Does type of intervention affects the endoscopic procedure outcome in female infertile patients? an experience at a single tertiary care centre

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Received: 01 November 2018
Accepted: 28 November 2018

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Introduction
Infertility is a medical condition that affects the couple, family, society rather than a single individual.1 The causes of infertility may be subdivided into isolated male factors (26-40%), ovulation dysfunction (21-25%), tubal factors (14-20) and others like cervical, peritoneal and uterine factors (10-13%), While 25-28% remain unexplained.2 One of the classifications for causes of infertility is anatomical and functional. The common anatomical causes of female infertility are ovarian cyst/ tumor, tubal damage, endometriosis, and uterine anomalies [congenital (septate uterus) /acquired (myomas and synechiae)] etc. In a single female, more than one anatomical cause may be coexisted and responsible for infertility.3

This is a known fact; that in the anatomical causes of the infertility, surgical intervention is important to improve the fertility outcome. Hysterolaparoscopy is a relatively well-established invasive modality to identify and
simultaneously for resolving the abdominopelvic anatomical pathologies. In our judgment we have a simple presumption that the infertile patients having more in number and type of the pelvic pathologies, will likely to get less success after endoscopic intervention than patients with single pathology, So, aim of present study was to compare single and multiple types of the hysterolaparoscopic interventions performed in the infertile female patients in terms of achieving pregnancy for 12 months or till achievement of fetal cardiac activity whichever is earlier.

**METHODS**

The present study was prospective interventional study and carried out between March 2016 to December 2017 at the Department of Obstetrics and Gynaecology at Santokba Durlabhji Memorial Hospital, Jaipur (Tertiary Care Centre).

**Inclusion criteria**

- Age 20-35 years.
- Regular and irregular menstrual cycle,
- Couple, who did not conceive even after at least one-year sexual intercourse
- Normal seminogram.

**Exclusion criteria**

- Age <20 year; >35 year
- Abnormal husband Semen analysis
- Abnormal Hormonal profile
- Active genitourinary infection
- Any treatment, chronic illness and MPA contraception which imparts a negative effect on fertility.

**Investigations**

- Hemoglobin, complete blood count (CBC), Erythrocyte sedimentation rate (ESR), Random blood sugar and chest X-ray PA view) - within normal limits
- Ovulatory function, husband semen analysis, hormonal profile (TSH/FSH/LH/Prolactin) and APLA (anti phosphor lipid antibody) levels (if available and only in secondary infertility) within normal limits.

Infertile female patients, age between 19-35 years were registered to participate in the study after taking the informed and written consent.

After detailed history (together as well as separately) and clinical examination (general, systemic and gynecological examination), routine investigations were performed. Pelvic ultrasonography findings were recorded in all enlisted patients. After considering the exclusion criteria and contraindications of the operative procedure, hysterolaparoscopic and laparoscopy were concurrently performed at SDMH, Jaipur, Rajasthan. The uterus, anterior and posterior cul-de-sacs, fallopian tubes, ovaries, ovarian fossae, pelvic peritoneum, appendix and liver surface were examined during the procedure, if some abnormalities was seen and it was noted down and therapeutic interventions were performed at the same sitting, if required and feasible.

These included ovarian drilling, adhesiolysis, ablation of endometriotic spots, cystectomy, syncheiolyisis, septum resection, polypectomy and cannulation. Chromopertubation (CPT) was performed in all cases. After offering the successful treatment, Patients were advised for regular sexual activity. The follow-up of all recruited patients was performed at an interval of three months for 12 months or till achievement of fetal cardiac activity. Approval of the institutional ethical committee was obtained for this prospective study. In view of the prospective study design, written informed consent was obtained.

**Statistical analysis**

All enlisted patients were divided into two subgroups, primary and secondary infertility and the detected pathologies and treatment in each group during the hysterolaparoscopic procedure were noted. The detected pathologies and interventions during the hysterolaparoscopic procedure were noted down and categorized as a single and multiple types of the hysterolaparoscopic interventions.

The analysis between the two groups and continuous variables were summarized as mean and standard deviation, whereas nominal/categorical variables were summarized as proportions. Parametric tests [Student t test] were used for analysis of continuous variables while Chi-square was used for nominal/ categorical variables. ‘p’ value < 0.05 was considered as significant. IBM-SPSS version 22.0 software was used for all statistical analysis.

