

Transabdominal Cervico-Isthmic Ultrasound Guided Injection of Peripheral Blood Mononuclear Cells in Cervical Insufficiency Abortion

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Abstract:**introduction:**Treatment of cervical insufficiency abortion is by Cerclage which either done vaginally (Schirodkar, McDonald) or abdominally and laparoscopically. In cases where the cervix is not accessible or when there is marked scarring, shortening or deformation of the cervix, precluding vaginal placement, transabdominal Cerclage (TAC) may be employed which means two times opening of the abdomen first time to do the Cerclage and second time to do caesarean section and this will cause extra economic burden specially in low resources , so a need for a new procedure is mandatory hence we introduced Transabdominal Cervico-Isthmic Ultrasound Guided Injection of Peripheral Blood Mononuclear Cells in Cervical Insufficiency Abortion. **Material and Methods:**Eight cases were enrolled in the study, all these cases were recruited to abdominal Cerclage. Mean age was 38.2 ± 1.2 years, mean number of abortion 10.2 ± 3.1 times. Mean gestational age 10.9 ± 0.6 weeks. Preparation of autologous peripheral blood mononuclear cells (PBMC): Blood samples were obtained from individual patients and PBMCs (1x10⁷ cells) were isolated by Ficoll-hypaque Centrifugation.**Results:**Seven cases continued to full term pregnancy (success rate 87.5%) and one case abortion (failure rate 12.5%), two cases out of the seven delivered vaginally and the rest by caesarean section. Statically significant increase in CD34 antibodies after the operation $P < 0.0001$.**Conclusion:** Transabdominal cervico-isthmic ultrasound guided injection of peripheral blood mononuclear cells is a new modality of treatment of cervical insufficiency abortion.

Keywords:Cervical insufficiency abortion, abdominal Cerclage, vaginal Cerclage, laparoscopic Cerclage, peripheral blood mononuclear cells

1 INTRODUCTION

The first recognition of cervical incompetence was reported in the literature in 1658 [1]. Treatment of cervical insufficiency abortion is by Cerclage which either done vaginally (Schirodkar [2], McDonald [3] or abdominally [4] and laparoscopically [5]. In cases where the cervix is not accessible or when there is marked scarring, shortening or deformation of the cervix, precluding vaginal placement, transabdominal Cerclage (TAC) may be employed. Nowadays there is a need to withdraw this operation because in this operation the abdomen is opened twice; first to do the Cerclage procedure and second to do caesarean section which is the method of delivery here after transabdominal Cerclage by elective caesarean section.

The catastrophic point here will be when the failure occur which result in two laparotomies with zero results, again the cost of two laparotomies specially in low resources

added to the negativity of this operation, another point this

learning curve, added to the contraindications for trans-abdominal Cerclage which are bulging membranes, ruptured membranes, intrauterine infections, vaginal blood loss, intrauterine foetal death, labour, and life-threatening maternal condition.

So the need for a new procedure is mandatory, the aim of this work is to introduce a new technique for treatment of cervical insufficiency abortion by ultrasound guided Transabdominal cervico-isthmic injection of human peripheral blood mononuclear cells (PBMC).

2 PATIENT AND METHODS

Eight cases were enrolled in the study, all these cases were recruited to abdominal Cerclage, four of them with absent vaginal cervix, one has very short vaginal cervix, and three with multiple high cervical tear. Mean age was 38.2 ± 1.2 years, mean number of abortion 10.2 ± 3.1 times. Mean gestational age 10.9 ± 0.6 weeks.

Preparation of autologous peripheral blood mononuclear cells (PBMC): Blood samples were obtained from individual patients and PBMCs (1x10⁷ cells) were isolated by Ficoll-hypaque Centrifugation [6]. The harvested MNC were evaluated for:

- Viability: Trypan blue dye exclusion test was done to know the percentage of live cells.
- Cell morphology: MNC were stained with Giemsa stain and observed under microscope.
- CD34+ counts: MNC were tagged with CD34 antibodies and assessed by flow cytometry to evaluate the

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operation needs an experienced surgeon with a good

hematopoietic stem cells.

- Total cell count: Cell numbers were assessed by counting the cell in the Neubauer chamber under microscope.

The procedure was conducted under intravenous sedation, combined abdominal and vaginal ultrasound was done to localize the area to be injected in isthmic region, depending upon the duration of pregnancy mean procedure time was 20 ± 8.2 minutes. The follow up will be carried out two weeks interval.

CD34 antibodies was done before and after the procedure.

