tolerability, and the remainder, judged the treatment as "good". Finally, the massage with Elastolabo® gel was considered "Completely Acceptable" or "Acceptable" by the patients in 85.4% at visit 1, with a significant increase to 92.6% at delivery ($p < 0.034$ at the Wilcoxon Test) (Figure 4).

Figure 4. Acceptability according to patients' judgements (ITT; N=118); Visit 1 vs Visit 2.



In summary, this study showed that Elastolabo® is a safe, effective and well-tolerated medical product. Statistically significant improvements compared to baseline were seen at delivery for incidence of episiotomy ($p < 0.01$ for Northern Italy, $p < 0.001$ for central Italy), for Perineal Tissues Extensibility ($p < 0.001$) and Perineal Tissues Elasticity ($p < 0.001$).

Only 2 (1.7%) patients reported a probably related Adverse Event to the product under study (irritation and feeling of discomfort, intolerable vulvar itch). One (0.8%) Serious Adverse Event (SAE) considered not related to the product under study, was recorded (haematoma postpartum). The application was interrupted in only 3 (2.5%) patients. 92.6% of patients considered Elastolabo® “Completely Acceptable” or “Acceptable”.

Discussion and Conclusion

Perineal trauma, following vaginal birth, can be associated with significant short-term and long-term morbidity. Although agreement about restricting the use of episiotomy is generally growing, no such consensus has emerged as to what is the optimal mode to reduce the episiotomy rate.

Perineal massage reduces the likelihood of perineal trauma (mainly episiotomies) and the reporting of ongoing perineal pain, and it is generally well accepted by women.

Elastolabo® gel is a class IIa medical product, composed mainly of Elastocell® (lysine carbonylmethyl cysteinate), vitamin E and sweet almond-oil, well-known compounds with elastic, soothing and lubricating properties. The experiment has confirmed that the active ingredients of Elastolabo® gel were able to statistically improve the elasticity and the extensibility of the perineal skin and muscles in pregnant women.

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As direct consequence of the aforementioned data, the results of the present study showed that Elastolabo® gel applied to primipara pregnant women, from the beginning of the eighth month until the moment of delivery, by means of perineal massage, is effective in the prevention of episiotomies, statistically decreasing the episiotomy incidence rate.

Statistically significant improvements compared to baseline were seen at delivery for incidence of episiotomy ($p < 0.01$ for northern Italy, $p < 0.001$ for central Italy), for Perineal Tissues Extensibility ($p < 0.001$) and Perineal Tissues Elasticity ($p < 0.001$). Of those patients that had a perineal tear, the majority (66.7%) had a first-degree tear and only 33.3% had a second-degree tear. This suggests an improvement in contrast with the literature that shows that second-degree tears are the most common tear following standard massage. None of the patients using Elastolabo® had third- or fourth-degree tears.

Moreover, Elastolabo® gel application was well tolerated and well accepted by the patients and by the investigators. In conclusion, the capacity to improve the elasticity and the extensibility of the perineal skin and muscles following Elastolabo® gel application makes a reduction in the episiotomy incidence rate possible and decrease the severity of perineal tears in primipara pregnant women.

We are aware that our study has a few limitations. In fact, a control group was not planned on, also due to the lack of a uniformly accepted reference. The professional who attended the woman in labour was the same one who had monitored her for the entire testing period. Lastly, since not all centres had an archive with historic data on the adoption of episiotomy, it was necessary to compare our data with the national and regional data. We naturally planned on performing a more thorough assessment containing a larger number of parameters in a subsequent future step. **TiM**

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