Comparison of the effect of compression stockings with heparin and enoxaparin in the prevention of deep vein thrombosis in lower limbs of hysterectomy patients

Abstract

Introduction: Deep vein thrombosis is a common complaint in patients which can be caused by factors such as surgery. Medical and mechanical methods as stockings are used to prevent this complication. Although several studies have examined and compared the effects of these methods, no study has compared these methods in hysterectomy. The purpose of the current research was to compare the use of heparin and enoxaparin alone and along with compression stockings in terms of incidence of deep vein thrombosis.

Methodology: To do the research, 80 patients were randomly assigned into 4 groups of heparin alone, heparin along with stockings, enoxaparin alone, and enoxaparin along with stockings (each contained 20 patients). In the first group, heparin at the dose of 5000 units per 12 hours for 3 days was used subcutaneously. In the second group, in addition to heparin, compression stockings were also utilized. In the third group underwent prophylaxis, enoxaparin at the dose of 40 mg per day for three days was used subcutaneously. In the fourth group, in addition to enoxaparin, compression stockings were also used. Two weeks after the completion of the medical and mechanical prophylaxis, thrombosis was examined through Doppler ultrasonography. Data were analyzed using SPSS, version 22, software and chi-square test (Fisher test) and ANOVA.

Results: Only two cases of thrombosis (one case in the first group and one case in the third group) were observed. No case of thrombosis was seen in groups receiving compression stockings along with medicine. Fisher’s exact test indicated that there was no significant difference among four groups in terms of incidence of thrombosis.

Conclusion: Adding compression stockings to heparin or enoxaparin had no significant effect on reducing the incidence of deep vein thrombosis in patients with hysterectomy.

Keywords: heparin, enoxaparin, stockings, deep vein thrombosis, hysterectomy.

Conclusión: la adición de medias de compresión a heparina o enoxaparina no tuvo un efecto significativo en la incidencia de trombosis.
reducción de la incidencia de trombosis venosa profunda en pacientes con hysterectomía.

**Palabras clave:** heparina, enoxaparina, medias, trombose venosa profunda, hysterectomía.

Venous thromboembolism, including deep vein thrombosis and pulmonary embolism, is a common complaint in ill patients. Ill patients are prone to deep vein thrombosis due to factors such as surgery, catheter, immobility, or the use of sedative or crippling medicines. Clinical processes of this disease can be very risky. For this reason, preventive measures such as the use of anticoagulants in patients prone to deep vein thrombosis are crucial. Venous thromboembolism is the second most common cardiovascular disease following myocardial infarction. The high prevalence of pulmonary embolism and its high mortality, especially when it is not diagnosed, indicates the need for proper use of imaging techniques for evaluation of patients suspected of pulmonary embolism.

The standard diagnostic method for patients suspected of pulmonary embolism starts with perfusion ventilation scanning. Almost half of the patients with pelvic vein thrombosis or proximal deep proximal vein thrombosis in lower limbs have pulmonary thrombosis, which is usually not symptomatic. In this regard, leg vein thrombosis alone has a lower risk for pulmonary embolism.

Deep vein thrombosis is considered as an immediate threat to the patient’s life with a potential to become a pulmonary embolism. It also leads to long-term venous insufficiency in the lower limb veins. These patients are mostly asymptomatic. Patients undergoing neurovascular surgery are more prone to venous thromboembolism. The factors predisposing these people to thromboembolism include long duration of surgery, the release of brain thromboplastic substances during surgery, the need for long rest after surgery and immobilization of the upper and lower limbs, the possibility of neurological injuries during surgery, the need for treatment with high doses of glucocorticoids in some patients, and the need for using osmotic and non-osmotic diuretics and dehydration.

Deep vein thrombosis diagnosis in the legs is usually difficult, since only one of several leg veins might be involved and might cause no disturbance in the blood flow of legs.

