Review Article

Ovarian hormone levels before and after tubal ligation: a systematic review and meta-analysis

Ping Li¹,², Hui-Li Wu², Bai-Hua Dong¹

¹Department of Gynecology and Obstetrics, Qilu Hospital, Shandong University, 107#, West Wenhua Road, Jinan 250012, PR China; ²Department of Gynecology and Obstetrics, Affiliated Hospital of Taishan Medical University, 706#, Taishan Street, Taian 271000, China

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Abstract: Background: Tubal ligation (TL) is an efficient, permanent, and convenient contraceptive method. However, there are conflicting results regarding postoperative ovarian hormone levels. The aim of this study was to determine whether TL alters ovarian hormone levels. Study design: Pubmed and Embase databases, from January 1980 to March 2017, were searched to identify relevant studies reporting ovarian hormone assessment before and after TL. Meta-analyses were performed with Stata 12.0. Results: Seventeen studies with a total of 620 women were included in this meta-analysis. Pooling of the results showed no significant differences in serum levels of follicle-stimulating, luteinizing and anti-Mullerian hormones, estradiol, and inhibin in pre-sterilization and post-sterilization assessments. However, progesterone levels were significantly decreased after TL when using Pomeroy or Falope-ring methods (P < 0.05). Conclusion: TL does not affect ovarian reserves but results in luteal function deficiency. However, further research is necessary to confirm the long-term effects of TL on ovarian function.

Keywords: Hormone, systematic review, tubal ligation

Introduction

Tubal ligation (TL) is a widely accepted method of destroying the fallopian tubes as a permanent method of contraception [1]. However, the effects of TL on ovarian function have been a matter of debate. Some patients have complained of irregular menstrual cycles, pelvic pain, dysmenorrhea, and spotting after TL [2-6]. Complications have been correlated with the degree of surrounding tissue damage, particularly affecting uterine-ovarian blood flow, which can influence short-term ovarian function. However, numerous studies have shown no side effects of TL on ovarian reserves and luteal function [7-15].

Various methods can be utilized to perform selective tubal sterilization, including vaginal colpotomy, post-partum laparotomy, minilaparotomy, laparoscopy, and hysteroscopy, which has been widely accepted as it is minimally invasive with rapid recovery [16]. However, hysteroscopic sterilization requires a hysterosalpingogram at least three months after the initial procedure to confirm bilateral tubal occlusion before women can rely on this method of contraception [17]. Therefore, minilaparotomy and laparoscopy methods of TL remain the preferred methods due to widespread use, cost-effectiveness, and fewer short- and long-term risks.

At present, many surgery methods are being employed to perform minilaparotomy and laparoscopy methods of TL, including Pomeroy, modified Pomeroy, Uchida, Hulka or Filshie clips, silastic bands, fimbriectomy, bipolar coagulation, and Falope rings. Pomeroy, modified Pomeroy, and Falope rings cause greater destruction of surrounding blood flow. To evaluate ovarian function, levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), anti-Mullerian hormone (AMH), and inhibin (INH) in the early follicular phase can be measured, as well as progesterone (P) in the mid-luteal phase. To assess the endocrine consequences of TL, this study conducted a
Materials and methods

Search strategy

Pubmed, Embase, China National Knowledge Infrastructure, and Chinese Biomedical Literature Service System were searched for articles published before July 2017, using the following terms: "tubal ligation", "tubal sterilization", "tubal blockage", "oviduct ligation", "fallopian tube ligation", "female sterilization", OR "tubal occlusion" AND "ovarian function", "ovarian reserve", "hormone", OR "luteal function". No search limits were set concerning study type, population, and language. However, no eligible articles were found in the Chinese database. Studies reporting levels of at least one of the ovarian hormones (FSH, LH, E2, AMH, INH, or P) were selected. After extracting full-text papers, reference lists were searched by hand to identify additional relevant studies.

Inclusion criteria

Criteria for inclusion in this meta-analysis were: 1) Human studies; 2) Prospective studies; 3) Blood-sample studies; 4) Discontinuation of hormone contraception > 3 months; and 5) Studies including before and after operation parameters. For studies reporting multiple endpoints, data for the longest end-point within one year was selected. Reviews, conference articles, letters to the editor, and case reports were excluded.

Data extraction

Two reviewers, independently, extracted data from eligible studies. Disagreements between the two reviewers were resolved by consensus with a third author. The following data were recorded from each study: name of first author, year and location (country) the study was performed, type of study, number and age of patients, patient body mass index (BMI), gravidity and parity information, study end-point duration, and method and type of hormone assessments.

