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ORIGINAL ARTICLE

EFFECTS OF CERVICAL VASOPRESSIN VERSUS NO CERVICAL VASOPRESSIN ON BLOOD LOSS DURING VAGINAL HYSTERECTOMY

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ABSTRACT: BACKGROUND: Minimizing blood loss during surgery is important because of the associated morbidity. In addition intraoperative bleeding can obstruct the view of operative field and lead to complications, in particular dissection during vaginal hysterectomy can be hampered by blood loss, because the main blood supply is not ligated until after much of the dissection has been done. Several methods to control blood loss have been used including hydro dissection with saline as well as with the injection of vaso constrictors. **AIMS:** To compare blood loss, operative time, post-operative complication rates in patients undergoing vaginal hysterectomy who were randomly assigned to receive pre-operative intra cervical vasopressin or no intra cervical injection. **SETTINGS & DESIGN:** This is a prospective case control study conducted in Kamla Raja hospital, Gajara Raja Medical College, Gwalior (M.P.) from August 2011 to September 2012. Sample size: 70 patients. **METHOD AND MATERIAL:** It is a prospective case control study. 70 woman undergoing vaginal hysterectomy to be randomly allocated to receive either 20 unit of vasopressin in 100 mL of normal saline intra cervically or control (no vasopressin or saline), preoperatively from August 2011 to September 2012. Patients were divided in two groups and various factors were compared and analysed. **STATISTICAL ANALYSIS:** Analysis was done by Chi-Square Test. **RESULT:** In this study average change in haemoglobin (gm %) ±SD in control group is 0.691±0.202 and in study group 0.328±0.144, p value=0.000000 (statistically significant). Maximum number of patients in study group had change in haemoglobin from 0.21 to 0.4 gm% while in control group maximum number of patients belonged to change in haemoglobin from 0.41 to 0.6 gm%. Whereas socio demographic factors & post-operative complications were comparable with no statistical significance among study groups. **CONCLUSION:** Use of vasopressin with judicious case selection during vaginal hysterectomy results in significant decrease in blood loss and minimal fall in Hb gm% thereby decreasing patients morbidity and improving post-operative outcome.

KEYWORDS: Intracervical Vasopressin, vaginal hysterectomy, operative blood loss.

INTRODUCTION: Hysterectomy is the most commonly performed gynaecological surgical procedure, next only to caesarean section.

The 1st documented case was reported by Bernengario Da Carpi, an Italian who lived in Bolonga in 1507. He performed partial vaginal hysterectomy.

Vaginal hysterectomy was done sporadically through 17th & 18th centuries. But the credit for performing 1st VH in France goes to Lauvarid in early 18th century.

Successful surgery depends on control of bleeding, infection & pain. Minimizing blood loss during surgery is important because of the associated morbidity. In addition, intraoperative bleeding can obstruct the view of the operative field and lead to complications. In particular, dissection during

vaginal hysterectomy can be hampered by blood loss, because the main blood supply is not ligated until after much of the dissection has begun.

Several methods to control blood loss have been used, including hydro dissection with saline as well as with the injection of vasoconstrictors. In previous reports, procedures that have shown reduced operative blood loss with the use of preoperative vasopressin include loop electrocautery of the cervix, hysteroscopic myomectomy, myomectomy, and abdominal hysterectomy.

One of the first reported uses of a vasoconstrictive agent in an attempt to decrease blood loss in vaginal hysterectomy was in 1983 by England et al.

Vasopressin, a vasoconstrictive drug with a short half-life of 20 minutes is often used in gynaecological surgery to decrease blood loss and improve visualization of the surgical field.

Through this study there has been an effort to correlate the use of intracervical vasopressin with decreased blood loss during vaginal hysterectomy. The aims and objectives has been to compare blood loss, operative time, rise in mean BP, Change in hemoglobin% & complication rates in patients undergoing vaginal hysterectomy.

Various methods have been used to promote hemostasis during vaginal hysterectomy;

1. Normal saline.
2. Nor – epinephrine.
3. Vasopressin.

Vasopressin: Vasopressin agents have played a role in gynaecologic surgery dating back to the late 1960's. Vasopressin (AVP) was one of the first synthesized peptide hormones, used to treat diabetes insipidus (DI) and gastro intestinal haemorrhage, discovered by Oliver and Schafer in 1895 by demonstrating the vasopressor effects of posterior pituitary extracts, while Farini and Velden described its antidiuretic effects by successfully treating DI with neuro-hypophyseal extracts, providing the name antidiuretic hormone.[1]

Later, Vigneaud and Turner isolated vasopressin and proved that the same neuro-hypophyseal hormone possessed both antidiuretic and vasopressor activity.[2,3] Currently, vasopressin and terlipressin (AVP/TP) have emerged as promising agents for the management of refractory shock in critically ill children. However, their effects on various vascular beds and tissues are complex and sometimes apparently paradoxical.

