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Effects of Intramesosalpingeal oxytocin injection in keep the tube in surgery of none ruptured ectopic pregnancy

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A B S T R A C T

Over the past decade, the incidence of ectopic pregnancy (EP) upward and early detection of this situation is so important. Ectopic pregnancy is seen in about 6-16% of cases of women in their reproductive years. The aim of this study was evaluation effects of Intramesosalpingeal oxytocin injection in keep the tube in surgery of none ruptured ectopic pregnancy. In a clinical trial that performed in the Department of Obstetrics gynecology, Tabriz University of Medical Sciences on women with none ruptured ectopic pregnancy, effects of Intramesosalpingeal oxytocin injection in keep the tube in surgery of none ruptured ectopic pregnancy evaluated. In our study, Drop rate of BHCG loss after surgery in patients with Intramesosalpingeal oxytocin injection was $21.36 + 27.25(P=0.141)$. The rate of intra-operative bleeding in patients with Intramesosalpingeal injection of oxytocin significantly less than intra-operative bleeding in patients treated without Intramesosalpingeal injection of oxytocin($P=0.010$). Of the ease of removal of the products of ectopic pregnancy in patients with Intramesosalpingeal injection of oxytocin was significantly easier and easier, and also the need to remove the tube during surgery in patients with Intramesosalpingeal injection of oxytocin was significantly lower($P<0.001$). Patency of the fallopian tubes in patients with Intramesosalpingeal injection of oxytocin at 2 months late postoperatively was significantly higher ($P=0.012$).The results show that Intramesosalpingeal injection of oxytocin in patients with un-ruptured EP decreases bleeding, increasing the ease of removal of the products of ectopic pregnancy and are decreasing tubal resection. The patency of the fallopian tubes at 2 months postoperatively in patients treated with Intramesosalpingeal injection of oxytocin was significantly higher. So it can be used in this surgical procedure that is performed to maintain the pipeline proposed.

Introduction

In the last decade the incidence of ectopic pregnancy (EP) had an increasing trend. EP is seen in 6 -16% of women in reproductive

age (1). The early diagnosis of this condition is so important. 3D vaginal Doppler ultrasonography with BHCG test has

provided a rapid diagnosis of this condition (2).

The supportive treatment for EP along with laparoscopy is improving and caused a rapid treatment. The supportive surgery for detaching the trophoblastic from endosalpinx, because of its high risk is so difficult which can cause salpingectomy (3). In most cases, the surgery can be prevented with medical therapy and follow up, with all of this, some patients are not good candidates for medical treatment and the surgery is the treatment of choice.

Hagenius and colleagues reported their results of an interventional study as an unsuccessful conservative therapy in the cases of EP and the need for intervention in most cases of this condition (4) the effect of oxytocin is not clearly understood in the studies. Oxytocin shows two phenomenons, first, it causes salpinx contractions, as the contractions in the myometrium. Second, it can produce a vasoconstriction in mesosalpinx artery (5).

In the study of Fedel and colleagues on the effect of the injection of 20 units of Oxytocin to mesosalpinx in laparoscopy, it is concluded that oxytocin improves the surgical treatment. With regard to the importance of bleeding and the reserve of urethral tubes, the need for intensive studies is felt (1).

Salpingectomy is the most common surgery for ectopic pregnancy. This option is chosen for torn urethral tubes, but in cases with torn urethral tubes, the conservative surgical methods such as salpingectomy and segmental resection are chosen. Surgery can be done in both laparoscopic and laparotomy methods. The recommended surgical method for the unruptured EP is the linear salpingectomy. A longitudinal tear is made

on the anti-mesenteric surface on the prominent mass using cutter, laser or scissor and the products are evicted using forceps or irrigation. The using of diluted vasopressin (1 unit/1 ml) or oxytocin (20 units) injection to the mesosalpinx can reduce the number of electro cutters needed for hemostasis. Incision can be kept open or can be closed, the long term reproductive results are equal in both methods (6).

The conservative management of EP is improved due to the early diagnosis of the disease, but in conservative surgery, the detachment of trophoblastic from the endosalpinx can causes severe bleeding and results in the salpingectomy. The linear salpingectomy is successful in about 80% of cases and in the rest of cases , the bleeding can lead to the tubectomy or in some cases the surgeon may use intensive coagulation which the aim of conservative is not achieved leading to relapse of EP(3).

