



Intramyometrium Autologous Platelet-Rich Plasma Injection after Primary caesarean Section for Promotion of caesarean Scar Healing: A Double Blind RCT

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
BMI.....	Body mass index
BFGF.....	Basic fibroblast growth factor
CAESAR.....	Caesarean section surgical techniques: a randomised factorial trial
CI.....	Confidence interval
CS.....	Caesarean section
CSD.....	Caesarean scar Defect
CSs.....	Caesarean sections
CTG.....	Cardiotocography
CVD.....	Cardiovascular disease
DEPA.....	Dose of the injected platelets, efficiency of production, purity of the PRP and activation of the PRP
EFM.....	Electronic fetal monitoring
GDM.....	Gestational diabetes mellitus
GIS.....	Gel instillation sonohysterography
HIV.....	Human immunodeficiency virus
HSG.....	Hysterosalpingography
IVF.....	In vitro fertilization
LGA.....	Large for gestational age
MSC.....	Mesenchymal stem cells
NICE.....	National Institute for Health and Care Excellence
PDGF.....	Platelet-derived growth factor
PRP.....	Platelet rich plasma
RCOG.....	Royal College of Obstetricians and Gynaecologists
RCT.....	Randomized clinical trial
RR.....	Relative risk
SCSH.....	Saline contrast sonohysterography

List of Abbreviations Cont...

Abb.	Full term
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TOLAC	Trial of labour after caesarean
TVS	Transvaginal sonography
US	Ultrasonography
UTI	Urinary tract infection
VEGF	Vascular endothelial growth factor
VTE.....	Venous Thromboembolism
WBCS	White blood cells
WHO	World health organization

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INTRODUCTION

Caesarean scar defect (CSD) is associated with increased risk of uterine rupture, abnormal placental implantation, uterine scar dehiscence in subsequent pregnancies and scar ectopic pregnancy, also CSD are reported to be associated with abnormal uterine bleeding and post menstrual spotting (*Uppal et al., 2011*).

Uterine wound healing is of great importance to achieve healthy future pregnancy and to allow for vaginal birth after caesarean section (CS), hence minimizing the rate of repeated caesarean sections (*Miller et al., 1997*).

Platelet rich plasma (PRP) is an autologous product derived from whole blood through the process of gradient density centrifugation. Autologous PRP has been shown to be safe and effective in promoting the natural processes of wound healing, soft tissue reconstruction, muscle healing, bone reconstruction and augmentation (*Smith et al., 2007*).

Recently, PRP has been used to promote endometrial growth and improve pregnancy outcome during in vitro fertilization (*Chang et al., 2015*).

PRP functions as a fibrin tissue adhesive with haemostatic and tissue sealing properties, its platelets provide a unique ability to promote wound healing through growth

factors. PRP accelerates endothelial, epithelial and epidermal regeneration, stimulates angiogenesis, promotes soft tissue healing and reverses the inhibition of wound healing caused by glucocorticoids. The high leukocyte concentration of PRP has an added antimicrobial effect. Since PRP is an autologous blood product, it carries no risk of transmitting infectious diseases (**Smith et al., 2007**).

While ultrasonography (US) is of great value in scar assessment in pregnant uterus (**Cheung, 2005**), its role in scar assessment in non-pregnant uterus is limited. Saline contrast sonohysterography (SCSH) is the method of choice for assessing the scar in non-pregnant uterus; in which the US of the uterus is enhanced by instillation of fluid into the uterine cavity to provide an anechoic contrast medium. Thus, SCSH combines the advantages of both US and hysterosalpingography (**Elsayes et al., 2009**).

The evolution of SCSH has contributed significantly in the assessment of the uterine cavity (**De Kroon et al., 2003**); it can be performed 6-12 weeks after caesarean section using gel or saline instillation (**Van Der Voet et al., 2014a**), to evaluate the thickness of the residual myometrium, thickness of myometrium bordering the scar, depth of the filling defect in the scar (niche) and scar related intrauterine adhesions (**Regnard et al., 2004**).

Sonohysterography has an overall accuracy of 96% in the diagnosis of CSD; and 91% in the diagnosis of intrauterine adhesions. In addition, the procedure of SCSH is well-tolerated, cost effective, not time-consuming, and can be performed as an office based gynaecological practice (*Fabres et al., 2003*).

The current study investigated the effect of platelet rich plasma on the healing of caesarean section scar evaluated by sonohysterography.

AIM OF THE STUDY

The aim of this study was to assess the efficacy of intramyometrial injection of PRP on uterine wound healing in women undergoing primary caesarean section.

Research question

In patients undergoing elective caesarean section for the first time; will intramyometrial injection of platelet rich plasma be more effective than placebo in improving uterine scar healing.

Research hypothesis

- ✓ **Alternative hypothesis:** intramyometrial injection of PRP is more effective than placebo on uterine scar healing after primary caesarean section.
- ✓ **Null hypothesis:** In women undergoing 1ry CS intramyometrial injection of PRP will have no effect on uterine wound healing

Chapter 1

CAESAREAN SECTION

The caesarean delivery is defined as the birth of a fetus through incisions in the abdominal wall (Laparotomy) and the uterine wall (Hysterotomy) (*Sholapurkar et al., 2018*).

The terms caesarean section, caesarean delivery, and caesarean birth may be used to describe the delivery of a fetus through a surgical incision of the anterior uterine wall. Caesarean section is a tautology; both words connote incision. Therefore, caesarean birth or caesarean delivery, are preferable terms (*Kapustian et al., 2019*).

Incidence:

According to the data from 150 countries, the average global rate of CS is 18.6%, ranging from 6.0% to 27.2% in the least and more developed regions, respectively. The lowest rates of CS are found in Africa (7.3%) and more specifically in Western Africa (3%). The highest rates of CS are found in Latin American and the Caribbean (40.5%) and South America is the sub region with the highest average CS rates in the world (42.9%) (*Betrán et al., 2016*).