
GYNAECOLOGY

The Effect of Cold Gel Pack on Pain Reduction in Patients Undergoing Complete Surgical Staging: A randomized controlled trial

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ABSTRACT

Objectives: To study the effectiveness of a cold gel pack for reducing surgical wound pain in patients undergoing complete surgical staging

Materials and Methods: We enrolled women 18 or older with gynecologic malignancy and undergoing complete surgical staging by gynecologic oncologists between November 2021 and May 2022. They were randomly assigned to two groups: the study group – who received a cold gel pack applied to the low midline surgical wound 6 h post-operatively, and the control group – who received standard post-operative care. Post-operative pain at 2, 6, and 12 h were evaluated.

Results: Forty eligible women were enrolled. Post-operative pain at 12 h was lower in the study group albeit not statistically significant (4.95 ± 1.67 vs 5.90 ± 1.65 , $p = 0.08$). Time to first flatus and additional opioids consumption were also not significantly different between groups ($2,506.50 \pm 85.86$ vs $2,473.50 \pm 189.69$ min, $p = 0.2$) and (11.80 ± 3.37 vs 12.05 ± 3.52 mg, $p = 0.85$). No adverse events were observed.

Conclusion: Cold gel pack did not significantly reduce post-operative pain compared with standard post-operative care in patients undergoing complete surgical staging.

Keywords: cold gel pack, post-operative pain, surgical wound pain, complete surgical staging.

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ผลของการประคบด้วยถุงเจลเย็นเพื่อลดระดับความเจ็บปวดหลังผ่าตัดประเมินระยะโรคของมะเร็งนรีเวช การศึกษาแบบสุ่ม

ญาณินท์ ศรีรัศมี, กิตติยา วุฒิเบญจรัศมี, ทুমวดี ตั้งศิริวัฒนา

บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาประสิทธิภาพของถุงเจลเย็นในการลดระดับความเจ็บปวดของแผลผ่าตัดประเมินระยะโรคของมะเร็งนรีเวช

วัตถุประสงค์และวิธีการ: ผู้ป่วยมะเร็งนรีเวชอายุ 18 ปีขึ้นไป ที่ได้รับการผ่าตัดเปิดช่องท้องเพื่อประเมินระยะโรคโดยแพทย์ผู้เชี่ยวชาญสาขามะเร็งนรีเวช ตั้งแต่เดือนพฤศจิกายน 2564 ถึงเดือนพฤษภาคม 2565 โดยแบ่งเป็น 2 กลุ่มโดยการสุ่ม สำหรับกลุ่มทดลองจะได้รับการวางถุงเจลเย็นประคบบริเวณแผลผ่าตัดแนวตั้ง ที่ 6 ชั่วโมงหลังการผ่าตัด และกลุ่มควบคุมได้รับการดูแลหลังการผ่าตัดตามมาตรฐานเพียงอย่างเดียว และทำการประเมินระดับความเจ็บปวดของแผลผ่าตัดที่ 2, 6 และ 12 ชั่วโมง

ผลการศึกษา: ผู้เข้าร่วมการศึกษาจำนวน 40 คน พบว่าระดับความเจ็บปวดของแผลผ่าตัดที่ 12 ชั่วโมงในกลุ่มที่ได้รับการวางถุงเจลเย็นน้อยกว่ากลุ่มควบคุม แต่ไม่มีนัยสำคัญทางสถิติ (4.95 ± 1.67 vs 5.90 ± 1.65 , $p = 0.08$) ระยะเวลาในการผายลมครั้งแรกหลังผ่าตัด การเข้ายาแก้ปวดเพิ่มเติมไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($2,506.50 \pm 85.86$ vs $2,473.50 \pm 189.69$ นาที, $p = 0.2$) และ (11.80 ± 3.37 vs 12.05 ± 3.52 มิลลิกรัม, $p = 0.85$) และไม่พบภาวะแทรกซ้อนหรือผลข้างเคียงจากการใช้ถุงเจลเย็น