Statistical analysis

Stata 12.0 software (StataCorp LP, College Station, TX, USA) was used to analyze data. Effect estimates were pooled using fixed effects meta-analysis with a non-standard method and statistical heterogeneity was assessed using
Table 1. Studies reporting hormone changes after tubal ligation included in meta-analysis

<table>
<thead>
<tr>
<th>Author et al.</th>
<th>Year</th>
<th>Location</th>
<th>Type</th>
<th>Method</th>
<th>n</th>
<th>Age (y)</th>
<th>BMI (kg/m²)</th>
<th>Gravity (n)</th>
<th>Parity (n)</th>
<th>Duration (mo)</th>
<th>Hormone (assay)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvarez et al. [18]</td>
<td>1989</td>
<td>Dominican Republic</td>
<td>CCT</td>
<td>Pomeroy</td>
<td>8</td>
<td>&lt;38</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>6</td>
<td>FSH, LH, E2, P (RIA)</td>
</tr>
<tr>
<td>Garza-Flores et al. [25]</td>
<td>1991</td>
<td>Mexico</td>
<td>CCT</td>
<td>Pomeroy</td>
<td>8</td>
<td>24.7±4.2</td>
<td>NR</td>
<td>NR</td>
<td>≥1</td>
<td>12</td>
<td>FSH, LH, E2, P (RIA)</td>
</tr>
<tr>
<td>Thranov et al. [29]</td>
<td>1992</td>
<td>Denmark</td>
<td>CCT</td>
<td>Falope-ring or Filshie clips</td>
<td>27</td>
<td>25 (28-36)</td>
<td>NR</td>
<td>NR</td>
<td>≥1</td>
<td>12</td>
<td>FSH, LH, E2, P (RIA)</td>
</tr>
<tr>
<td>Hakverdi et al. [4]</td>
<td>1994</td>
<td>Turkey</td>
<td>CCT</td>
<td>Pomeroy, silastic bands or fimbriectomy</td>
<td>43</td>
<td>32.6±4.1</td>
<td>6.8±2.1</td>
<td>5.7±1.6</td>
<td>12</td>
<td>FSH, LH, E2, P (RIA)</td>
<td></td>
</tr>
<tr>
<td>Sumiala et al. [28]</td>
<td>2000</td>
<td>Finland</td>
<td>CCT</td>
<td>Hulka or Filshie clips</td>
<td>46</td>
<td>(31-43)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>12</td>
<td>FSH, LH, E2, P (RIA)</td>
</tr>
<tr>
<td>Bulent Tiras et al. [20]</td>
<td>2001</td>
<td>Turkey</td>
<td>CCT</td>
<td>Bipolar coagulation</td>
<td>13</td>
<td>33.1±3.9</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>3</td>
<td>FSH, LH, E2, P (ELISA)</td>
</tr>
<tr>
<td>Timonen et al. [30]</td>
<td>2002</td>
<td>Finland</td>
<td>CCT</td>
<td>Hulka or Filshie clips</td>
<td>23</td>
<td>37 (31-43)</td>
<td>37 (24-40)</td>
<td>NR</td>
<td>NR</td>
<td>12</td>
<td>FSH, LH, E2, P (RIA)</td>
</tr>
<tr>
<td>Carmona et al. [21]</td>
<td>2003</td>
<td>Spain</td>
<td>CCT</td>
<td>Bipolar caugulation</td>
<td>12</td>
<td>36.4±1.1</td>
<td>27.1±2.1</td>
<td>NR</td>
<td>1.9±0.2</td>
<td>12</td>
<td>FSH, LH, E2, P (ECLIA), INH (ELISA)</td>
</tr>
<tr>
<td>Yazici et al. [31]</td>
<td>2004</td>
<td>Turkey</td>
<td>CCT</td>
<td>Bipolar caugulation</td>
<td>15</td>
<td>36.9±3.8</td>
<td>28.3±2.8</td>
<td>3.0±0.9</td>
<td>2.4±0.4</td>
<td>6</td>
<td>FSH, LH, E2, P (ECLIA)</td>
</tr>
<tr>
<td>Cevrioglu et al. [22]</td>
<td>2004</td>
<td>Turkey</td>
<td>RCT</td>
<td>Pomeroy</td>
<td>14</td>
<td>35.8±3.6</td>
<td>27.5±3.1</td>
<td>3.3±0.9</td>
<td>2.5±0.4</td>
<td>3</td>
<td>FSH, LH, E2, P (ECLIA)</td>
</tr>
<tr>
<td>Kutlar et al. [26]</td>
<td>2005</td>
<td>Turkey</td>
<td>Unblinded RCT</td>
<td>Pomeroy</td>
<td>11</td>
<td>36.4±2.5</td>
<td>34.1±1.3</td>
<td>NR</td>
<td>NR</td>
<td>6</td>
<td>FSH, LH, E2, P (ECLIA)</td>
</tr>
<tr>
<td>Fagundes et al. [24]</td>
<td>2005</td>
<td>Brazil</td>
<td>CCT</td>
<td>Modified Pomeroy</td>
<td>13</td>
<td>36.8±2.0</td>
<td>36.7±2.2</td>
<td>NR</td>
<td>4.7±1.8</td>
<td>3.8±1.2</td>
<td>FSH, LH, E2, P (ECLIA)</td>
</tr>
<tr>
<td>Baloglu et al. [19]</td>
<td>2005</td>
<td>Turkey</td>
<td>RCT</td>
<td>Bipolar electrocaugulation</td>
<td>15</td>
<td>36.7±2.2</td>
<td>34.1±1.3</td>
<td>NR</td>
<td>4.3±1.9</td>
<td>4.1±1.2</td>
<td>FSH, LH, E2, P (ECLIA)</td>
</tr>
<tr>
<td>Dede et al. [23]</td>
<td>2006</td>
<td>Turkey</td>
<td>CCT</td>
<td>Bipolar electrocautery</td>
<td>20</td>
<td>34.2±4.2</td>
<td>4.8±1.8</td>
<td>2.9±1.0</td>
<td>3</td>
<td>FSH, LH, E2, P (RIA)</td>
<td></td>
</tr>
<tr>
<td>Goynumer et al. [3]</td>
<td>2006</td>
<td>Turkey</td>
<td>Unblinded RCT</td>
<td>Electrocaugulation</td>
<td>44</td>
<td>(35-40)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>10</td>
<td>NR</td>
</tr>
<tr>
<td>Ercan et al. [8]</td>
<td>2012</td>
<td>Turkey</td>
<td>CCT</td>
<td>Bipolar electrodesication and transection</td>
<td>49</td>
<td>36.6±3.4</td>
<td>42 (2-7)</td>
<td>3 (2-5)</td>
<td>3</td>
<td>FSH, LH, E2, P (ECLIA), AMH (ELISA)</td>
<td></td>
</tr>
<tr>
<td>Silva et al. [27]</td>
<td>2013</td>
<td>Brazil</td>
<td>Prospective cohort</td>
<td>Bipolar electrocaugulation or Pomeroy</td>
<td>52</td>
<td>32.5±4.5</td>
<td>29.9±4.8</td>
<td>NR</td>
<td>NR</td>
<td>12</td>
<td>AMH (ELISA)</td>
</tr>
</tbody>
</table>

