TITLE:

A STUDY TRIAL ON PROTESCAL IN PREVENTING POST CAESAREAN SECTION HYPERTROPHIC SCAR AND KELOID

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1.0 INTRODUCTION

Every year several million women worldwide acquire an abdominal scar as a result of caesarean delivery. Obstetricians often consider skin closure after a caesarean section as a trivial aspect of the procedure, because the skin scar is deemed the normal and inevitable price we pay foe tissue repair. Moreover, the anatomical location of caesarean scars, which hide easily beneath underwear, and the generally held belief that all transverse suprapubic incision heal about equally well further contribute to the underestimation by practitioners of the importance of scar appearance to patients.

Young women place supreme importance on cosmetic outcomes, but scarring can also affect patient in term of symptoms (pain, tenderness, and itching) and has the potential to have a negative impact overall quality of life, being a source of considerable distress, loss of self esteem and stigmatization.

The final appearance and the function of the healed skin is dependent on patient and wound factors, which are often outside the control of a surgeon, and technical factors, which are completely within the control of the surgeon and include closure material and technique of skin apposition.

There were few study trial done with the aims of preventing hyperthropic scar formation following caesarean section. Antonella Cromi et al (obstet Gynaecol 2010, 203: 36.el-8) did a randomized trial on 123 patient to compare scar quality associated with different types of wound closure method after caesarean section. The result showed that the were no difference in scar quality in either staples or 3 different types of subcurticular sutures.

Atkinson et al (2005 American Society of plastic surgeon) performed a randomized controlled trial involving 70 patient to determine the efficacy of paper tape in preventing hyperthrophic scar formation in surgical incisions that traverse Langer's skin tension lines.
Result suggest that tension acting on a scar is the trigger for hyperthrophic scarring, and paper tape is likely to be an effective modality for prevention of hypertrophic scarring through its ability to eliminate scar tension.

The aims of this study is to prevent hypertrophic scar and keloid formation post caesarean section using PROTESCAL adhesion barrier. PROTESCAL, a combination of hyaluronic acid, methylcellulose, and alginate was manufactured by Korean pharmaceutical companies and became available since 2012. PROTESCAL was developed to prevent complications such as ileus, pain and infertility due to postoperative adhesion.

Hyaluronic acid is a natural polymer of disaccharides, one of the components of the extracellular matrix. It is present in the skin, cartilage, bone and brain. Because of its biocompatibility, moisture capacity, and viscoelasticity, hyaluronic acid has been used as

artificial tears in drug delivery systems, and tissue restoration materials, and it plays a role in inflammation, granulation and re-epithelization for wound healing. It has proved valuable in neurosurgery and dermatology because hyaluronic acid and degradation products can modulate wound healing. There is wide scientific evidence on the positive role of hyaluronic acid in tissue regeneration and wound healing.

Carboxymethylcellulose is a high molecular weight polysaccharide that has a concentration and volume that are inversely correlated with its antiadhesive agent. The combination of carboxymethylcellulose and hyaluronic acid has had a preventive effect on the formation of adhesion in various surgical fields.

Alginate has been used as a wound dressing agent, its calcium or sodium form has hemostatic and antimicrobial effects, and it has been shown to prevent adhesion formation in animal studies.

With the combination of hyluronic acid, methylcellulose and alginate, which already proven scientifically benefit in wound healing, we aims to prevent the hypertrophic scar and keloid formation following caesarean section by applying PROTESCAL in subcutaneous layer prior to skin closure.

2.0 OBJECTIVE OF THE STUDY

2.1 General Objective

To evaluate the effectiveness of Protescal in preventing post caesarean section hypertrophic scar and keloid and pelvic adhesion.

2.2 Specific Objectives

To determine the effectiveness of Protescal in preventing hypertrophic scar and keloid compared to control group.

To determine the effectiveness of Protescal in preventing pelvic adhesion

3.0 OUTCOMES

3.1 Primary

To assess the outcome of healing of the external scar

3.2 Secondary

To look for adhesion formed during next caesarean section

4.0 RESEARCH METHODOLOGY

4.1 Study design

Prospective, randomized controlled clinical trial

4.2 Place of study

Obstetric ward and maternity operation theatre of Department of Obstetrics and Gynaecology, Universiti Kebangsaan Malaysia Medical Centre (UKMMC).

4.3 Study Population

All women undergoing elective caesarean section, without any history of previous abdominal surgery; who planned for further pregnancy and consented to participate in this study.

4.4 Duration of study

6 months duration; from April 2017 to October 2017

4.5 Inclusion Criteria

Pregnant women without any history of previous abdominal surgery

Plan for elective caesarean section for this current pregnancy section

Transverse suprapubic scar

4.6 Exclusion Criteria

Patient who are allergic to protescal

Patient with previous abdominal surgery

Patient with surgery complication

4.7 Randomization

The randomization sequence, either to Protescal group or control group, was generated by using a computer randomization program; in the maternity operation theatre or antenatal clinic .