สรุป: การใช้ถุงเจลเย็นประคบบริเวณแผลผ่าตัดในผู้ป่วยที่ผ่าตัดประเมินระยะโรคของมะเร็งนรีเวช ไม่ได้ช่วยลดความเจ็บปวดของแผลผ่าตัดที่ 12 ชั่วโมงหลังการผ่าตัด เมื่อเปรียบเทียบกับการดูแลหลังผ่าตัดตามมาตรฐาน

คำสำคัญ: ถุงเจลเย็น, ความเจ็บปวดหลังผ่าตัด, ความเจ็บปวดของแผลผ่าตัด, ผ่าตัดทางมะเร็งนรีเวช, ผ่าตัดประเมินระยะของโรค

Introduction

Surgery often causes tissue injury and inflammation. In response, nociceptors are activated and transmit nerve signals (i.e., prostaglandins, interleukins, cytokines, and neurotrophins), which travel through the spinal cord towards the brain, where the sensation of pain is recognized. The neurotransmitters initiate a spinal reflex, resulting in increased muscle activity and tonicity at the site of injury. Other skin receptors include (a) thermoreceptors that are activated by changes in skin temperature, and (b) proprioceptors that detect physical changes in tissue pressure and movement – the activation of both inhibit nociceptors resulting in muscle relaxation and enhanced tissue blood flow^(1, 2).

Surgery-related morbidities impact patient outcomes and quality of life. Most gynecologic malignancies require surgical management to remove the macroscopic tumor and stage the disease to plan proper adjuvant therapies⁽³⁾. Complications often develop when post-operative pain management is inadequate, such as delayed ambulation, bowel ileus, lung atelectasis, venous thromboembolism, and infection, resulting in delayed post-operative recovery and prolonged hospitalization, especially in oncologic patients. Most surgical patients experience post-operative pain, and less than 50% receive adequate pain control management⁽⁴⁾.

There are two categories of post-operative pain management, medication and non-medication. Multimodal therapies (multimodal anesthesia plus adjunctive therapy) are usually recommended. As the innervation of the anterolateral abdominal wall arises from the anterior rami of spinal nerves T7 to L1, including intercostal nerves (T7-T11), subcostal nerve (T12), and iliohypogastric and ilioinguinal nerves (L1). Transversus abdominis plane (TAP) blocks are additional local anesthesia widely used to

diminish the post-operative pain of the required low midline incision. The target of the TAP block is the space between the internal oblique and transverse abdominis muscle where the nerves are located. The innervation to abdominal skin, muscles, and parietal peritoneum may be blocked, but tissue injury and inflammation are not eliminated⁽⁵⁾. The anesthetic effect of the TAP block ranges from 6 to 36 h⁽⁶⁾.

Several studies argue that non-medical pain management could be more appropriate because of fewer side effects, and it could synergize with other medical approaches, including thermal therapy⁽⁴⁾.

Cryotherapy is any application that removes heat from the body, causing vasoconstriction, reducing tissue metabolism, oxygen consumption, inflammation, and muscle spasms. Likewise, cryotherapy minimizes the inflammatory processes by activating thermoreceptors and proprioceptors, thereby aiding recovery after soft tissue trauma^(1,2). The most effective cryotherapy is between 10 - 15 °C within 72 h of injury, for 20 to 30 min, 2 to 4 times per day, or 30 to 45 min every 2 h^(7,8). Using an ice pack or cold gel pack applied to the surgical wound is a simple way to reduce post-operative pain. Other non-medical pain management include (a) transcutaneous electrical nerves stimulation, typically applied at the incision site (note: contraindicated in patients with a pacemaker or implanted defibrillator, lymphedema, and/or broken skin); and (b) cognitive modalities that include guided imagination and relaxation, which often require pre-operative education or training⁽⁴⁾.