Abbreviations: AMH, anti-Mullerian hormone; BMI, body mass index; CCT, controlled clinical trial; E2, estradiol; ECLIA, electrochemiluminescence immunoassay; ELISA, enzyme-linked immunosorbent assay; FSH, follicle-stimulation hormone; INH, inhibin; LH, luteinizing hormone; NR, not reported; P, progesterone; RCT, randomized controlled trial; RIA, radioimmunoassay. Note: data are expressed as mean ± standard deviation, or as median (range).
TL resulting in luteal function deficiency

Figure 2. Quality of studies included in the meta-analysis.

Table 2. Comparison of hormones before and after tubal ligation

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Studies (n)</th>
<th>Patients (n)</th>
<th>WMD (95% CI)</th>
<th>I²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH</td>
<td>11</td>
<td>364</td>
<td>0.046 (-0.233-0.325)</td>
<td>0.0%</td>
<td>0.745</td>
</tr>
<tr>
<td>LH</td>
<td>10</td>
<td>290</td>
<td>-0.024 (-0.230-0.182)</td>
<td>70.0%</td>
<td>0.821</td>
</tr>
<tr>
<td>E2</td>
<td>9</td>
<td>349</td>
<td>0.728 (-1.669-3.125)</td>
<td>0.0%</td>
<td>0.552</td>
</tr>
<tr>
<td>P</td>
<td>8</td>
<td>264</td>
<td>-1.528 (-2.753-0.304)</td>
<td>69.1%</td>
<td>0.014</td>
</tr>
<tr>
<td>INH</td>
<td>2</td>
<td>114</td>
<td>-1.370 (-6.726-3.987)</td>
<td>0.0%</td>
<td>0.616</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; E2, estradiol; FSH, follicle-stimulation hormone; INH, inhibin; LH, luteinizing hormone; P, progesterone; WMD, weighted mean difference.

Figure 3. Sensitivity analysis of the effects of tubal ligation on luteinizing hormones in the early follicular phase. CI, confidence interval.

Results

Study selection

A total of 12,132 studies were initially retrieved from Pubmed and Embase databases (Figure 1). After excluding duplicates, studies that were not self-controlled trials, cross-sectional studies, and those without a comparison group were excluded, as well as studies including patients that did not meet the inclusion criterion (premenopausal or menopausal, use of hormone contraception < 1 mo before TL). A total of 17 studies comprising 620 patients remained for further analyses [3, 4, 8, 18-31] (Table 1). Risk of bias assessment of included trials is presented in Figure 2.

