Inflammatory response and tissue trauma in laparoscopic hysterectomy: comparison of electrosurgery and harmonic scalpel

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Summary

Objective: Our aim was to quantify and compare clinical outcome and surgical inflammatory response and tissue trauma after laparoscopic hysterectomy for a benign disorder which was performed by electrosurgery or harmonic scalpel.

Methods: Sixty patients scheduled for laparoscopic hysterectomy were selected according to patient preference to undergo either electrosurgery or an ultrasonic operative technique. Blood samples for assay of markers of tissue trauma (C-reactive protein, interleukin-6, creatine kinase, white blood cell count) were taken preoperatively, on the first and third postoperative day. Three patients with intraoperative complications or incomplete records were excluded from tissue analysis.

Results: No differences were present in the demographic characteristics and clinical outcomes (blood loss, uterine weight, operating time and hospital stay) in 57 uncomplicated laparoscopic hysterectomies. Both electrosurgery (n = 36) and use of the harmonic scalpel (n = 21) resulted in statistically significant changes in the inflammatory and systemic immune response in comparison with preoperative values. No significant differences were observed in the studied inflammatory and tissue markers (C-reactive protein, interleukin-6, creatine kinase and white blood cells) between the compared groups.

Conclusion: The harmonic scalpel and electrosurgery in laparoscopic hystsrectomy were equally traumatic in terms of surgical inflammatory response and tissue trauma.

Key words: Laparoscopic hysterectomy; Electrosurgery; Harmonic scalpel; Stress; Tissue trauma.

Introduction

Surgical trauma induces a series of hormonal, metabolic, and inflammatory changes, that together constitute the stress, and the magnitude of the responses reflects the severity of tissue trauma [1-3]. Clinical and experimental experience demonstrate that perioperative stress is lower for laparoscopic surgery than for laparotomy [4].

Several authors have evaluated blood cells, cytokines, cortisol, catecholamines, creatine kinase, CA 125 and acute-phase proteins to try to quantify and compare the metabolic and inflammatory changes after laparoscopic and abdominal hysterectomy. Three authors also observed that serum markers of tissue trauma were significantly higher in the laparotomy group [1,3,5]. One study showed no difference between these operative techniques [6]. Falcone [7] suggests that the use of electrocautery can potentially explain the differences in the serum markers. In our previous randomized clinical study a comparison of perioperative parameters of two groups of women with different operative techniques in laparoscopic hysterectomy was performed [8]. There were no significant clinical differences between the electrosurgery and harmonic scalpel group in any intraoperative or postoperative follow-up variables.

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For this reason we decided to compare perioperative parameters and stress response and tissue damage markers of the harmonic scalpel and electrosurgery in laparoscopic hysterectomy.

Subjects and Methods

A prospective comparative study was undertaken at Baby Friendly Hospital Kladno which included 60 women treated with laparoscopic hysterectomy (LH) for benign disorders from October 2000 to June 2001. The patients were allocated to laparoscopic electrosurgery (bipolar and monopolar procedures) or the harmonic scalpel as a primary method of hemostasis and discission. Selection of the groups was done by means of patient preference. Laparoscopic procedures were performed by three experienced laparoscopic surgeons. Written informed consent was obtained and the differences in the operative procedure were explained to every woman.

The two variants of laparoscopic hysterectomy were used as follows: total laparoscopic hysterectomy (TLH) and laparoscopically assisted vaginal hysterectomy (LAVH) with laparoscopic colpotomy (LC) or vaginal colpotomy (VC). We opted for laparoscopic hysterectomy in patients with a history of pelvic surgery, those suspected of having an adhesive process after pelvic inflammation, and in those with fixation of a retroflexed uterus, a uterus size more than 14 weeks, poor vaginal access or expected difficulties in removal of the adnexa. We preferred TLH or LAVH with laparoscopic colpotomy mostly with smaller uterine sizes or poor vaginal access, given the impor-

tance of performing the hysterectomy quickly and preserving the uterosacral complex. Table 1 shows the patient characteristics and clinical outcome.

The parameters monitored were as follows: surgery duration (skin to skin), blood loss, hemoglobin drop, perioperative complications, hospital stay, recovery and inflammatory response and tissue damage markers (serum creatine kinase (CK)), serum C-reactive protein (CRP), and white blood cell (WBC) count). In the last 15 patients – the ELC (electro) group, n = 7 vs the LCST (laparoscopic) group, n = 8 – interleukin-6 (IL-6) was assessed as well.

The study was approved by the Regional Research Ethics Commitee of Hospital Kladno and supported by a Grant Fund of the Minister of Health.