Vasopressin has a short plasma half-life of 10-20 min and pressor effect lasts for 30 to 60 minutes. Repeat injection 45 to 60 minutes after the first may be safe.

Vasopressin receptors: There are at least 3 kinds of vasopressin receptors: V1A, V1B and V2. All are G protein coupled. The V1A and V1B receptors act through phosphatidyl inositol hydrolysis to increase the intracellular Ca^{2+} concentration. The V2 receptors act as though to increase the cAMP levels.[4,5,6]

Mechanism of action: Vasopressin regulates plasma volume, blood pressure and osmolality. Under normal conditions, its main role is in regulation of water balance with minimal effect on BP. It causes vasoconstriction by acting through the vasopressin (V1) receptor and exerts its antidiuretic action through the V2 receptor in the kidney. The major mechanism by which vasopressin reduces blood loss is vasoconstriction.[7,8]

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Vasopressin also stimulates uterine contraction by acting through myometrial V1a receptors. Unlike oxytocin receptors, which are plentiful in term uterus but far less abundant in the non-pregnant uterus, vasopressin receptors are present in the myometrium of both pregnant and non-pregnant women. Thus it is a uterotonic in the non-pregnant uterus.

METHODS: It is a prospective case control study.

70 woman undergoing vaginal hysterectomy to be randomly allocated to receive either 20 unit of vasopressin in 100mL of normal saline intra cervically or control (no vasopressin or saline), preoperatively from August 2011 to September 2012.

Inclusion Criteria for selection of cases is as follows:

1. Informed consent
2. Vaginal hysterectomy of benign pathology.

Exclusion Criteria:

1. Patients not giving consent.
2. Patient with significant medical conditions.
    - Hypertension.
    - Ischemic heart disease.
    - Peripheral vascular disease.
    - Epilepsy.
    - Severe liver disease.
    - Impaired renal function as determined by elevated s. creatinine.
    - Asthma.
    - History of recurrent migraines.

1. **Patient with malignant pathology:** Detailed history (medical & obstetrical) and examination (General physical examination & obstetrical) was done. Pre-operative work-up of selected patients was done. Patients were taken up for elective surgery after pre anaesthetic check-up.

Anaesthesia used: Subarachnoid Block (↓SAB).

Preparation of vasopressin solution: 20 unit of vasopressin in 100 ml of normal saline was used.

Instillation of vasopressin: A total of 30-40 ml solution of vasopressin was injected at 2, 4, 8 and 10 o'clock circumferentially around the cervix at cervico-vaginal junction.

All the patients undergoing vaginal hysterectomy were included even if other concurrent procedures were scheduled, as long as hysterectomy was the first procedure. Vaginal hysterectomy was performed and important steps were timed, including time until entering the posterior cul-de-sac, removal of the uterus, and reattachment of the cardinal ligaments to the vaginal cuff. Only data from hysterectomy portion of the surgery were included in the analysis.

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OBSERVATIONS NOTED:

(a) Measurement of blood loss: All the mops and gauze pieces used during vaginal hysterectomy were weighed before and after the procedure.
The total amount of blood loss was determined.
(b) Time required for surgery.
(c) Vitals (B.P., Pulse & ECG) were monitored, pre-operatively, intra operatively and post operatively.
(d) Any intra operative problem during vaginal hysterectomy.
(e) Febrile morbidity: Defined as oral temp of 101^0 or greater on any 2 days of the first 10 post-operative days excluding the first 24 hrs.
(f) Haemoglobin on 5th day post-operative.
(g) C/o post-operative discharge p/v.
(h) C/o increase in frequency of micturition or burning micturition (UTI).

RESULTS: Present study was conducted in Department of Obstetrics and Gynaecology, Kamla Raja Hospital, G. R. Medical College, Gwalior from August 2011 to September 2012.

A total of 70 patients undergoing vaginal hysterectomy for benign pathologies of uterus were selected and divided into two groups.

Group A - 35 cases with cervical vasopressin (Study group).

Group B - 35 cases with no cervical vasopressin (Control group).

Amongst the 70 patients studied, maximum number of patients belonged to 30-50 years of age, 68.58% and 71.43% in control group and study group respectively (Table 1). The mean age in both, the control and study group was 47.14 yrs and 47.85 yrs respectively.

Maximum number of patients were para 4 in both groups (45.71% in control group and 42.85% in study group) (Table 2).

In both groups vaginal hysterectomy alone was most commonly performed (48.58%) (Table 3).