In this group of patients, D dimer, as a molecule resulting from fibrin breakdown, is a sensitive indicator, although its specialty is low. Venous duplex ultrasonography, as a non-invasive and simple method, is commonly used in this group of patients for diagnosis. The sensitivity of this diagnostic method is 75% in deep vein thrombosis and 75% for symptomatic cases in leg. Anticoagulants reduce the blood coagulation. These medicines are known as blood diluents and are used to stop the formation of clots in people who are at risk of formation of clots and preventing the growth of current clots. These substances break down the clots which have not been present before (the body will dissolve the current clots over time). Anticoagulants can be used as pills or in injecting form. In the study conducted by Geerts et al., it was shown that in patients who used mechanical prophylaxis, ultrasound findings were found in the favor of thrombosis, while in patients who used medicine prophylaxis, no finding in favor of thrombosis was found.

In a study conducted by Mohammad Zadeh Ghare Baghi et al., in Tabriz, 75 patients with traumatic spinal cord injury were divided into three groups (each contained 25) and three methods of compression stockings along with enoxaparin and compression stockings along with heparin and compression stockings alone were compared to prevent deep vein thrombosis. No significant difference was found in the method of prevention of thrombosis among the three groups in terms of adding medical prevention methods of heparin and enoxaparin to mechanical methods in these patients.

Hysterectomy is one of the most commonly used surgeries. Following cesarean section, it is the second most common surgery in the United States. In this country, about 40% of women have hysterectomy before the age of 60. The likelihood of this surgery in women depends on a number of factors such as age, race, living place, gender, physician.

The most important indications for this surgery include leiomyoma, abnormal uterine bleeding, adenomyosis, endometriosis, uterine prolapse, pelvic pain, and treatment-resistant dysmenorrhea. This surgery is performed in severe vaginal bleeding after labor. Cervical, uterine and ovarian malignancies and inflammatory diseases are some of the causes for this surgery. In a study, 2704 patients were evaluated for the risk of thrombosis before the surgery and it was found that 74 of them faced a risk for thrombosis. In the mentioned study, 70% of patients re-
ceived heparin before and after surgery, and 28% received only heparin after surgery. A total of 7 patients had thrombosis\(^2\). In another study, the incidence and consequences of deep vein thrombosis in gynecological surgery were examined. The results showed that 53 patients had thrombosis or pulmonary embolism after 30 thousand surgeries (1 case per 500 surgeries). In the mentioned study, 91% of patients received a type of prevention. The rate of embolism and thrombosis was very low in patients with benign disease, anesthesia less than 3 hours, and no history of embolism or thrombosis or v-factor reduction (one case per 4,000 surgeries)\(^3\).

Several studies have been conducted on the effects of different methods of medical and mechanical prevention of thrombosis in various surgeries and diseases such as trauma\(^4\), spinal cord injury\(^5\), hip joint replacement\(^6\), brain tumor patients under craniotomy\(^7\), stroke\(^8\), spinal surgery\(^9\) and even gynecological diseases\(^10,11\). In some cases, a significant difference between the use of different medical and mechanical methods alone or in combination with each other has been reported. In some cases, their effects have been reported equal. However, it seems that no study has yet been conducted to compare the effects of heparin and enoxaparin and compression stockings on prophylaxis of deep vein thrombosis in hysterectomy patients. Thus, conducting a study to compare heparin and enoxaparin and compression stockings in prophylaxis of deep vein thrombosis seems to be necessary in hysterectomy patients, so that if the reduction in the incidence of thrombosis was seen in people using any prophylaxis, the same treatment could be used in patients to reduce thrombosis and its complications\(^12\).

Inclusion criteria of study included women requiring hysterectomy and aged less than 60 years. Patients referring to the radiology unit of Afzalipour Hospital in Kerman during the years 2017-2018 who had undergone hysterectomy were selected as the participants of the current study.