Previous studies reported that cryotherapy effectively reduced post-operative pain and reduced post-operative additional opioid consumption without serious adverse events after repairing the inguinal hernia, benign gynecologic operations, exploratory laparotomy, episiotomy wound, and cesarean section⁽⁹⁻¹⁶⁾ using varies

rationale, for example cold pack applied at 2 h after the procedure for 20 minutes in study of Nuangpho, applied at 2 hours post operative and changed every 2 h for 2 consecutive times in study of Chumkam and Suwannalert. Furthermore, gynecologic malignancy operations—including total abdominal hysterectomy, bilateral salpingo-oophorectomy, partial omentectomy, and bilateral pelvic lymph nodes dissection—frequently have a longer incision length and include more traction force to provide good exposure of the intra-abdominal and pelvic organs. The consequence of these invasive procedures is severe tissue injury, inflammation, and greater post-operative pain.

The current study aimed to evaluate the effects of cryotherapy by applying a cold gel pack to reduce post-operative pain at the surgical wound after completing surgical staging for gynecologic malignancy.

Materials and Methods

This randomized controlled study was performed at the Department of Obstetrics and Gynecology, Khon Kaen Hospital, Thailand. The objective was to study the effectiveness of a cold gel pack in reducing post-operative pain in patients undergoing complete surgical staging compared with standard post-operative care without a cold gel pack. The study was approved by the Khon Kaen Hospital Institute Review Board in Human Research (KEF64017). The study included 40 women, 18 or older, diagnosed with gynecologic malignancy, undergoing complete surgical staging with a midline incision between November 2021 and May 2022. We excluded women who had cold hypersensitivity, active skin disease at the surgical site, received patient-controlled analgesia, or had any perioperative complications (including torn internal organs, drainage tube, or needed post-operative intensive care).

Computer-generated block randomization was performed and allocated using opaque sealed envelopes. Women who met the inclusion criteria were informed, and the gynecologic residents obtained consent after completing the surgical staging surgery and immediate post-operative care in recovery room. Participants were assigned to group 1 or 2 per number in the envelope.

Demographic data were recorded, including age, underlying disease, body weight (BW), height, body mass index (BMI), history of previous abdominal surgeries, and the gynecologic malignancy diagnosis. The physician recorded perioperative data and findings, including time start or surgery open and closed, operative findings, estimated blood loss (EBL), suture materials, surgical incision length measured in centimeters. The histopathological report was recorded when the findings were made available.

The study group received standard post-operative care and a cold gel pack (Nanomed: CSI-CH-I 450), which was refrigerated for 1 h. The gel pack was between 10 and 15°C when applied for 1 h above the surgical wound at 6 h after surgery by using stopwatch to ensure the exact time for applying the cold gel pack. The control group received standard post-operative care. Standard pre- and post-operative care included: (a) complete surgical staging by gynecologic oncologists; (b) standard general anesthesia with endotracheal tube TAP block using 1% lidocaine with adrenaline and 0.25% bupivacaine, corresponding to a maximum dose of 7 mg/kg lidocaine with adrenaline and 3 mg/kg bupivacaine injected between the transversus abdominis and internal oblique with ultrasound guided; (c) post-operative antibiotics prophylaxis of cefazolin 1 g (2 g if BW > 90 kg) intravenous every 6 h for 24 h or clindamycin 300 mg intravenous every 8 h for 24 h if patients had a drugs allergy; (d) post operative opioids; morphine

sulfate 2 mg (if body weight < 50 kg) intravenous every 4 h or 3 mg intravenous (if body weight > 50 kg) every 4 h for 24 h; (e) additional morphine sulfate to breakthrough pain if pain score ≥ 5 ; (f) post-operative prokinetic drug - metoclopramide 10 mg intravenous every 8 h if they had nausea or vomiting as the morphine sulfate side effects; and, (g) surgical wound covered with sterile gauze and waterproof patch and wound dressing if there was bleeding or oozing.