In the past, vasoconstrictors such as Adrenalin and Vasopressin was used in controlling the bleeding (7) but was abandoned due to the systemic complications (8). Based on the known constrictor effects of Oxytocin on the urethra, Fedele and colleagues have studied its effects on the muscular fibers of salpinx in women with tubal pregnancy and showed that the intra mesosalpinx injection of oxytocin can accelerate the conservative surgery of EP (1) but since the sample size of this study was limited the study on reproductive prognosis of this methods had been suggested. The aim of this study is the evaluation of the topical oxytocin as a supportive treatment in conservative treatment in patients with EP who underwent open or laparoscopic surgery with diagnosis of unruptured EP. In this study, we evaluated the effect of oxytocin plus normal saline in controlling the

bleeding during and after the salpingectomy and reserving the urethral tubes and compared with the cases which were received the normal saline alone. The primary outcome criteria included the control of bleeding during the salpingectomy and the ease of eviction of pregnancy products and the need for change the procedure to the salpingectomy the secondary outcome is Tube patency 2 months after surgery.

Methods and Materials

In a clinical trial in the Department of Obstetrics and gynecology, in Tabriz University of Medical Sciences, Center for Research on Women's reproductive health in women with ruptured ectopic pregnancy the effect the oxytocin injection in mesosalpinx in reserving the urethral tubes in the surgeries of unruptured ectopic pregnancy was investigated.

During the year 2012, 67 patients with ectopic pregnancy were enrolled into the study they were randomly divided into two groups.

67 women who were diagnosed with unruptured ectopic pregnancy by laparoscopy or laparotomy were enrolled. Patients were divided into two groups: the first group received 20 units oxytocin diluted in 20 ml saline that was injected in mesosalpinx under the ectopic pregnancy and the second group received normal saline only.

3 min after injection was salpingectomy was tried and the pregnancy products were evicted. Amount of blood loss during surgery, requiring removal of the tube due to the severity of bleeding, coagulation times were noted. Based on the amount, bleeding severity was scored (mild - moderate and

severe). (3 = abundant, 2 = moderate, 1 = minimal). Bleeding at the site of pregnancy, as well as the ease of removal of the products of pregnancy was scored. (Difficult = 3, moderately difficult = 2 easy = 1), and require of the conversion of surgery to salpingectomy was investigated. β HCG levels were measured before surgery, after surgery and then every 3 days until the β HCG measurements were negative. Preoperative hematocrit levels were measured 6 hours after surgery. Two months later, all patients were treated and the degrees of openness of the fallopian tube were recorded.

Statistical analysis

Data were entered into statistical software Spss 17.0. The statistical test, Chi-square, Man-Whitney U, X² and T-test was used for statistical analysis with P <0.05 was considered statistically significant.

Ethical considerations

For all patients who entered the study, written informed consent has been obtained after giving the necessary information and the effects and consequences of the acts described to patients in the language understandable.

Results and Discussion

In this study, 67 patients with EP with and without Intramesosalpingeal injection of oxytocin have been treated and the following results were:

The mean gestational age in patients treated with and without Intramesosalpingeal injection of oxytocin were 5.4 ± 1.07 and 5.34 ± 1.37 weeks respectively (P=0.835). Mean baseline β HCG levels in patients treated with and without Intramesosalpingeal injection of oxytocin

were $3811.78 \pm 4173 \pm 72$ and 7581.91 ± 14184.96 respectively ($P=0.141$). Mean baseline hematocrit in patients treated with and without Intramesosalpingeal injection of oxytocin were ... and 32.6 ± 3.59 respectively ($P=0.192$). Mean BHCG level after 1 day of surgery in patients treated with and without Intramesosalpingeal injection of oxytocin were 2560.77 ± 2991.40 and 3426.38 ± 5020.05 IU / ml respectively ($P=0.413$). The mean hematocrit at 6 hours after surgery in patients treated with and without Intramesosalpingeal injection of oxytocin were 30.12 ± 2.53 and 28.62 ± 3.54 percent ($P=0.053$). The mean rate of reduction in BHCG in the day after surgery in patients treated with and without Intramesosalpingeal injection were 1234.25 ± 2686.87 and 2177.19 ± 1069.02 respectively ($P=0.636$).