Biochemical investigations

Three blood samples were collected from a brachial vein at 6 a.m. on the day of surgery and 24 h and 72 h later, respectively. The operations were started at the same time (8:00 a.m.),to avoid any influence of the circadian biorhythm. Only patients who underwent surgery during the morning were included in the study. The interval between the end of surgery and the first postsurgical sample collection varied between 18 and 20 hours.

The overall activity of creatine kinase (EC 2.7.3.2) was assessed using the kinetic method in the ultraviolet (UV) range, total CK activity was measured by the IFCC method at 37°C (Dade, USA) with a calibrator traceable to enzyme-reference materials ERM 1 and ERM 2. The upper limit for females was 2.4 μkatl/l. The CRP was measured by turbidimetric immunoassay at 37°C (Merck, Germany) with a calibrator traceable to CRM 470. The upper limit of reference values was 10 mg/l. The concentration of IL-6 in the serum was determined by the DPC chemiluminiscence test on a DPC Immulite (Los Angeles, CA, USA) system.

Operative technique

Laparoscopy was done with the patient under general anesthesia, with the introduction of a 10-mm laparoscope through the umbilicus and using 5-mm suprapubic trocars. Two or three 5-mm ports were each placed in the lower quadrant beside the lateral edge of the direct muscle. In the electrosurgery (ELC) group, after the diagnostic laparoscopy, bipolar and monopolar electrocautery devices (Karl Storz Endoscope, Tuttlingen, Germany) were used, whereas in the laparosonic (LCS) group, the harmonic scalpel and ultrasonically activated shears (LCS-K5) (Ultracision, Ethicon Endo Surgery, Johnson & Johnson Ltd., Cincinnati, Ohio,USA) were applied. The Ultracision was applied at power levels from 1 up to 5 (full power). Lower power levels allowed better coagulation but slower cutting. Higher power levels allowed faster transsection of relatively avascular tissue.

Our technique of total laparoscopic hysterectomy and laparoscopically-assisted vaginal hysterectomy with vaginal or laparoscopic colpotomy has been described in more detail elsewhere [8, 9].

Statistical analysis

Statistical analysis was performed with the Mann-Whitney U test. Differences within groups were analyzed by the Wilcoxon-signed rank test for two related samples. Data are presented as median and interquartile range, number or percentage. Statistical significance was defined as $p < 0,05$.

Results

Sixty patients were recruited for the study. For tissue trauma analysis 57 uncomplicated hysterectomies in both groups were included. As a result, 36 patients were placed in the electrosurgery group and 21 in the laparosonic group. One woman with a ureteral injury was excluded from the ELC group in addition to one woman with an incomplete result of the biochemical analysis. In the previously mentioned patient with cervical fibromyoma, the right ureter was accidentaly coagulated by bipolar cauter approximately 4 cm from its entry into the bladder. A partial ureteral lesion was identified 36 hours after the primary operation. Ureteroneocystostomy by laparotomy was performed and a ureteral stent was placed for six weeks. Postoperatively she did very well and has been asymptomatic for eight months. In the LCS group one woman with intraoperative complications (cystotomy) was also excluded. The bladder lesion was repaired laparoscopically without further complications.

Indications for laparoscopic hysterectomy in the ELC group were uterine fibroids (n = 31), adenomyosis (n = 2), menorrhagia (n = 2) and atypical endometrial hyperplasia (n=1) and for laparosonically assisted laparoscopic hysterectomy, uterine fibroids (n = 16), adenomyosis (n = 1), menorrhagia (n = 1) and atypical endometrial hyperplasia (n = 3). Demographic characteristics and uterine weight were similar between the two groups (Table 1), and uterine fibroids were the most common indication for hysterectomy (81.6.% in the ELC group vs 75,2% in the LCS group). No difference in age, weight, previous surgery, uterine weight, TLH/LAVH rate, operation times and hospital stay were found between the two groups (Table 1). Only the two above-mentioned major complications were observed.

The circulating concentrations of CRP, CK, and number of white blood cells increased significantly after surgery in both groups (Table 2). An increase of IL-6 over 5 μg/l was seen in two cases from the ELC group and in four cases from the LCS group on the first postoperative

Table 1. — *Patient characteristics and clinical outcome (n = 60)*

Variables	ELC group (n = 38)	LCS group (n = 22)	p
Age (yrs)	48.0 (32.6-57.0)	49.0 (36.0-78.7)	NS
Weight (kg)	69.5 (56.0-93.0)	68.0 (51.0-89.9)	NS
Prior surgery n (%)	14 (36.8)	6 (27.5)	NS
Uterine weight (g)	240.0 (100.0-486.0)	190.0 (51.0-519.0)	NS
Operating time (min)	80.0 (47.0-168.0)	80.0 (60.0-149.5)	NS
Estimated blood loss (ml)	100.0 (50.0-230.0)	100.0 (50.0-298.8)	NS
Decline of hemoglobin (g/dl)	0.9 (0.8-1.2)	0.9 (0.4-0.2)	NS
Hospital stay (days)	4.0 (3.0-14.4)	4.0 (3.0-7.0)	NS
Major complications n (%)	1 (2.7)	1 (4.5)	NS