The primary outcome of the present study was a post-operative pain score at 12 h. Participants were asked to assess their post-operative pain score using a visual analog scale (VAS) (0 = no pain and 10 = worse pain) at 2, 6, and 12 h post-operatively. Those with a pain score ≥ 5 (severe pain)⁽⁴⁾ received additional analgesia (opioids). The secondary outcomes include time to first flatus and opioid consumption in the first 24 h post-operatively. Registered nurses checked and recorded the outcomes and any adverse events.

The sample size was based on the pilot study of 30 women (n = 15 in each group) using two independent mean formula. Mean \pm standard

deviation (SD) of post-operative pain score in study group and control group were 4.27 ± 1.28 and 6.07 ± 1.98 , respectively. The sample size was 40 participants (20 in each group), calculated per a type 1 error of 0.05 and a power of 90%, and dropout rate of 5%. The data were analyzed using STATA statistical software version 13.0. The student's t-test was used for continuous variables and reported as means and SD. The Chi-square and Fisher's exact test for categorical variables were reported as numbers and percentages. A p value < 0.05 was considered statistically significant.

Results

Forty women scheduled for elective complete surgical staging surgery were enrolled in the study, of whom 22 were diagnosed with ovarian cancer, 13 with endometrial cancer, 4 with uterine sarcoma, and 1 with fallopian tube cancer. All participants were randomized into the study group (cold gel pack) and the control group post-operatively. None of the participants was excluded, withdrew, or dropped out from the study (Fig. 1).

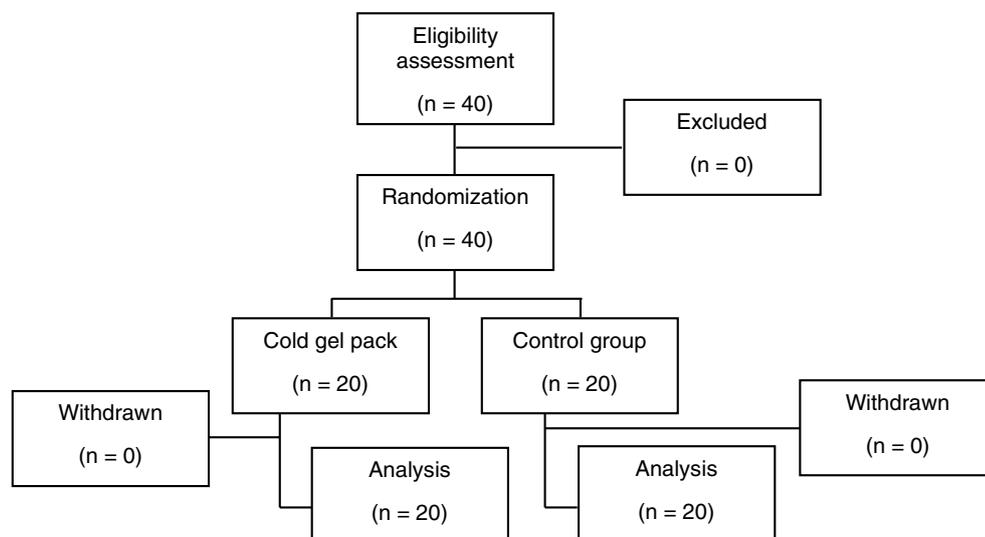


Fig. 1. Study flow diagram.

The demographic data between groups were similar, including ages, BMI, underlying diseases, and prior abdominal surgery. The peri-operative data and findings revealed that EBL was significantly lower in the study group than in the control group (227.50 ml \pm 72.95 vs. 347.50 ml \pm 96.8, $p = 0.01$) and there were

no significant differences in incision length, operative time, suture materials, and opioids consumption before intervention. The post-operative pain scores at 6 h (before applying the cold gel pack) was higher in study group than control group but were not statistically significant (7.90 \pm 2.12 vs 6.65 \pm 1.81, $p = 0.05$) (Table1).

Table 1. Baseline Characteristics.