The amount of bleeding during surgery in 17 patients (5 patients treated without Intramesosalpingeal injection of oxytocin and 12 patients treated with injections of oxytocin Intramesosalpingeal) were mild, in 43 patients (24 patients treated without Intramesosalpingeal injections of oxytocin and 19 patients treated with Intramesosalpingeal injections of oxytocin) were moderate and in 7 patients (6 patients treated without injection of oxytocin and 1 patient treated with oxytocin) was severe.

The rate of intraoperative bleeding in patients treated with Intramesosalpingeal injection of oxytocin was significantly less than intraoperative bleeding in patients treated without injection of oxytocin ($P=0.01$).

Ease of removal of the products of ectopic pregnancy in 17 patients (4 patients without Intramesosalpingeal injection of oxytocin and 13 patients treated with Intramesosalpingeal injection of oxytocin)

was Easy, in 40 patients (22 patients treated with Intramesosalpingeal injection of oxytocin and 18 patients treated with Intramesosalpingeal injection of oxytocin) was moderate and in 10 patients (9 patients treated without Intramesosalpingeal injection of oxytocin and 1 patients treated with Intramesosalpingeal injection of oxytocin) was difficult.

Ease of removal of the products of ectopic pregnancy in patients treated with Intramesosalpingeal injection of oxytocin was significantly easier compared to patients treated without Intramesosalpingeal injection of oxytocin ($P=0.001$).

Number of times of cutter using for controlling the intraoperative bleeding in 6 patients treated with Intramesosalpingeal injection of oxytocin was low (less than 3 times), in 52 patients (28 patients treated with Intramesosalpingeal injection of oxytocin, 24 patients received no injection of oxytocin) was moderate (6-4 times) and in 9 patients (7 patients treated without Intramesosalpingeal injection of oxytocin and 2 patients treated with Intramesosalpingeal injection of oxytocin) were high (more The six-time respectively). Number of times of cutter using for controlling the intraoperative bleeding in patients treated with Intramesosalpingeal injection of oxytocin was significantly lower than the frequency of times of cutter using for controlling the intraoperative bleeding in patients without injection of oxytocin ($P=0.005$).

Need to remove the tube during surgery in 23 patients (20 patients treated without Intramesosalpingeal injection of oxytocin and 3 patients treated with Intramesosalpingeal injection of oxytocin) was present. Need to remove of the tube during surgery in patients treated without

Intramesosalpingeal injection of oxytocin was significantly more than the numbers to remove the tube during surgery in patients treated with Intramesosalpingeal injection of oxytocin ($P < 0.001$)

The fallopian tubes at 2 months postoperatively in 26 patients (5 patients treated without Intramesosalpingeal injection of oxytocin and 21 patients treated with Intramesosalpingeal injection of oxytocin) was open and in 18 patients (10 patients treated with Intramesosalpingeal injection of oxytocin and 8 patients treated with Intramesosalpingeal injection of oxytocin) was closed. The evaluation was not possible in 23 patients due to surgical removal of the tube. Patency of the fallopian tubes in patients treated with Intramesosalpingeal injection of oxytocin at 2 months after surgery, was significantly more than patients treated without Intramesosalpingeal injection of oxytocin ($P = 0.021$).

EP is one of the most common emergencies in obstetrics and gynecology and is one of the first differential diagnosis of acute abdomen in women of reproductive age (9). Treatment of ectopic pregnancy depends not only on the patient's age and desire for future pregnancy, but also depends on gestational age of patients during laparoscopic findings (10). Obviously, the older patient with no intention for the next pregnancy, the treatment of choice is a simple method of salpingectomy using laser, cutter or 3 rings (5 loop method) (11). Conservative surgery for ectopic pregnancy is associated with risk of recurrence and that is the fact that the patient and her family should be informed (12-14).

Incidence rate:

Given the evidence recorded in the hospitals, the incidence of ectopic pregnancy

is rising steadily, so that the incidence has reached from 4.5 per 1000 in 1970 to 16.8 per 1000 in 1992.

Direct injection of cytotoxic drugs, injection of prostaglandins, hyperosmolar glucose, potassium chloride and saline to the place of EP as an alternative to Methotrexate is pending. In these methods, the success rate is low and needs to have a laparoscopic or vaginal aspirations are practically unavoidable. Delivery to the site of ectopic pregnancy Methotrexate via hysteroscopy is also under study (1).