In both groups, 54.29% of patients belong to premenopausal group and 45.71% belong to menopausal group (Table 4).

As regards time required for surgery, 74.29% patients in control group and 65.72% in study group required the time between 46-60 min (Table 5).

From the above table it is calculated that average time required (min) ±SD

In control group = 55±6.75.

In study group = 51.71±7.75.

P value = 0.06 (not significant).

Maximum number of patients in control group had blood loss between 201-300 ml (74.28%) and study group had blood loss between 101-150 ml (57.14%) (Table 6).

From the above table it is calculated that average blood loss (ml)±SD.

In control group = 250±46.90.

In study group = 140.57±33.51 p value = 0.000000 (statistically significant).

Rise in BP was observed after vasopressin infiltration. Mean rise was 15.91 mmHg after 5 mins of vasopressin infiltration in study group as compared to 4.85 mmHg in control group (Table 7).

There was no significant difference in the postoperative complications in both control and study group (Table 8).

P value = 0.00000 (statistically significant).

Maximum number of patients in control group had change in haemoglobin between 0.41 to 0.6 gm% (40%).

DISCUSSION: Vaginal extirpation of uterus for non-malignant indication is recognized by many gynaecologists as a preferential method for the management of benign pelvic disease. As stated by Pratt (1976), "If a uterus is to be removed it is best removed vaginally."

Vasoconstrictors to minimize blood loss have been shown to be effective in many gynaecological procedures. Historically vaginal hysterectomy has been performed without any intracervical injection or with a saline injection intracervically to create a mechanical temponade and potentially to assist in creating an easier plane of dissection.

Specifically vasopressin has been shown to decrease blood loss in myomectomy, hysteroscopy and abdominal hysterectomy.

In present study main operation performed was vaginal hysterectomy alone (48.58%) in both groups. Other concomitant procedures being anterior and/or posterior colporrhaphy.

In our study there was a significant decrease in mean blood loss of about 109.43 ml between two groups. We also noticed that rise in mean BP was significant intraoperatively at 5 mins after vasopressin injection as compared to rise at 10 mins & 15 mins and control group. Julian et al (1993) concluded that vasopressin group had significantly less intraoperative blood loss (296±37 ml) versus 435±55 ml (control group) ($p<0.02$).[9] Frederick et al (1996) showed a decrease in median blood loss from 675 ml in the placebo group to 225 ml in the vasopressin arm ($p<0.001$) during myomectomy.In present study average change in haemoglobin (gm%)±SD in control group is 0.691±0.202 and in study group 0.328±0.144, p value=0.000000 (statistically significant). Maximum number of patients in study group had change in haemoglobin from 0.21 to 0.4 gm% while in control group maximum number of patients belonged to change in haemoglobin from 0.41 to 0.6 gm%.[10]

Whereas sociodemographic factors & post-operative complications were comparable with no statistical significance among study groups.

Thus this study reinforces the fact that use of vasopressin with judicious case selection during vaginal hysterectomy results in significant decrease in blood loss and minimal fall in Hb gm% thereby decreasing pateints morbidity and improving post-operative outcome. However further clinical work is needed to prove universal role and use of vasopressin in decreasing blood loss during vaginal hysterectomy.

No gynaecological procedure is more rewarding than one completed successfully with minimal blood loss, with the operating field as pristine at the end as a it was at the beginning, with one sponge with a spot of blood and with the patient safely in the recovery room. Vasopressin has a role in reaching for this ideal, but it must be used in dilution and at a low total dosage.

It should not be used in patients with history of myocardial infarction, bradycardia, angina, hypertension and arrythmias.

Further studies are needed to prove the role of vasopressin in vaginal hysterectomy.

REFERENCES:

1. Oliver H, Schafer E. On the physiological action of extracts of pituitary body and certain other glandular organs: preliminary communication. J Physiol (Lond). 1895; 18: 277-9.