	Cold gel pack group (n = 20)	Control group (n = 20)	p value
Ages (years)* (95% CI)	59.80 \pm 1.74 (56.17 - 63.43)	57.55 \pm 2.07 (53.20 - 61.90)	0.41
BMI (kg/m2)* (95% CI)	24.28 \pm 1.0 (22.26 - 26.29)	24.30 \pm 1.21 (21.76 - 26.84)	0.56
Underlying diseases n (%)			
DM, HT	9 (45)	8 (40)	
No	11 (55)	12 (60)	0.37
Prior abdominal surgery n (%)			
Yes	13 (65)	12 (60)	0.74
Length (cm)* (95% CI)	14.58 \pm 0.68 (13.14 - 16.01)	12.95 \pm 0.41 (12.09 - 13.81)	0.45
Operative time (min) * (95% CI)	98.15 \pm 5.86 (85.88 - 110.42)	112.40 \pm 9.77 (91.95 - 132.84)	0.05
EBL (ml)* (95% CI)	227.50 \pm 72.95 (74.81 - 380.19)	347.50 \pm 96.8 (144.84 - 550.15)	0.01
Suture materials n (%)			0.53
Nylon	9 (45)	11 (55)	
Staples	11 (55)	9 (45)	
Post-operative diagnosis n (%)			0.09
CA ovary	8 (40)	14 (70)	
CA endometrium	10 (50)	3 (15)	
CA fallopian tube	0 (0)	1 (5)	
Uterine Sarcoma	2 (10)	2 (10)	
Pre-intervention opioids consumption (before 6 h) (mg)	3.30 \pm 0.80	3.45 \pm 0.94	0.56
Post-operative pain score at 6 h	7.90 \pm 2.12	6.65 \pm 1.81	0.05

* mean \pm standard deviation

BMI: body mass index, DM: diabetes mellitus, HT: hypertension, EBL: estimate blood loss, CI: confidence interval

The results indicated that a cold gel pack reduced post-operative pain score at 12 h in the study group compared to the control group (4.95 \pm 1.67 vs. 5.90 \pm 1.65, $p = 0.08$), albeit not statistically significant. In terms of the secondary outcomes, there was no significant difference in time to first flatus between

groups (2,506.50 min \pm 85.86 vs 2,473.50 min \pm 189.69, $p = 0.2$), or post-operative additional opioid consumption (11.80 mg \pm 3.37 vs 12.05 mg \pm 3.52, $p = 0.85$) (Table 2). However, the study group had less additional opioid consumption than the control group. It was noted that there were no post-operative

complications in either group, such as re-exploring laparotomy or infection, and none of the participants

had any adverse events after applying the cold gel pack.

Table 2. Outcomes of the study.

	Cold gel pack group (n = 20)	Control group (n = 20)	p value
Primary outcome			
Post-operative pain score at 12 h	4.95 ± 1.67	5.90 ± 1.65	0.08
Secondary outcomes			
Time to first flatus (min)* (95% CI)	2,506.50 ± 85.86 (2,326.78 - 2,686.22)	2,473.50 ± 189.69 (2,076.47 - 2,870.53)	0.20
Opioid consumption (mg)* (95% CI)	11.80 ± 3.37 (9.26 - 15.25)	12.05 ± 3.52 (9.15 - 17.28)	0.85

* mean ± standard deviation
CI: confidence interval

Discussion

To minimize post-operative pain, multimodalities anesthesia takes more role nowadays. In this study, we used the combined general anesthesia with TAP block in all participants and additional cold gel pack in the study group. While Nuangpho et al and Chumkam et al applied cold gel pack for 20 minutes and 2 h postoperative, then changed every 2 h for 2 consecutive times, respectively. They found that the cold gel pack was effective in reducing post-operative pain without adverse events. However, complete surgical staging

takes longer time than in benign gynecologic surgery and cesarean section. Hence, we chose the duration of applying cold gel pack for 1 h in study group for the convenience, avoid adverse event especially frostbite and anticipated to improve the efficacy of cold gel pack. And post-operative pain score at 12 h may least the effect of TAP block. The primary outcome of this study found that the difference in post-operative surgical wound pain at 12 h in women undergoing complete surgical staging trended to be less in the study group than in the control group albeit not statistically significant (Fig. 2).