4.8 Data Collection And Statistical Analysis

SPSS (Statistical Package of Social Science) version 20.0 will be employed proportional data will be compared with chi square. The Fisher exact test will be chosen if the expected size of any cell of the contingency table is less than 5. Continuous data will be compared using the Wilcoxon rank-sum test. Multiple logistic regressions will be use to model the relationship between group assignment, controlling for possible confounders. $P<0.05$ will be considered significant.

4.9 Sample Size Calculation

- The sample size was calculated based on computerized generated formula, Cohen's (1988) formula.
- Effect size calculator for T Test
- For the independent samples T-test, cohen's d id determined by calculating the mean difference between two groups, and then dividing the result by pooled standard deviation

$$\text{cohen's d} = M2 - M1 / SD \text{ pooled}$$

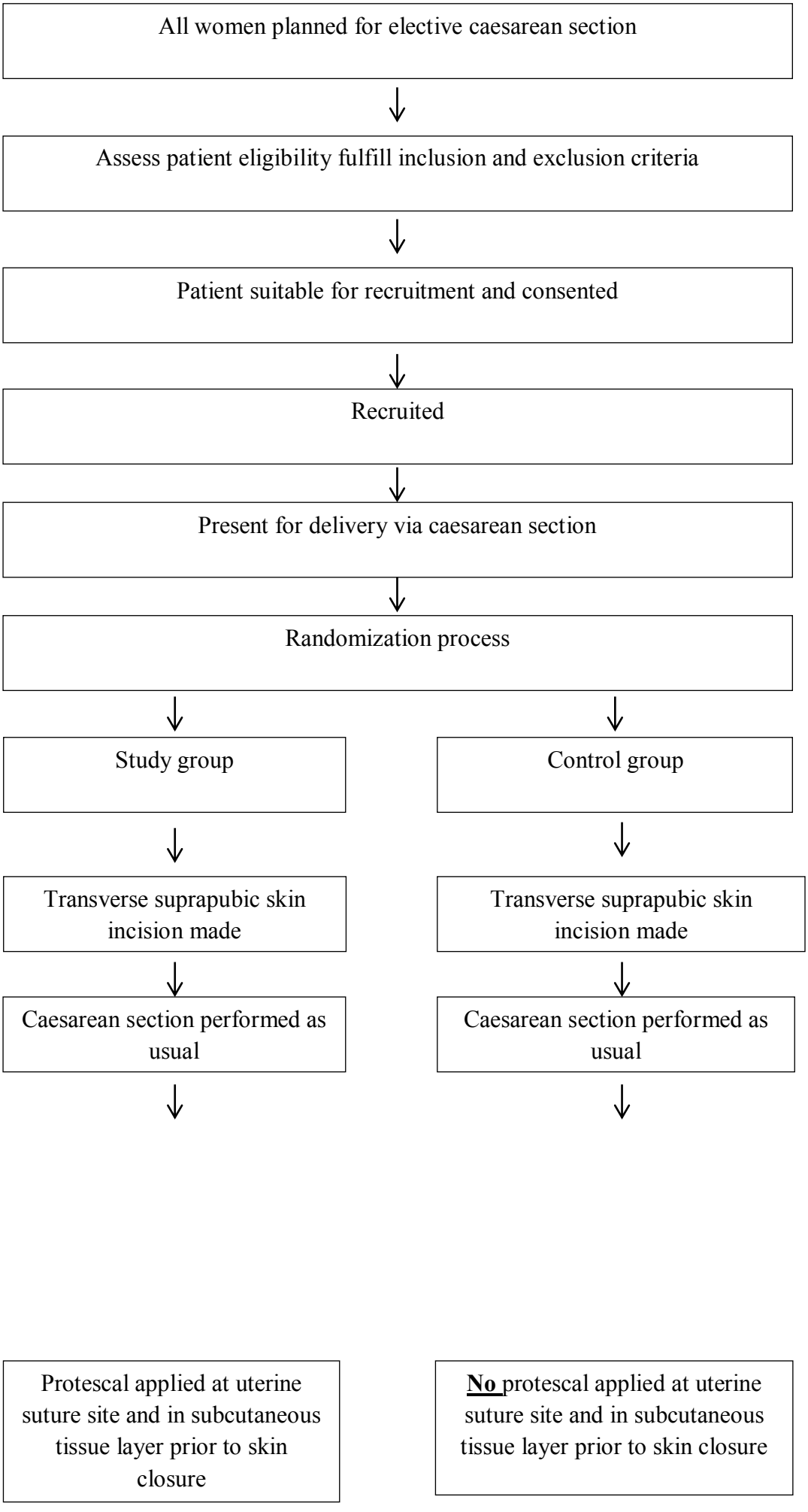
$$SD \text{ pooled} = \sqrt{((SD1^2 + SD2^2) / 2)}$$