In this study, the effect mesosalpinx injection of oxytocin in on treatment of EP and decrease of bleeding and reduce in tubal resection was investigated.

We may fail In the MTX treatment. Severe enduring pain, declining hematocrit, orthostatic hypotension. Rapid diagnosis and surgical treatment in most cases will prevent the EP from rupture. Nowadays laparotomy and laparoscopy with salpingectomy is the first treatment of choice for ruptured ectopic pregnancy. Almost all patients with hypovolemic shock due to rupture of the EP are in need of blood transfusions. If Laparoscopist is expert enough as well as cardiac monitoring and anesthesia for laparoscopic salpingectomy is appropriate alternative if Methotrexate is contraindicated is.

EP rate of relapse is slightly higher after conservative surgery. In following cases laparoscopic salpingectomy is preferred on Salpingostomy: the uncontrollable bleeding untreatable conservatively. Extensive damage to the tubes, recurrence EP in the same tube, linear Salpingostomy with surgical sterilization is the surgical method conservatively recommended for the EP. In a study by Laatikainen and colleagues conducted on patients with tubal EP, The

Effect of osmolar glucose topical infusion during surgery was evaluated, they stated that reduction of β HCG in patients with osmolar glucose infusion and patients with Salpingostomy alone were 37% and 53%, respectively (15). In our study the rate of the post operative reduction in β HCG in patients with injection of oxytocin was 21.36 ± 27.26 %.

In a study by Stock et al conducted on patients with EP, The Effect of Vasopressin on infusion during surgery of EP was studied. They reported that vasopressin is effective in controlling bleeding and hemostasis in patients, but there was no significant difference in hematocrit levels in patients with and without injection of vasopressin (16).

In our study, the mean hematocrit at 6 hours after surgery in patients treated without Intramesosalpingeal injection of oxytocin was 28.62 ± 3.54 and in patients treated with Intramesosalpingeal infusion of oxytocin was 30.12 ± 2.53 there was no significant difference between hematocrit at 6 hours after surgery in patients treated with and without injection of oxytocin ($P=0.053$), but the amount of bleeding during surgery in patients treated with Intramesosalpingeal injection of oxytocin was significantly less than intraoperative bleeding in patients treated with Intramesosalpingeal injection of oxytocin I ($P=0.001$).

In a study by Porpora et al on patients with EP, the effect of topical Methotrexate with linear Salpingostomy was evaluated and it was concluded that the rate of β HCG normalization and the patency of fallopian tubes is equal in both methods (17). In our study like the study above, there was not a significant difference between the mean reduction rate of β HCG level in the day after the surgery in patients with and without

Intramesosalpingeal oxytocin ($P=0.636$). But the eviction of pregnancy products was easier in patients with Intramesosalpingeal oxytocin injection ($P=0.001$) the need for tubectomy in patients receiving Intramesosalpingeal oxytocin was significantly lower than patients not receiving Intramesosalpingeal oxytocin ($P<0.001$).

Zilber and colleagues had carried out a study on the patients with EP and evaluated the laparoscopic Salpingostomy with topical Methotrexate on patients with unruptured EP; they concluded that the normalization time for β HCG is equal in both methods (18). In another study by Moon et al on patients with EP, the effect of injection of vasopressin during the surgery was studied on patients with a mean age of 33.5 years and mean gestational age of 6.7 weeks; they reported this method as a safe method which can decrease the risk of bleeding during the surgery (19).

In our study the times of using of cutter for controlling the bleeding in the patients receiving Intramesosalpingeal oxytocin was significantly lower than the times of cutter use in patients not receiving the Intramesosalpingeal oxytocin ($P=0.005$), and the patency of fallopian tubes in the patients who underwent the injection of Intramesosalpingeal oxytocin was significantly higher 2 months after the surgery comparing the patients who did not receive Intramesosalpingeal oxytocin ($P=0.012$)

Conclusion

The results show that the intra mesosalpinx injection of oxytocin in patients with unruptured EP can reduce the bleeding increase the ease of evicting the pregnancy products and reduce the tubal resection. The

patency of fallopian tubes in patients with Intramesosalpingeal injection of oxytocin had been increased meaningfully 2 month after the surgery. So this method is recommended in surgeries with tubal reserve.

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