Effects of TL on follicular phase ovarian hormones

Meta-analyses demonstrated that TL had no effect on post-procedural levels of FSH, LH, E2, or INH (Table 2). However, moderate heterogeneity was observed among studies with respect to LH assessment, which may have been due to differences in operation techniques and methods of detection. Therefore, sensitivity analysis was performed to verify the robustness of the outcome (estimate = 0.323, 95% CI: -1.840-0.829) (Figure 3).

AMH levels were measured in three studies. However, values reported by Silva et al. [27] were not normally distributed and Ercan et al. [8] reported median (range), whereas Goynume et al. [3] reported means and standard deviations. Although AMH could not be assessed by

their own control. The ≥ 80% completion rate per study group indicates a lack of attrition bias. Hormone concentrations are presented as mean ± standard deviation. P < 0.05 is considered statistically significant.
**TL resulting in luteal function deficiency**

TL resulting in luteal function deficiency

**Meta-analysis**

Each of the three studies found no changes in AMH after TL.

**Effects of TL on mid-luteal phase ovarian hormone**

Pooled data from eight studies showed significant alteration in P levels after TL ($P = 0.014$) (Table 2). However, there was significant heterogeneity among the studies ($I^2 = 69.1\%$; $P < 0.001$). Thus, subgroup analyses according to surgery type were performed. As Pomeroy and Falope-ring methods tend to more seriously damage surrounding tissue, they were included together as subgroup 1. The remaining operation types were classified as subgroup 2. Data reported by Hakverdi et al. [4] was not included in subgroup analyses, as P levels were not distinguished among the three methods used (Pomeroy, silastic bands, and fimbriectomy). Subgroup analysis revealed a significant decrease in P levels after TL in subgroup 1 ($P < 0.001$), but not in subgroup 2 ($P = 0.358$) (Figure 4). There was no heterogeneity within the subgroups.

**Discussion**

Results of the present meta-analysis indicate that TL does not influence the secretion of FSH, LH, INH, or E2. Furthermore, although TL by bipolar electrocoagulation, fimbriectomy, or Hulka and Filshie clips did not significantly alter P levels in the mid-luteal phase, levels were significantly decreased when using Pomeroy or Falope-ring methods. These techniques resulted in the formation of a loop in the tube, which could impair the mesosalpinx vessels and damage circulation to the ovaries, as well as contribute to tubal ligation syndrome. This may lead to irregular menstrual cycles and spotting. Alternative methods leave the mesosalpinx vessels intact, reducing the probability of influencing ovarian function. For example, laparoscopic tubal bipolar coagulation has no permanent effects on luteal function, particularly in younger women [32].

Although the heterogeneity among studies concerning the effects of LT on P was not significant, the presence of mild heterogeneity may be attributed to the inclusion of various operation techniques that could not be further subdivided. In addition, most studies collected blood samples on the 21st day of the menstrual cycle, though some studies obtained samples eight to ten days post-ovulation. For example, time of blood draw can influence levels of P, which change rapidly in the corpus luteum maturation period. It is also possible that varying methods of sample management and testing contributed to these findings.

There were several limitations to the present study. First, the limited number of studies restricted the ability to clarify the effects of

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**Figure 4.** Subgroup analysis of the effects of tubal ligation on progesterone in the mid-luteal phase. CI, confidence interval; WMD, weighted mean difference.
specific surgical techniques, particularly in subgroup analysis. Thus, these results should be interpreted carefully. Second, the quality of evidence was insufficient. More adequately powered clinical trials are needed. Third, only one study included patients that were over 30 years of age. Thus, future studies are needed to more clearly describe the effects among women of various ages. Because the secretion of P is pulsatile, additional studies with larger samples and definitive blood draw timing are necessary to verify the influence of TL on the corpus luteum maturation period. Moreover, recent studies have suggested that AMH is an indicator of ovarian function [33-35] and should, therefore, be included in future studies evaluating the impact of TL.

**Conclusion**

This meta-analysis demonstrates that TL does not significantly alter the profile of follicular phase ovarian hormones. However, procedures utilizing Pomeroy or Falope-ring methods may damage the vasculature and impact luteal function, evidenced by an alteration in P levels. It is, therefore, important to apply the appropriate method resulting in the least tubal damage.

**Disclosure of conflict of interest**

None.

**Address correspondence to:** Bai-Hua Dong, Department of Gynecology and Obstetrics, Qilu Hospital, Shandong University, 107#, West Wenhua Road, Jinan 250012, PR China. Tel: +8618254880409; E-mail: 18254880409@163.com

**References**


[17] Garfpey AM, Creinin MD, Schwarz EB, Smith KU. Reliability of laparoscopic compared with
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