The research exclusion criteria included cases of hysterectomy due to malignancy, patients with the history of taking aspirins, patients with a history of pelvic trauma, patients with a history of diabetes, patients with a history of heart failure and lung disease, patients with a history of previous thrombosis, patients with history of long-term hospitalization, and obese patients (20% ideal weight<). Convenient sampling was used in this study. The sample size was determined to be 80 people based on cases of hysterectomy surgery in women. Patients were randomly divided into four groups, including prophylaxis along with heparin, heparin along with compression stockings, prophylaxis along with enoxaparin, and enoxaparin along with compression stockings. They were assigned randomly into these groups using random numbers’ table. In the first group, subcutaneous heparin at the dose of 5000 units per 12 hours for 3 days was used. In the second group, in addition to heparin, compression stockings were utilized. In the third group underwent prophylaxis, subcutaneous enoxaparin at the dose of 40 mg per day for three days was used. In the fourth group, in addition to enoxaparin, compression stockings were also used.

The compression stockings used by patients were top of knee type and they were made in Iran. The medical treatment lasted up to three days after surgery. The use of stockings was also continued immediately after leaving the operating room up to two weeks at home. Two weeks after the completion of the medical and mechanical prophylaxis, the patients underwent Doppler ultrasound by a radiologist who did not have information on prophylaxis method. Doppler ultrasound findings were recorded in the checklist (presence or absence of thrombosis). Data were analyzed using SPSS, version 22, software. Chi-square (Fisher’s test) and ANOVA tests were used to analyze the data and compare the groups. The significance level was considered less than 0.05.

All ethical considerations were observed in this research. All steps and research objectives were explained for them. Their unwillingness to participate in the study had no effect on the normal course of treatment, and patients were allowed to leave the study at any time. Moreover, no additional cost including ultrasound was imposed on the patients. The license was obtained from Ethics Committee of Kerman University of Medical Sciences before the study began and the necessary code was obtained for the clinical trial study.

The mean age of the patients was 50.16 ± 5.66. The minimum and maximum age was 40 and 60 years, respectively. The mean age of the patients in four groups is presented in the table. As shown, there was no significant difference among the groups in terms of age.

Based on (Table 1), only two cases of thrombosis (one case in the groups used only heparin and one case in the group used only enoxaparin) and no case of thrombosis was seen in the groups using compression stockings in addition to medicines. Fisher’s exact test showed that there was a significant difference between the use of heparin alone or heparin along with compression stockings (P=0.5), between heparin group and enoxaparin group (P=0.756), and between the group used enoxaparin alone and the group used enoxaparin along with stockings (P=0.5) in terms of incidence of thrombosis.
In this study, 80 patients in 4 groups were studied. In two groups, heparin and enoxaparin were used alone. In two other groups, in addition to these medicines, compression stockings were used. The results revealed that only two cases of deep vein thrombosis occurred (2.5%). The mentioned two cases included 1 case in the heparin group and 1 case in the enoxaparin group. There was no case of thrombosis in the groups using these stockings. All research hypotheses were confirmed and it was found that there was no significant difference between the four groups in terms of incidence of deep vein thrombosis. There are not many studies regarding the use of medical methods to prevent thrombosis along with mechanical methods in hysterectomy. Previous studies had mainly focused on the risk factors of thrombosis in gynecological surgery or the effects of different types of medical therapy in prevention of this complication. Studies have also been conducted on other surgical procedures.

In short, the results showed that deep vein thrombosis was very low in hysterectomy (2.5%). In a retrospective case-control study, the rate of complications of abdominal and vaginal hysterectomy during the years 2001 and 2002 in Shahid Yahyanejad Hospital of Babol was reported as follows: 32.7% in abdominal group and 5.3% in the vaginal group. Rate of thrombosis was not reported in this study20. Another study showed that out of a total of 2704 patients undergoing gynecological surgery, only 74 had risk for thrombosis, and only 7 patients had thrombosis. The researchers concluded that the incidence of thrombosis in gynecological surgery was not high and had a close association with the risks of thrombosis20. Another study examined the incidence and consequences of deep vein thrombosis in gynecological surgery. It was found that 53 patients had thrombosis or pulmonary embolism after 30000 gynecological surgeries (one case per 500 surgeries).