2. Du Vigneaud V, Gash DT, Karsoyannis PG. A synthetic preparation possessing biological properties associated with arginine vasopressin. J Am Chem Soc. 1954; 76: 4751-2.
3. Turner RA, Pierce JG, Du Vigneaud V. The purification and the amino acid content of vasopressin preparation. J Biol Chem. 1951; 191: 21-8.
4. Holmes CL, Landry DW, Granton JT. Science Review: Vasopressin and the cardiovascular system part-I – receptor physiology. Crit Care. 2003; 7: 427-34.
5. Barrett LK, Singer M, Clapp LH. Vasopressin: mechanisms of action on the vasculature in health and in septic shock. Crit Care Med. 2007; 35: 33-40.
6. Holmes CL, Patel BM, Russell JA, Walley KR. Physiology of vasopressin relevant to management of septic shock. Chest. 2001; 120: 989-1002.
7. Treshcan TA, Peters J. The vasopressin system: Physiology and clinical strategies. Anesthesiology. 2006; 105: 599-612.
8. Dunser MW, Hasibeder WR, Wenzel V, Schwarz S, Ulmer H, Knotzer H, et al. Endocrinologic response to vasopressin infusion in advanced vasodilatory shock. Crit Care Med. 2004; 32: 1266-71.
9. Julian TM, Johnson GW, Gosewhr JA, et al. Vasopressin as a chemical tourniquet during vaginal surgery. J Gynecol Surg 1993; 9: 161–4.
10. Okin CR, Guido RS, Meyn LA, Ramanathan S. Vasopressin during abdominal hysterectomy: a randomized controlled trial. Obstet Gynecol 2001; 97: 867–72.

Age group (in yrs)	Vaginal hysterectomy (Control group)	Vaginal hysterectomy with intracervical vasopressin
30-40	12 (34.29%)	11 (31.43%)
41-50	12 (34.29%)	14 (40%)
51-60	9 (25.71%)	9 (25.71%)
> 60	2 (5.71%)	1 (2.86%)

Table 1: Distribution of cases according to age who underwent vaginal hysterectomy

Parity	Vaginal hysterectomy (Control group)	Vaginal hysterectomy with intracervical vasopressin
Primipara	0 (0%)	0 (0%)
2nd para	0 (0%)	1 (2.86%)
3rd para	11 (31.43%)	12 (34.29%)
4th para	16 (45.71%)	15 (42.85%)
5th para	4 (11.43%)	6 (17.14%)
Above 5th para	4 (11.43%)	1 (2.86%)

Table 2: Distribution of cases according to parity

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Type of operation done	Vaginal hysterectomy (Control group)	Vaginal hysterectomy with intracervical vasopressin
Vaginal hysterectomy	17 (48.58%)	17 (48.58%)
Vaginal hysterectomy + anterior colporrhaphy	14 (40%)	12 (34.28%)
Vaginal hysterectomy + posterior colporrhaphy	2 (5.71%)	0 (0%)
Vaginal hysterectomy + anterior and posterior colporrhaphy	2 (5.71%)	6 (17.14%)

Table 3: Distribution of cases according to type of operation done

Menstrual Status	Vaginal hysterectomy (Control group)	Vaginal hysterectomy with intracervical vasopressin
Premenopause	19 (54.29%)	19 (54.29%)
Menopause	16 (45.71%)	16 (45.71%)

Table 4: Distribution of cases according to premenopausal and menopausal status

	Vaginal hysterectomy (Control group)	Vaginal hysterectomy with intracervical vasopressin
30-45 min	5 (14.29%)	10 (28.57%)
46-60 min	26 (74.29%)	23 (65.72%)
61-75 min	4 (11.42%)	2 (5.71%)

Table 5: Distribution of cases according to time required for surgery (Only up till hysterectomy portion)

Blood loss (ml)	Vaginal hysterectomy (Control group)	Vaginal hysterectomy with intracervical vasopressin
< 100	0 (0%)	7 (20%)
101-150	2 (5.71%)	20 (57.14%)
151-200	6 (17.15%)	7 (20%)
201-250	13 (37.14%)	1 (2.86%)
251-300	13 (37.14%)	0 (0%)
301-350	1 (2.86%)	0 (0%)
> 350	0 (0%)	0 (0%)

Table 6: Distribution of cases according to blood loss

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	Pre-operative	Intraoperative		
		5 min	10 min	15 min
Vaginal hysterectomy (control group)	92.47	97.32	95.32	93.80
Vaginal hysterectomy with intracervical vasopressin (study group)	92.56	108.47	103.42	98.37

Table 7: Distribution of cases according to mean BP preoperatively, intraoperatively and its rise

	Control group	Vasopressin group
Febrile morbidity	4	3
UTI - Frequency during micturition	1	2
- Burning sensation during micturition	0	0
Vaginal discharge	4	4
Other	0	0

Table 8: Distribution of cases according to postoperative complications

Change in haemoglobin (gm%)	Control group	Vasopressin group
< 0.2	1 (2.86%)	15 (42.86%)
0.21 to 0.4	4 (11.43%)	16 (45.71%)
0.41 to 0.6	14 (40%)	4 (11.43%)
0.61 to 0.8	10 (28.57%)	0 (0%)
0.81 to 1	6 (17.14%)	0 (0%)
> 1	0 (0%)	0 (0%)

Table 9: Distribution of cases according to change in hemoglobin

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