3 ETHICS:

Informed Consent and explaining all the details of the procedure to the patients, and all procedures involving human subjects complied with the declaration of Helsinki 1975 and revised in 2000, again all the procedures accepted from the ethical committee of Heliopolis research center and Heliopolis Hospital.

4 RESULTS

Ultrasound Follow up two weeks interval revealed continuation of pregnancy to full term (37 weeks) for seven cases (success rate 87.5%) and one case abortion. Regarding the method of delivery two cases delivered vaginally and the rest of the cases by caesarean section. Mean birth weight 3.700 ± 0.1 kg, mean Apgar score 1 and 5 minutes 8.7 ± 0.1 and 9.4 ± 0.2 respectively. The result of CD34 antibodies was demonstrated in table (1)

TABLE (1): SERUM CD34 ANTIBODIES BEFORE AND AFTER TRANSABDOMINAL CERVICO-ISTHMIC ULTRASOUND GUIDED INJECTION OF PERIPHERAL BLOOD MONONUCLEAR CELLS

Serum level	Before the operation	After the operation	P value
CD34 antibodies	4 ± 0.3	111.2 ± 5.3	< 0.0001

Statistically significant increase in CD34 antibodies after the operation $P < 0.0001$

5 DISCUSSION

The incidence of cervical insufficiency in the general obstetric population is reported to vary from 1:100 to 1:2,000 [7, 8]. Cervical surgery to prevent recurrent pregnancy loss was introduced in 1902 by Herman [9], Cervical Cerclage was first proposed by Shirodkar in 1955 [2], in 1957 it was considerably simplified by McDonald [3],

in those who conventional Cerclage by the vaginal route is not accessible, a transabdominal procedure can be attempted. Transabdominal cervical Cerclage (TAC) was first described in 1965 [4] this procedure has also been reported laparoscopically [5]. We introduced for the first time in literature a new treatment of cervical insufficiency abortion by transabdominal cervico-isthmus ultrasound guided injection of peripheral blood mononuclear cells (PBMC), As mononuclear cells is a potential regulator of cell proliferation [10, 11], stimulate progesterone by luteal cells [12], promote embryo invasion [13], stimulate Adenosine triphosphate [14], improving mitochondrial respiration [15], express HCG receptors, strong anti-microbial [16], and anti-oxidant effect. Hence comes its application in cervical injection.

We demonstrated in our previous work the biochemical basis of human peripheral mononuclear cells (PBMC) in treatment of cervical insufficiency which based upon statistically significant decrease of IL8, collagenase, AQP3, AQP4 and AQP5 in addition to it's a rich source of early pregnancy factor which has an immunosuppressive and growth factor properties [17].

We put a new theory to explain the therapeutic effect of our new procedure that there's ample evidence that cervix contains adult stem cells population and hence it might be possible to activate endogenous cervical stem cells / progenitor cells. We demonstrate that incorporate to the cervix mononuclear cells that resulting in increasing collagen and increasing in the fibromuscular activity of the cervix.

The implanted peripheral blood mononuclear cells (PBMC) may trans- differentiate into resident stem cells of the cervix and this will correct the cervix. In supporting this we found CD34 increased in the peripheral blood, this is a marker of angiogenesis and proliferation so the implanted peripheral blood mononuclear cells (PBMC) promote angiogenesis, tissue repair and modulate inflammatory and immune reaction.

Again it activates specific progenitor cells, in comparison of our results to previous other trans-abdominal approach we found that our procedure is easy, no anesthesia, no opening of the abdomen, in addition a possibility of vaginal delivery in contrast to the trans-abdominal approach. In addition our technique has positive fetal impact which is not present in the other abdominal approach.

In comparison of our technique to laparoscopic Trans-abdominal Cerclage the previous points were applied to this situation but laparoscopic trans-abdominal Cerclage need highly experienced laparoscopist we reported a case of abortion on table due to creation of pneumoperitoneum which caused increased pressure over the uterus, again we encountered abortion on table in trans-abdominal Cerclage

due to injury of the amniotic sac during placement of the sutures.

So, we find that our new technique is safe, effective, and cheap with positive fetal impact and no fetomaternal complications, plus the possibility of vaginal delivery unless there is other obstetric contraindication.

6 CONCLUSION

Transabdominal cervico-isthmic ultrasound guided injection of peripheral blood mononuclear cells is a new modality of treatment of cervical insufficiency abortion this technique is safe, effective, and cheap with positive fetal impact and no fetomaternal complications, with chance of vaginal delivery and more easy learning curve but more cases and randomization are needed before elucidation the effectiveness of the procedure.

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