**RESULTS**

157 female patients with the complained of infertility were included in the present study. The mean age of patients was 27.7 years (range of 19-35 years). All enlisted patients fulfilled the inclusion criteria of the present study. On the basis of obstetric history, patients were divided in primary and secondary infertility. The characteristics of all patients are given in Table 1. After the detail history, clinical examination and biochemical evaluation, all patients underwent the pelvic ultrasound examination.

**Hysterolaparoscopic findings (diagnostic)**

After the initial evaluation, all patients underwent hysterolaparoscopy. Out of 157 patients, abnormalities
were detected in 125/157 (79.6%) patients during Hysterolaparoscopy. These abnormal findings in the laparoscopy and hysteroscopy are summarized in Table 2 and 3 respectively.

**Table: 1 Characteristics of infertility patients (Age, BMI).**

| Infertility (Total number of patients) | No. |
|---------------------------------------|-----|
| Age (Years) Mean ± standard deviation | 27.72 ± 3.82 |
| Range                                 | 19-35 |
| BMI (Kg/m²) Mean ± standard deviation | 21.80 ± 3.03 |
| Range                                 | 15.6-33.3 |

**Primary infertility (No. of patients)**

| Age (Years) Mean ± standard deviation | 26.59 ± 3.23 |
| Range                                 | 19-34 |
| BMI (Kg/m²) Mean ± standard deviation | 21.84 ± 3.30 |
| Range                                 | 16-33.3 |

**Secondary infertility (No. of patients)**

| Age (years) Mean ± standard deviation | 29.35 ± 4.04 |
| Range                                 | 20-35 |
| BMI (Kg/m²) Mean ± standard deviation | 21.7 ± 2.62 |
| Range                                 | 15.6-28.8 |

**Table 2: Summary of the abnormalities detected in the laparoscopic examination in primary and secondary infertility patients.**

| Laparoscopic organ abnormality | Primary infertility | Secondary infertility | Sub-categorization of abnormalities | Primary infertility | Secondary infertility |
|-------------------------------|----------------------|------------------------|-------------------------------------|----------------------|------------------------|
| Ovarian abnormalities         | 54/93 (58.4%)        | 24/64 (37.5%)          | Cystic abnormality                  | 38/54 (70.4%)        | 18/24 (75%)            |
|                               |                      |                        | (Polycystic, single cystic)         | (Polycystic - 34     | (Polycystic-13 Single cyst-5) |
|                               |                      |                        |                                     | Single cyst-4)       |                        |
|                               |                      |                        | Adherent                            | 9                    | 5                      |
|                               |                      |                        | Endometriotic                       | 6                    | 1                      |
|                               |                      |                        | Streak                              | 1                    | 0                      |
| Fallopian tube abnormalities   | 20/93 (21.5%)        | 14/64 (21.8)           | Dilated and tortuous                | 8                    | 2                      |
|                               |                      |                        | Endometriotic patches               | 1                    | 1                      |
|                               |                      |                        | Hidden fimbral end                  | 1                    | 2                      |
| Uterine abnormalities         | 20/93 (21.5%)        | 10/64 (15.6%)          | Bulky uterus                        | 7/20 (35%)           | 4/10 (40%)             |
|                               |                      |                        | Fibroid / adenomyosis               |                      |                        |
|                               |                      |                        | Endometriotic patches               | 3                    | 2                      |
|                               |                      |                        | Tubercle                            | 4                    | 0                      |
|                               |                      |                        | Adherent and congested              | 3                    | 2                      |
|                               |                      |                        | Hypoplastic uterus                  | 2                    | 0                      |
|                               |                      |                        | Acutely retroverted uterus          | 1                    | 2                      |
| Adhesions                     | 20/93 (21.5%)        | 17/64 (26.6%)          | Flimsy adhesions                    | 9/20 (45%)           | 12/17 (70.6%)          |
|                               |                      |                        | Dense adhesions                     | 11/20 (55%)          | 5/17 (29.4%)           |
| POD abnormalities             | 33/93 (35.5%)        | 15/64 (23.4%)          | Clear fluid                         | 22/33 (66.7%)        | 12/15 (80%)            |
|                               |                      |                        | Hemorrhagic fluid                   | 8                    | 1                      |
|                               |                      |                        | Caseous material                    | 3                    | 2                      |
Table 3: Summary of the abnormalities detected in the hysteroscopic examination in primary and secondary infertility patients.

