

REGENERATION OF ENDOMETRIUM AFTER TERMINATION OF PREGNANCY WITH INTRA-AMNIOTIC HYPERTONIC SALINE INFUSION

by

R. C. MISRA,* M.D.

U. K. NANDA,** M.S.

and

S. PATNAIK***

Introduction

Interruption of pregnancy with intra-amniotic injection of hypertonic salt solution is an accepted method of termination of pregnancy in midtrimester. Although this is a widely practised method, the sequence of events regarding endometrial regeneration have not found appropriate place in the available literature, unlike after, vacuum aspiration (Andrew, 1968) and normal delivery (Willams, 1931).

In the present study, attempts have been made to study the sequential changes of endometrial regeneration through repeated biopsies after termination of pregnancy in the midtrimester by intra-amniotic injection of hypertonic salt solution.

*Prof. and Head of the Department of Pathology.

**Prof. and Head of the Department of Obstetrics and Gynaecology.

*** Medical Officer, Sunabeda, Dist. Koraput, Orissa.

Department of Pathology and Department of Obstetrics & Gynaecology V.S.S. Medical College, Burla, Sambalpur (Orissa).

Address for correspondence:—

Dr. R. C. Misra, M.D.

Prof. & H.O.D. of Pathology,

V.S.S. Medical College, Burla-768017.

Accepted for publication on 12-12-79.

Material and Methods

The study was conducted in the departments of Pathology and Obstetrics and Gynaecology, VSS Medical College, Burla during the years from 1976-1978.

The material in the present work constitutes of 30 women who underwent medical termination of pregnancy (MTP) during the gestation periods between 14th to 20th week by intra-amniotic hypertonic saline injection (IAHSI) and 10 women undergoing normal delivery served as control.

Clinical findings and results of routine laboratory findings were noted in all the cases. Pregnancies were terminated in all patients by IAHSI. Endometrial biopsies were taken repeatedly during post-abortal periods (PAP) between first to fifth days in 30 cases, 6th to 10th days in 24 cases, 11th to 15th days in 24 cases, 16th to 20th days in 18 cases, 21st to 25th days in 12 cases and 26th to 30th days in 12 cases. Slides were prepared by usual histological techniques and were examined for the presence of necrotic tissue, surface epithelialisation endometrial stroma and glands, products of conception and inflammatory cells.

Observations

The 10 cases of the control group were between the age group of 15 to 30 years. Three patients were primigravidae and rest were from 2nd to 5th gravidae.

In the study group all the 30 patients were distributed between 15 to 40 years of age except a slight increase (30%) between 26th to 30 years. Seven women presented for MTP during their first pregnancy.

The period of gestation was, 9 between 15th to 16th weeks, 6 between 17th to 18th week and 15 between 19th to 20th week.

Table I illustrates the sequential regenerative changes of the endometrial tissue taken at intervals from 10 women after normal delivery.

In the study group of 30 women, sequential changes of endometrial tissue were observed as following (Table II).

(a) Surface epithelium of endometrium was not detected till the 5th post-abort day in any of the 30 cases. Subsequent specimens relating to the period between 6th and 10th post-abort days, 75% of the cases showed areas of epithelialisation; localised areas in 50% and multifocal in 25%. In all cases the surface epithelial cells were of low cuboidal type. From 11th day onwards surface epithelialisation was observed in all cases and the epithelial cells assumed tall columnar pattern.

(b) Endometrial glands first appeared during the post-abort period, between 6th and 10th day, lined by low cuboidal epithelium. From 11th to 15th day period and onwards endometrial glands were found in all specimens. Glands with tall columnar epithelium were first detected between 11th to 15th day period in 25% of cases and thereafter its number gradu-