In the mentioned study, 91% of patients received a type of prevention. The rate of thrombosis or embolism was significantly lower in patients with benign disease, anesthesia less than 3 hours, and no history of embolism or thrombosis, or v-factor reduction (one case per 4,000 surgeries). The researchers concluded that the rate of embolism and thrombosis in women undergoing gynecological surgery was low21.

The present study revealed no significant difference between two types of medicines (heparin and enoxaparin) in terms of incidence of deep vein thrombosis (1 case of thrombosis was observed in each group). Various studies have been conducted to compare the effects of various medicines. For example, a study compared the effects of heparin and enoxaparin in preventing deep vein thrombosis after hip joint replacement surgery. The first group received heparin at a dose of 5,000 units per 8 hours for 20 days, the second group received enoxaparin at the dose of 40 mg per day for 10 days, and the third group received enoxaparin at the dose of 40 mg per day for 20 days.

In this study, 31 patients (77.5%) in the first group, 23 patients (57.5%) in the second group, and 4 (10%) patients in the third group had symptoms of thrombosis during hospitalization. The difference between the first and second groups (p = 0.047), the difference between the first and third groups (p < 0.001) and the difference between the second and third groups (p < 0.001) were significant. Hence, enoxaparin at the dose of 40 mg per day for 20 days was recognized more appropriate23. In another study, the effect of normal heparin and low molecular weight heparin (clexane) on the prevention of deep vein thrombosis in patients with brain tumor under craniotomy was compared. The first group received clexane at the dose of 40 mg subcutaneously and the second group received normal heparin at the dose of 5000 units per 12 hours after craniotomy surgery. The rate of deep vein thrombosis included 14 (18.2%) people in the normal heparin group and 3 (3.9%) people in the second group. This difference was significant. Generally, it was found that clexane was more appropriate than normal heparin24.

Some studies have also been conducted on gynecological surgery. For example, a study was conducted to compare low molecular weight heparin with the lack of receiving this medicine in gynecological surgery. In the non-treated group, 4 cases of pulmonary embolism (0.22%), two cases of fatal embolisms (0.11%), 13 cases of proximal deep vein thrombosis (72.0%) and 41 cases of distal deep vein thrombosis (2.3%) were seen. In the second group, no case of embolism was observed. Rather, 3 cases of proximal deep vein thrombosis (0.16%) and 18 cases of distal deep vein thrombosis (0.96%) were observed. Among

### Table 1. Comparison of mean age and thrombosis in the studied group

<table>
<thead>
<tr>
<th>Groups studied</th>
<th>Age mean and SD</th>
<th>Thrombosis *</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin</td>
<td>50.2 ± 5.7</td>
<td>(5) 1</td>
<td>0.8160</td>
</tr>
<tr>
<td>Heparin and compression stockings</td>
<td>50.5 ± 5.7</td>
<td>-</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>49.15 ± 5.7</td>
<td>(5) 1</td>
<td></td>
</tr>
<tr>
<td>Enoxaparin and compression stockings</td>
<td>50.8 ± 5.8</td>
<td>(100) 20</td>
<td></td>
</tr>
</tbody>
</table>

*Numbers are presented in number (percentage)
patients with vaginal hysterectomy, in the control and treatment groups, only 1 patient out of 41 (2.4%) patients and 2 patients out of 40 patients (5%), respectively, had deep vein thrombosis.