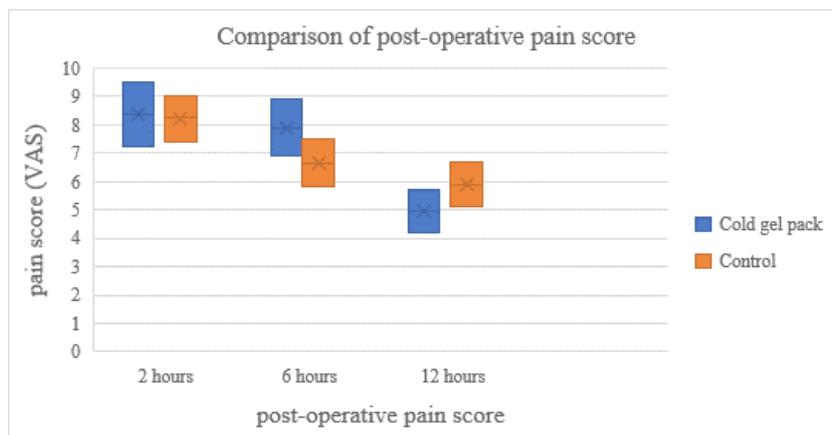


Fig. 2. Comparison post-operative pain scores between groups.

The lesser EBL may reflect the easier procedures and less intraabdominal adhesion but the operative time did not significantly difference between groups, so that the period of traction or tissue injuries were not difference. Moreover, we randomized the participants into 2 groups and baseline characteristics were not statistically difference, this factor might not have a difference effect to the outcome.

Our findings were consistent with Finan et al who reported no effect of cold gel pack in improving post-operative pain control in gynecologic patients undergoing exploratory laparotomy, measured as the amount of post-operative morphine sulfate consumption on the first operative day⁽¹¹⁾. To contrast, Ammara et al⁽⁹⁾, Nuangpho et al⁽¹³⁾, Chumkam et al⁽¹⁴⁾, Suwannalert et al⁽¹⁵⁾, and Siripanthong et al⁽¹⁶⁾ reported that ice packs or cold gel packs significantly lowered post-operative pain scores without any adverse events. The variation across studies might be due to differences in study design (e.g., type of operation and incision, operative time, time to first applying and duration for applying the cold gel pack on the surgical wound, type of cold gel pack, and the anesthesia used general anesthesia with/without additional TAP block). TAP block blocks the innervation at the abdominal wall so that the patients experience less post-operative pain. Type or length of incision wound that in malignant operations might be larger incision and require more traction than benign operations to provide optimized approach. The more traction and larger incision, the more tissue injuries, and inflammation.

Suwannalert et al⁽¹⁵⁾ reported that patients undergoing cesarean section with a low midline incision and receiving post-operative cold gel packs applied at the surgical site have significantly lower post-operative pain scores from 6 h to 24 h. We identified a similar trend in our cold gel group.

Notwithstanding, the decreasing trend in post-operative pain scores at 12 h in the study group could be helpful for designing future studies. It is expected that observing post-operative pain scores for a longer period could provide more insightful data. Cold gel

packs may still be helpful in patients who are allergic to analgesic drugs, have adverse events from opioids, or suffer from breakthrough pain. In such cases, cold gel packs could be used to mitigate the pain with a low risk of adverse events.

The strengths of this study were (a) it was a randomized controlled trial, and (b) no participants were lost or dropped out. Limitations included that (a) it was not blinded to both participants and medical workers, and (b) environmental factors may have interfered with temperature measurement of the cold gel pack.

Conclusion

In conclusion, the effect of a cold gel pack was not significant in reducing post-operative pain compared with standard post-operative care in patients undergoing complete surgical staging and receiving regional anesthesia for post-operative pain control.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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