| Hysteroscopic organ abnormality | Hysteroscopic abnormalities in primary infertility | Sub-categorization of hysteroscopic abnormalities in primary infertility | Patients No. | Hysteroscopic abnormalities in secondary infertility | Sub-categorization of hysteroscopic abnormalities in secondary infertility | Patient No. |
|---------------------------------|-----------------------------------------------|-----------------------------|-------------|------------------------------------------------|------------------------------------------------|-------------|
| Cervix (external and internal os), Uterine cavity and osteal web abnormality | 18/93 (19.4%) | Hypertrophied endometrium | 3 | 8/64 (12.5%) | Hypertrophied endometrium in Bicornuate uterus and cervical stenosis | 1 |
|                                 |                                              | Uterine septum              | 6           |                                              | Uterine septum                                  | 2           |
|                                 |                                              | Cervical stenosis           | 2           |                                              | Uterine polyp/ fibroid                           | 1           |
|                                 |                                              | Uterine polyp/ fibroid      | 2           |                                              | Tubercles/White patches                          | 1           |
|                                 |                                              | Synechiae                   | 1           |                                              | Tubercles/White patches and uterine septum       | 1           |
|                                 |                                              | Tubercles                   | 1           |                                              |                                              |             |
|                                 |                                              | Osteal webbing              | 1           |                                              | Osteal webbing                                  | 1           |
|                                 |                                              | Tubercle and Osteal webbing | 1           |                                              | Osteal webbing and uterine septum                | 1           |
|                                 |                                              | Vaginal septum              | 1           |                                              |                                              |             |

Table 4: Summary of the distribution of different interventions during the hysterolaparoscopy.

| Infertility       | Number of recruited patients | Abnormalities detected in hysterolaparoscopy | Interventions performed by hysterolaparoscopy | Single site intervention | Multiple site intervention |
|-------------------|------------------------------|-----------------------------------------------|-----------------------------------------------|--------------------------|----------------------------|
| Combined          | 157                          | 125                                           | 121                                           | 81                       | 40                         |
| Primary           | 93                           | 77                                            | 73                                            | 47                       | 26                         |
| Secondary         | 64                           | 48                                            | 48                                            | 34                       | 14                         |

**Hysterolaparoscopic interventions**

Out of 157 patients, abnormalities were detected in 125 patients (~79.6%) during hysterolaparoscopic examination. Out of these 125 patients, 121 (~96.8%) underwent therapeutic interventions in form of ovarian drilling (Figure-1), adhesiolysis, Successful cannulation, fluid drainage, fulguration of white patches, septum resection and chocolate cystectomy etc.

Table 5: Summary of the single site interventions during the hysterolaparoscopy in primary infertility patients.

| Type of intervention          | Patient’s No. |
|-------------------------------|---------------|
| Ovarian drilling              | 24/47 (51.1%) |
| Adhesiolysis                  | 9             |
| Successful cannulation        | 4             |
| Unsuccessful cannulation      | 4             |
| Fluid drainage                | 3             |
| Fulguration of white patches  | 1             |
| Septum resection              | 1             |
| Anatomical restoration of uterus (of acutely retroverted uterus) | 1 |
Table 6: Summary of multiple site interventions during the hysterolaparoscopy in primary infertility patients.

| Type of intervention                                                                 | Patient’s No. |
|--------------------------------------------------------------------------------------|---------------|
| Ovarian drilling and Successful cannulation                                           | 3             |
| Ovarian drilling and adhesiolysis                                                    | 3             |
| Hysteroscopic polypectomy/ fibroid removal                                            | 2             |
| Partial oophorectomy and successful cannulation                                       | 2             |
| Ovarian drilling and septum resection                                                | 2             |
| Adhesiolysis, fulguration of endometriotic patches                                   | 2             |
| Chocolate cystectomy and fluid aspiration                                            | 1             |
| Surgical removal of paraovarian cyst lesion                                           | 1             |
| Ovarian drilling and septum resection                                                | 1             |
| Adhesiolysis; paraovarian cyst removal, ovarian drilling and unsuccessful cannulation | 1             |
| Adhesiolysis of fimbrial adhesions, ovarian drilling and unsuccessful tubal cannulation| 1             |
| Adhesiolysis and removal of polyp                                                    | 1             |
| Adhesiolysis and Chocolate cystectomy                                                | 1             |
| Adhesiolysis and suction irrigation                                                  | 1             |
| Adhesiolysis and unsuccessful cannulation                                            | 1             |
| Open myomectomy due to laparoscopic failure                                          | 1             |
| Septum resection and myomectomy                                                      | 1             |
| Ovarian drilling and Unsuccessful cannulation                                         | 1             |