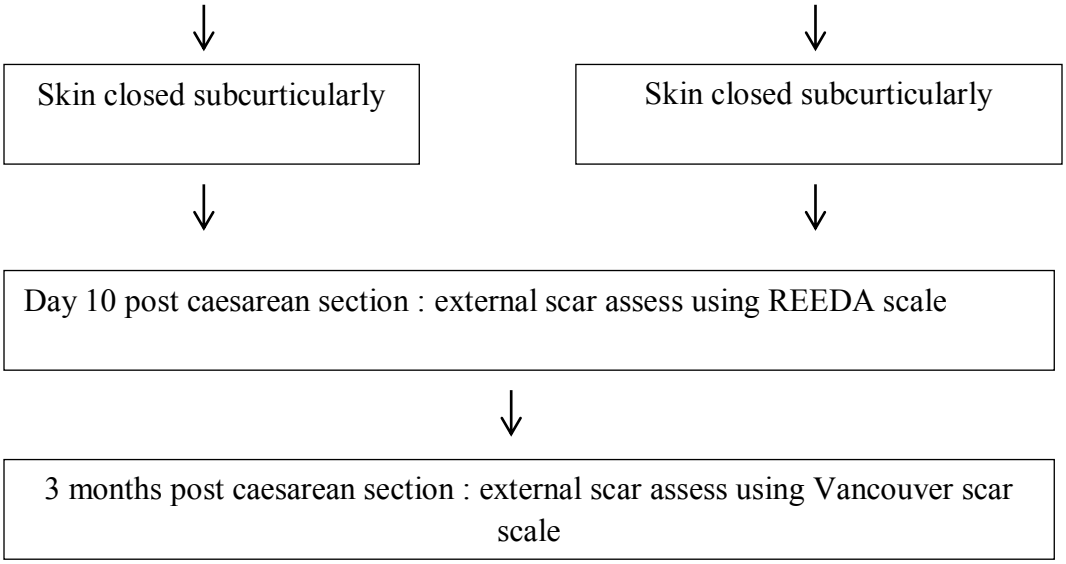
- Using effect size f = 0.60, alpha = 0.05 and power = 0.80, the appropriate number of participants was calculated as 45 in each group.

Cohen's Sample Size Table

D											
Power	**0.10**	**0.20**	**0.30**	**0.40**	**0.50**	**0.60**	**0.70**	**0.80**	**1.0**	**1.20**	**1.40**
0.25	332	84	38	22	14	10	8	6	5	4	3
0.50	769	193	86	49	32	22	17	13	9	7	5
0.60	981	246	110	62	40	28	21	16	11	8	6
2/3	1144	287	128	73	47	33	24	19	12	9	7
0.70	1235	310	138	78	50	35	26	20	13	10	7
0.75	1389	348	155	88	57	40	29	23	15	11	8
0.80	1571	393	175	99	64	**45**	33	26	17	12	9
0.85	1797	450	201	113	73	51	38	29	19	14	10
0.90	2102	526	234	132	85	59	44	34	22	16	12
0.95	2600	651	290	163	105	73	54	42	37	19	14
0.99	3675	920	409	231	148	103	76	58	38	27	20

4.10 Study Flow Chart


All women planned for elective caesarean section
Assess patient eligibility fulfill inclusion and exclusion criteria
Patient suitable for recruitment and consented
Recruited
Present for delivery via caesarean section
Randomization process
Study group
Control group
Transverse suprapubic skin incision made
Transverse suprapubic skin incision made
Caesarean section performed as usual
Caesarean section performed as usual
Protescal applied at uterine suture site and in subcutaneous tissue layer prior to skin closure
No protescal applied at uterine suture site and in subcutaneous tissue layer prior to skin closure



4.11 Study Protocol

After delivering the baby through caesarean section, uterine muscle is closed in 2 layers with braided absorbable suture, polyglactin 910 (vicryl no 1).

After haemostasis secure, 4 ml Protescal gel apply at the uterine suture site.

Peritoneal layer close using braided absorbable suture, polyglactin 910 (vicryl no 1).

Rectus sheath suture using braided absorbable suture, polyglactin 910 (vicryl no 1).

Subcutaneous tissue close interruptedly using braided absorbable suture, polyglactin 910 (vicryl no 1).

1 ml Protescal gel apply in subcutaneous tissue prior to skin closure.

Skin close with subcuticular method using braided absorbable suture, polyglactin 910 (vicryl 3-0).

Wound healing assess on 10th day post caesarean section using REEDA scale, which had criteria including redness, edema, ecchymosis, discharge and approximation.

On 3rd month, the degree of scarring assess using the Vancouver scar scale including pigmentation, height, pliability and vascularity.

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