TABLE I
Histological Findings in Endometrial Curettings After Normal Delivery (Control Group)

| Days | 1-5 | 6-10 | 11-15 | 16-20 | 21-25 | 26-30 |
|---|---------|---------|---------|--------|---------|--------|
| No. of cases studied | 10 | 6 | 8 | 5 | 7 | 5 |
| Decidua | 9(90) | 3(50) | 0 | 0 | 0 | 0 |
| Villi | 6(60) | 0 | 0 | 0 | 0 | 0 |
| Necrotic tissue | 8(80) | 1(16.7) | 1(12.5) | 1(20) | 1(14.3) | 0 |
| Haemorrhage | 10(100) | 6(100) | 8(100) | 4(80) | 5(71.4) | 3(60) |
| Localized surface epithelization | 0 | 2(33.3) | 6(75) | 2(40) | 2(28.6) | 1(20) |
| Multifocal area of surface epithelization | 0 | 3(50) | 2(25) | 3(60) | 5(71.4) | 4(80) |
| Total No. of glands | 0 | 6(100) | 8(100) | 5(100) | 7(100) | 5(100) |
| Low cuboidal | 0 | 6(100) | 8(100) | 5(100) | 5(71.4) | 4(80) |
| Tall columnar | 0 | 0 | 0 | 0 | 2(28.6) | 1(20) |
| Acute inflammatory cell | 10(100) | 4(66.7) | 4(50) | 1(20) | 0 | 0 |
| Chronic inflammatory cell | 0 | 2(33.3) | 4(50) | 2(40) | 3(42.8) | 2(40) |
| Dense stroma | 0 | 4(66.7) | 6(75) | 2(40) | 0 | 0 |
| Loose stroma | 0 | 0 | 2(25) | 3(60) | 7(100) | 5(100) |
| Proliferative phase | 0 | 6(100) | 8(100) | 5(100) | 5(71.4) | 4(80) |
| Secretory phase | 0 | 0 | 0 | 0 | 2(14.3) | 1(20) |

(Figures in parenthesis indicated percentage).

TABLE II

Histological Findings from Serial Endometrial Curettings After Termination of Pregnancy with LAHSI (Study Group)

| Days | No. of cases studied | Localised area of epithelization | Multifocal area of epithelization | Proliferative phase | Early secretory phase | Late secretory phase |
|------|----------------------|----------------------------------|-----------------------------------|---------------------|-----------------------|----------------------|
| 1 | 16 | 0 | 0 | 0 | 0 | 0 |
| 2 | 3 | 0 | 0 | 0 | 0 | 0 |
| 3 | 5 | 0 | 0 | 0 | 0 | 0 |
| 4 | 3 | 0 | 0 | 0 | 0 | 0 |
| 5 | 3 | 0 | 0 | 0 | 0 | 0 |
| 6 | 6 | 3 | 0 | 3 | 0 | 0 |
| 7 | 9 | 3 | 3 | 6 | 0 | 0 |
| 8 | 5 | 3 | 2 | 5 | 0 | 0 |
| 10 | 4 | 3 | 1 | 4 | 0 | 0 |
| 11 | 14 | 5 | 9 | 14 | 0 | 0 |
| 15 | 10 | 3 | 7 | 4 | 6 | 0 |
| 16 | 5 | 1 | 4 | 4 | 1 | 0 |
| 17 | 6 | 1 | 5 | 3 | 3 | 0 |
| 18 | 7 | 1 | 6 | 2 | 3 | 2 |
| 21 | 4 | 2 | 2 | 2 | 1 | 1 |
| 22 | 4 | 1 | 3 | 1 | 2 | 1* |
| 23 | 4 | 1 | 3 | 0 | 2 | 2 |
| 26 | 6 | 2 | 4 | 1 | 3 | 2 |
| 30 | 6 | 1 | 5 | 0 | 4 | 2 |

* Arias stella reaction.

ally increased. Evidence of early secretory phase was detected between 11th to 15th day in 25% and late secretory activity was seen between 16th to 20th day in 11.1%. Subsequently late secretory phase was seen in 33.3% cases during the period between 21st to 25th days and 26th to 30th days. The rest of the specimens showed proliferative activity only.

Arias-Stella reaction was seen in only 1 case on 22nd day.

(c) Stromal tissue was first observed between 6th and 10th day and thereafter appeared loose from 11th or 15th day period onwards.