ELC = Electrosurgery
LCS = Laparosonic

Table 2. — *Tissue and inflammatory markers in the ELC and LCS groups (n = 57).*

Variables	Postoperative day	ELC	LCS	p (ELC vs LCS)
CRP (mg/l)	0	5.0	5.0	NS
	1	16.0*	20.0*	NS
	3	27.5*	33.5*	NS
CK (μkat/l)	0	1.10	1.11	NS
	1	1.89*	1.72*	NS
	3	1.49	1.19	NS
WBC count	0	8.25	8.5	NS
(10^9/l)	1	11.20*	10.30*	NS
	3	7.35	8.25	NS

Data are presented as median and interquartile range
NS = not significant
FPD = first postoperative day
SPD = second postoperative day
* statistically significant change from preoperative value
CRP: ELC - 0 vs ELC FPD ($p < 0.001$)
LCS - 0 vs LCS FPD ($p < 0.01$)
ELC - 0 vs ELC SPD ($p < 0.001$)
LCS - 0 vs LCS FPD ($p < 0.001$)
CK: ELC - 0 vs ELC FPD ($p < 0.001$)
LCS - 0 vs LCS FPD ($p < 0.01$)
WBC: ELC - 0 vs ELC FPD ($p < 0.001$)
LCS - 0 vs LCS FPD ($p < 0.01$)

day, respectively (Figure 1). The difference was statistically insignificant.

The increase of CK was greatest on the first postoperative day in both groups and that of CRP on the third postoperative day in both groups. No differences were seen in CRP, IL-6 and CK levels and white blood cell counts between the compared groups (Table 2).

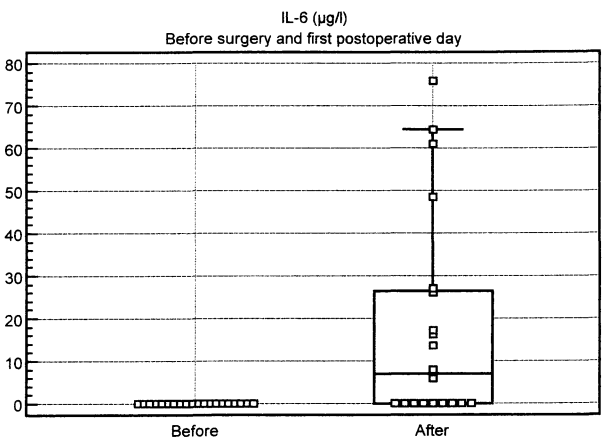

Figure 1. — *Plasma concentrations of IL-6 (μg/l) in both groups measured immediately before surgery and on the first postoperative day. All concentrations before surgery less than 5 μg/l.*

Discussion

Standard methods evaluating the duration of surgery, blood loss, perioperative morbidity, damage of tissue, subsequent pain, duration of hospital stay and hospitalization costs were used as comparative criteria for regular scalpel, laser or electrosurgery and harmonic scalpel in laparoscopic hysterectomy [8, 10, 11, 12]. Some authors, however, do not consider the assessment of the surgical method using the above-mentioned criteria to be sufficiently objective [13]. It is also more objective to measure perioperative stress by means of metabolic, hormonal and inflammatory response markers.

The harmonic scalpel was developed so that surgeons could make surgicial incisions without blood loss [14]. Hemostasis is achieved through coaptive coagulation. Tissue proteins are denatured,thus producing a protein coagulum that seals coapted vessel walls. Laser, electrical and ultrasonic energy all obtain hemostasis by coaptive coagulation. Laser and electrical energy denature tissue proteins through production of heat, whereas ultrasonic energy does this mechanically. Ultrasonic energy operates in the temperature range of 50° to 150°C, when protein coagulation occurs. Laser and electrosurgical energies create a temperature range of 100° to 400°C, when tissue desiccation (100-150°C) and charring (>150°C) occur [15]. Minimal heat production in the harmonic scalpel leads to a minimal zone of thermal injury and better healing compared with electrosurgery and lasers [16]. Our histopathology laboratory has also found less tissue damage in the uterus and round ligament when the ultrasonically activated scalpel was compared to electrosurgery. In our previous randomized study the perioperative clinical parameters of electrosurgery and the harmonic scalpel in laparoscopic hysterectomy were compared [8]. There were no significant differences between the groups in intraoperative or postoperative follow-up variables. In three patients with larger fibromyomas, the harmonic scalpel was ineffective (successful procedure rate 91.6%). Electrosurgery was effective in all cases without exception. The advantage of the ultrasonic technique included less charring and plume, better visualisation, and fewer thermal injuries, particularly with respect to the important surrounding pelvic structures. Electrosurgery was demonstrated to be superior to the harmonic scalpel in cases of larger fibromas as well as better in terms of cost effectiveness.