In the control group undergoing abdominal hysterectomy, 2 cases of pulmonary embolism (0.27%), 1 fatal embolism (0.13%), 9 cases of proximal deep vein thrombosis (1.2%) and 20 cases of distal deep vein thrombosis (2.7%) were observed. In patients undergoing abdominal hysterectomy and received heparin, 1 case of proximal deep vein thrombosis (0.13%) and 10 cases of distal deep vein thrombosis (1.4%) were observed. Thus, the use of heparin with low molecular weight was effective in preventing thrombosis in women undergoing surgery. Another study was conducted to compare the effect of low molecular weight heparin along with dihydroergotamine (LMWH-DHE) and conventional heparin-DHE along with Acenocoumarol (heparin-DHE / A) in 191 patients undergoing gynecological surgery.

It was found that LMWH-DHE was not different from heparin-DHE/A in preventing thrombosis and the rate of bleeding and side effects. Only one case of thrombosis occurred in each group and only one case of non-fatal pulmonary embolism occurred in the LMWH-DHE group. The authors concluded that LMWH-DHE was an attractive, safe and effective method in preventing thrombosis in gynecological surgery.

In general, above-mentioned studies suggested that medical methods were effective in preventing thrombosis in surgery, and lower molecular weight heparin was more appropriate than normal heparin in surgeries, including gynecological surgery. Although the rate of thrombosis was low in both groups in the present study (1 case out of 20 cases), no significant difference was seen between the two medical groups, which might be due to the small sample size of the study.

In the present study, no case of deep vein thrombosis was seen in the groups using the medicine along with compression stockings. However, the comparison of these two groups (heparin along with stockings and enoxaparin along with stockings) and their comparison with medicine alone showed that using stockings along with medicine did not significantly reduce the incidence of thrombosis. In this regard, no study was found in the area of hysterectomy or gynecological surgery. In other surgeries, the use of medical and mechanical methods such as stockings has been compared. For example, a study was conducted to compare the effect of using compression stockings alone or along with low doses of heparin or enoxaparin in preventing deep vein thrombosis in patients with spinal cord injury. Compression stockings along with enoxaparin (40 mg/day) were subcutaneously used in the first group, compression stockings along with low doses of heparin (5000 units per 12 hours daily) were subcutaneously used in the second group, and only stockings were used in the third group. Based on the findings, a total of 5 patients (6.7%) had deep vein thrombosis (3 patients in the first group and 1 patient in each of the other groups). No significant difference was observed among three groups.

In another study, the effect of compression stockings and heparin on the prevention of deep vein thrombosis in stroke patients was compared.

In the first group, heparin at a dose of 5000 units per 12 hours was subcutaneously used, and in the second group, compressions stockings were used during the hospitalization. In general, 5 patients (5%) had thrombosis during the study, which 2 (4%) of them were in the heparin group and 3 (6%) were in the stockings group. As a result, no significant difference was seen in terms of the incidence of thrombosis. A study was conducted in India in 2009 on patients with spinal cord injuries. In this study, 279 patients receiving physiotherapy were studied in two groups of heparin and mechanical prevention (physical therapy alone). Based on the results, the rate of thrombosis was 1.8% in the heparin group and it was 3% in the second group. Thus, the use of heparin with a preventative dose had no effect on reducing thrombosis. Moreover, the use of mechanical methods was effective in reducing deep vein thrombosis. These studies suggested that although the use of mechanical methods was effective, adding them to medical method, did not necessarily produce a significant difference in the reduction of deep vein thrombosis. These results were in line with those of the present study.

Conclusions

In summary, this study revealed no significant difference between heparin and enoxaparin alone or in combination with compression stockings in terms of incidence of deep vein thrombosis. Based on the research results, the following recommendations are presented:

1- Replication of the current research in other centers and conducting similar research on other gynecological surgeries.

2- The current research did not reveal a significant difference among different groups in terms of incidence of deep vein thrombosis, which might be due to a small sample size. Therefore, it is recommended that the current research can be replicated with a larger sample size.

3- It is recommended that in addition to deep vein thrombosis, other complications such as the duration of hospitalization and pulmonary embolism can be considered in future studies.
References