(d) Infiltration by polymorphonuclear neutrophils (PNM) was observed in 100% cases between days 1 to 5, 62.5% between days 6 to 10, 25% between days 11 to 15, 11.1% between 16th to 20 and

8.3% between 21 to 25. Moderate infiltration by round cells were seen throughout the study period. Towards later half of the study period mild eosinophilic infiltration was seen in occasional cases.

(e) Involutionary changes.

Placental villi were found in 66%, 12.5% and 8.3% of patients between 1 to 5, 6 to 10 and 11 to 15 days period respectively. Decidual cells were detected till 11th to 15th day period. Necrotic tissue were found till the period between 16th to 20th day. Uterus assumed normal length, e.g. 7.5 cm from 16th to 20 days period onwards in all cases.

Discussion

The findings regarding the regeneration of endometrium after normal delivery in

the control group is in agreement with the report published by William (1931). Regarding the regeneration of endometrium at the site of placental attachment is beyond the scope of the present work as hysterectomy specimens have not been examined.

Age matched control cases have been studied although their number was small. Another difference noted is that, in the control group the parity of the subjects was slightly higher than the study group.

The surface epithelialisation appeared in both groups during the same time i.e. between 6th to 10th days of PAP. But in the IAHSI group more number of patients revealed such epithelialization than the control cases.

Endometrial glands appeared during the same period in both the groups. But secretory phase was found quicker in the study group.

Neutrophilic infiltration disappeared more quickly in the control cases. Since bacteriological investigations have not been conducted it is difficult to exclude concomittant mild infestive process. None of the patients were febrile.

Regeneration of endometrial stroma was found during the same period in both groups of cases. Arias-Stella reaction was found only in one case on 22nd day. Such reactions indicate association of intra and extra uterine pregnancies or presence of chorionic tissue in the body (Novak, 1974).

In the study group, products of conception were not found in the curetted material in any of the patients beyond 20 days during PAP. Although products of conception were not found in the endometrial curetting of the patient showing Arias-Stella reaction, it cannot be assumed that uterine cavity was free of such products without careful examination of hysterec-

tomy specimens. Therefore it is concluded that in some patients products of conception persist for more than 20 days after MTP with IASHI.

Placental villi and decidual cells were present for longer time in the study group than the control group.

Therefore from the present study it would be justified to conclude that in IAHSA group, the endometrial regeneration is quicker than after normal delivery although complete expulsion of products of conception takes longer time. It is assumed that this difference is probably due to size of uterus which attains much bigger dimension at the time of normal delivery and therefore complete expulsion of product of conception becomes an easier process.

The present study also indicates that the regenerative process of endometrium after IAHSI is almost similar to the regenerative activity of the tissue seen after endometrial curattage (Rutherford and Mezer, 1942), termination of pregnancy with vaccum aspiration (Andrew, 1968) and spontaneous abortion (Sharman, 1966).

Summary

Serial endometrial biopsy specimens were examined from 30 women after termination of midtrimester pregnancy with intra-aminotic hypertonic saline infusion. Ten age matched women after normal delivery served as control.

Histological examination of curetted material revealed that MTP after IAHSI does not interfere with regeneration of endometrium, ovulation and uterine involution and instead the process is rather accelerated when compared with the regenerating activity of endometrium after full term normal delivery.

Acknowledgements

The authors are indebted to the staff members of Obstetrics and Gynaecology department and Pathology Department for their co-operation and skillful assistance while carrying out this work. Our special thanks are to Prof. P. K. Kar, M.D., Principal, VSS Medical College, Burla for his constant encouragement and permission to publish this article.

References

1. Andreev, D.: Folia Medical, 11 :221, 1969.
2. Williams, J. W.: Am. J. Obst. & Gynaec. 22: 664, 1931.
3. Ruther Ford, R. N. and Mezer, J.: J. Am. Med. Assoc. 119: 124, 1942.
4. Novak, E. R. and Woodruff, J. D.: Novak's Gynaecologic and Obstetric Pathology, 7th Ed. p. 1195, Saunders Co., Philadelphia, 1974.
5. Sharman, A. 1966: Reproductive physiology of post partum period, Livinstone Edinburgh.