Surgical trauma, tissue injury, infection and inflammation are followed by a release of cytokines from monocytes, macrophages, fibroblasts and endothelial cells of damaged tissue. The major cytokine is interleukin-6 (IL-6). Receptors for interleukin-6 are found in cells with various functions, and when activated by this cytokine, they release secondary substances that mediate inflammation and tissue remodeling. IL-6 induces specific hepatic proteins,the most important of which is C-reactive protein [17,18]. CRP is the most extensively studied acute-phase response (APR) protein following trauma and surgery. CRP levels usually rise approximately 4-12 h after surgery and peak at 24-72 h, thereafter remaining

raised for about two weeks [2]. The expression of IL-6 is believed to be directly proportional to the extent of surgical trauma [19]. Both interleukin-6 and C-reactive protein have been shown to correlate with the severity of tissue trauma, blood loss and duration of surgical procedure [17, 18, 20].

Laparoscopic surgery is believed to lessen surgical trauma and thus cause less disturbance of immune function. The usual physiological reaction to injury, surgical or non-surgical, is an early rise in stress hormone levels together with a decrease in cellular immune response. The latter manifests as a reduction in lymphocyte and macrophage interaction, decreased activity of natural killer cells, decreased lymphocyte and neutrophil chemotaxis, and a reduction in delayed-type hypersensitivity. Polymorhponuclear (PMN) leucocytes play a key role in the host defence against invading micro-organisms. Surgical stress affects PMN function during the postoperative period [17, 21]. Despite a few contradictory reports, systemic immunity appears to be better preserved after laparoscopic surgery than after open surgery. However, the applicability of animal studies to the clinical situation, and the clinical significance of better preserved imunity in terms of postsurgical outcome, require further elucidiation [21].

During surgical stress, adrenergic activation occurs in both the adrenal medulla and peripheral symphathetic neurons and release of corticotrophin, cortisol and catecholamines follows. The site, extent and duration of surgery as well as the patient´s position and type of anesthesia may all contribute to the degree of adrenergic-sympathetic response during laparoscopy; an increase in arterial tension of carbon dioxide was closely associated with adrenergic-sympathetic activation [22, 23].

In the present study no difference in the perioperative clinical parameters (blood loss, duration of surgery, hospital stay and convalescence) between studied groups was found. Our results show that laparoscopic hysterectomy, whether performed by electrosurgery or harmonic scalpel is associated with significant stress response, with increases in the biochemical markers measured. Serum level of creatine kinase was significantly increased in both groups on the first postoperative day. CK has three subtypes of isoenzyme composed of two subunits, M (muscle) and B (brain). Isoenzyme MM typically is found in skeletal muscle. During operations where a transmuscular approach to the surgical field is used, the creatinie kinase isoenzyme MM is released into the circulation together with a lesser amount of isoenzyme MB. In gynecological surgery, therefore, the overall activity of CK may derive from the abdominal muscle wall and from the uterus, which however, contains almost exclusively isoenzyme BB [5]. The CK concentrations were highest on the first postoperative day, followed by elevation of CRP on the third day after both types of operative techniques. Shakespeare *at al.* [24] reported that the maximal concentrations of CRP were detected after 48 hours, but the severity of tissue damage, and complications, were also correlated with elevated CRP levels. According to the findings in laparoscopic cholecystectomy reported by Sietses *et al.* [25], the surgical immune response markers were similar to those with electrosurgery compared with those having the ultrasonic operative technique. The role of IL-6 in assessment of local immune changes in two different operative techniques of laparoscopic hysterectomy needs to be studied prospectively in larger groups of patients. In addition, the magnitude of tissue damage in laparoscopic hysterectomy may be important, as one study has shown the laparovaginal approach to result in fewer complications than with others [26].

In conclusion, our study demonstrates that electrosurgery and harmonic scalpel in laparoscopic hysterectomy were associated with similar clinical outcomes . Both the operative techniques results in a series of local and general immune and metabolic changes and responeses to stress. This may indicate that the difference in local thermal tissue injury measured by biochemical markers may be masked by systemic changes. The harmonic scalpel and electrosurgery are eaqually traumatic in terms of activation of the systemic immune response.

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