Table 7: Summary of the single site interventions during the hysterolaparoscopy in secondary infertility patients.

| Type of intervention                    | Patient’s No. |
|-----------------------------------------|---------------|
| Ovarian drilling                        | 8             |
| Adhesiolysis                            | 7             |
| Successful cannulation                  | 5             |
| Unsuccessful cannulation                | 4             |
| Septum resection                        | 3             |
| Fibroid / polyp removal                 | 3             |
| Fluid drainage                          | 1             |
| Chocolate cyst removal                  | 1             |
| Unsuccessful septum resection           | 1             |
| Right salpingectomy                     | 1             |

Table 8: Summary of the multiple site interventions during the hysterolaparoscopy in secondary infertility patients.

| Type of intervention                                                                 | Patient’s No. |
|--------------------------------------------------------------------------------------|---------------|
| Successful cannulation, Adhesiolysis and paraovarian cystic removal                  | 2             |
| Adhesiolysis and suction irrigation in POD                                            | 2             |
| Adhesiolysis and ovarian drilling                                                    | 1             |
| Adhesiolysis and successful cannulation                                              | 1             |
| Ovarian drilling and fluid drainage from POD and cervical erosion cauterization       | 1             |
| Adhesiolysis, cyst removed, suction irrigation in POD                                 | 1             |
| Septum resection and fluid drainage                                                  | 1             |
| Adhesiolysis, ovarian drilling and removal of polyp                                   | 1             |
| Fulguration of the endometriotic patches                                             | 1             |
| Septum resection, chocolate cystectomy and endometriotic patches fulguration         | 1             |
| Successful cannulation, adhesiolysis and paraovarian cystic removal and successful cannulation | 1             |
| Ovarian drilling and adhesiolysis and cervical erosion cauterization                 | 1             |
| Ovarian drilling and successful cannulation                                          | 1             |
Of the 121 patients, 81 (66.9%) underwent for single type intervention while remaining 40 (33.1%) patients underwent for multiple type interventions (Table 4).

Separately in primary infertile patients, out of 77 patients with abnormal hysterolaparoscopic findings, 73 underwent various therapeutic interventions. While in secondary infertility, 48 patients had abnormal hysterolaparoscopic findings and all underwent therapeutic interventions (Table 5-8 and figure 1).

Out of 77, 4 patients with abnormal hysterolaparoscopic finding were not underwent active intervention. These patients have streak ovaries and hypoplastic uterus, few small fibroids and adenomyosis in 1, 1 and 2 patients respectively.

**Post hysterolaparoscopic interventions outcomes**

After the hysterolaparoscopic intervention, 43 patients were successfully conceived. Out of 43 patients who conceived after the hysterolaparoscopic intervention, 28 underwent single type of intervention and remaining 15 patients underwent multiple type interventions. An illustration case of multiple type of intervention (Figure 2), a 26-year-old female of primary infertility underwent infertility work up with past history of successfully treated pulmonary tuberculosis.

The husband seminogram was within normal limits Figure 2. She underwent hysterosalpingography, which shows normal uterine cavity outline (arrow) and absent of the bilateral spillage of the contrast agent (dashed arrow).

In Figure 3, during hysterolaparoscopy, we performed the chromoperturbation (CPT) mediated successful cannulation and finally found patency of bilateral ostia (arrow b, c) and bilateral spillage of methylene blue dye in the pelvis (dashed arrow d, e).

Out of 77, 4 patients with abnormal hysterolaparoscopic finding were not underwent active intervention. These patients have streak ovaries and hypoplastic uterus, few small fibroids and adenomyosis in 1, 1 and 2 patients respectively.

**Figure 1: Distribution of abnormalities and intervention in hysterolaparoscopy in the female infertile patients**

**Figure 2: Hysterosalpingogram shows normal uterine cavity (arrow) and absent of the bilateral spillage (dashed arrow).**

**Figure 3: Chromoperturbation (CPT) bilateral spillage of blue dye.**

**Figure 4: Additionally, multiple white patches in endometrial surface and we fulgurated these patches.**
Another illustration case of single type of intervention (Figure 5), a 31-year-old secondary infertile female underwent for infertility work up. She has complained of recurrent first trimester abortions (3 in number) since three years.

Figure 5: A case of single type intervention, a 31-year-old secondary infertile female with history of recurrent abortions Figure 3 a, b-USG shows uterine septum. Figure 3 c, d- during hysterolaparoscopy, we found the uterine septum (c) and hysteroscopic removal of septum (d).

The husband semenogram was within normal limits. Figure 5 a, b- She underwent for USG, which shows uterine septum. Figure 5 c, d- during hysterolaparoscopy, we found the uterine septum (c) and hysteroscopic removal septum was performed (d). And on follow-up patient was conceived after 4 months of the hysterolaparoscopy.

Independently in primary infertility, 28 patients who conceived after the hysterolaparoscopic intervention, 17 patients underwent single type intervention and remaining 11 patients underwent multiple type interventions. While in secondary infertility, 15 patients who conceived after the hysterolaparoscopic intervention, 11 patients underwent single type intervention and remaining 4 patients underwent multiple type interventions. All the above describe findings are summarized in Table 9.

There was no statistically significant difference in the pregnancy outcome in both groups. Independently in primary and secondary infertile patients, there was no significant difference in the pregnancy outcome in infertile female patients who experienced either single or multiple type intervention. In all hysterolaparoscopic patients, during and after the procedure no major surgical and anesthetical complications were reported. Few patients were reported with mild abdominal pain and low-grade fever of short duration.

| Infertility  | Conceived with intervention (patient’s Number) | Conceived with single site intervention (patient’s Number) | Conceived with multiple site intervention (patient’s Number) | P value |
|--------------|--------------------------------------------------|----------------------------------------------------------|-----------------------------------------------------------|---------|
| Combined     | 43                                               | 28/43 (65.1%)                                             | 15/43 (34.9%)                                             | 0.973   |
| Primary      | 28                                               | 17/28 (60.7%)                                             | 11/28 (39.3%)                                             | 0.616   |
| Secondary    | 15                                               | 11/15 (73.3)                                              | 4/15 (26.7%)                                              | 0.803   |

DISCUSSION

The proposal of the study came because of at the time of evaluation of the infertile female when we found that more than one types of the anatomical abnormalities in a single female, the expectations of the fruitful outcome after successful hysterolaparoscopic intervention has been reduced.

In the published literature for single type interventions, Amer et al, Kong et al and Kaur et al found in their study that conception rate in PCOS patients with infertility, following ovarian drilling, was 49%, 37% and 47% respectively.8-7 While Freud A et al, Selvaraj et al, Hollett-Caines J at al, Bakas et al and Esmaeilzadeh et al also found significant improvement in pregnancy rate (70-95%) after the septum resection.8-12 Lee et al and Nesbitt-Hawes EM et al calculated the conception rate for infertile women with endometriosis after laparoscopic surgery.13,14 They found overall pregnancy rate 41.9% and 73 % respectively after successful management of the endometriosis. But to the best of my knowledge, there is no study in the published literature that addressed the comparison of single and multiple types of interventions in infertile female patients.

Authors found that in present study, most of the detected pathologies were of the ovarian origin and cystic ovarian disease was the more common as an isolated and combined with others pathologies. In present study, the achievement of the successful pregnancy rate in female infertile patient after the successful hysterolaparoscopic intervention was 34.6%. Independently in the single type intervention was 34.6% and multiple type intervention was 34.9%, which was not statistically different in both groups. When we compare isolate in the primary and...
secondary infertile patients, the conception after the successful single type and multiple type intervention were no significantly different. So, the final outcome in the infertile female patients were not depend on the type of the pathologies independently in primary or secondary and combinedly. The limitations of the study are single center study so discrepancy in outcomes may be possible, relatively short time (12 months) follow-up, the numbers of the multiple types of the interventions are relatively low in number.

CONCLUSION

We concluded that the conception rate was not significantly different in the infertile female patients, who underwent either single or multiple type hysterolaparoscopic intervention. In short Hysterolaparoscopy intervention should be performed in infertile female patients irrespective of extent of the pelvic abnormality.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Agrawal N, Fayyaz S. Does type of intervention affects the endoscopic procedure outcome in female infertile patients? an experience at a single tertiary care centre. Int J Reprod Contracept Obstet Gynecol 2019;8:192-9.