

# Adrenalin versus terlipressin: blood loss and cardiovascular side-effects in the vaginal part of laparoscopically-assisted vaginal hysterectomy or vaginal hysterectomy

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## Summary

The purpose of the study was to compare blood loss and cardiovascular side-effects in the course of the vaginal part of laparoscopically-assisted vaginal hysterectomy (LAVH) or single vaginal hysterectomy (VH) [1]. Blood loss was evaluated in relation to local application of two haemostatic agents, e.g. adrenalin as a gold standard versus terlipressin. The investigation was designed as a prospective randomised study. A prospective group of 40 patients selected for LAVH or VH was randomised into two groups, e.g. 20 patients in each group. In both of these groups, the blindly selected haemostatic agent was applied locally immediately before circular colpotomy, the surgeon not being aware which agent was being used. Because of the claimed delayed effect of terlipressin a third group of another 20 patients was randomly selected. For comparison in this group terlipressin was locally already applied before the laparoscopic part of LAVH, e.g. 20-25 minutes before performing circular colpotomy. Thus, this particular group could not be made blind to the surgeon.

The study confirmed a significantly superior haemostatic effect of adrenalin. On the other hand after the adrenalin application a higher frequency of hypertensive reactions and mild arrhythmias were observed but without any clinical sequelae.

*Key words:* Local haemostasis in vaginal surgery; Haemostatic agents; LAVH; LH; Blood loss; Cardiovascular side-effects.

## Introduction

To diminish blood loss during surgery is indeed the aim of every surgeon. A clear operative field with minimal bleeding enables safer and faster surgery and this aspect is especially important during vaginal procedures [2]. Because of this in recent years we have seen a greater application of local vasoconstrictive and haemostatic agents especially during the course of vaginal surgery [3-6].

Our study was controversially linked to the application of various vasoconstrictive agents during vaginal surgery. In the Czech Republic these controversions have increased even further after the disappearance of trusted agent ornipressin (POR 8, Sandoz) [7] from local markets and because of the subjective feeling of many surgeons that the recommended replacement terlipressin was very ineffective. Thus, a return of many surgeons to a gold standard of adrenalin followed against the background of some anaesthesiological and surgical opinions [8] that the local adrenalin or vasopressin application might have a serious adverse effect on the cardiovascular system.

## Material and Methods

Sixty women who were randomly selected and operated on by means of LAVH or LH in the Department of Operative Gynaecology and Minimally Invasive Surgery of Na Homolce Hospital, Prague, Czech Republic between 4/1/99 and 30/3/99 were included. The Department is a teaching unit for minimally invasive surgery in gynaecology of the Czech Endoscopic Society and all women were operated on by senior surgeons. Patients with accompanying diseases such as ischaemic heart disease, hypertension, cardiac arrhythmias and bronchial asthma were not excluded from the study. The mean age was 45.6 years (range 30-60 years). The women were further randomly assigned to three groups. In the first group adrenalin was locally applied intra/paracervically immediately before performing circular colpotomy. In the second group terlipressin was applied in the same manner. A third group of the last 20 women had terlipressin already applied before the laparoscopic part of LAVH in order to take into account a proclaimed delayed effect of terlipressin. Adrenalin was applied at a ratio of 1:200,000 in 20 ml of normal saline; terlipressin in a dosage of 400 mg.

Blood loss was measured in two stages to minimize any bias caused by additional blood loss from places which were not influenced by the application of local vasoconstrictive agents [1]. This meant that in the first stage the blood loss was measured from the moment of circular colpotomy until ligation of the uterine arteries. In the second stage the blood loss was measured from the beginning of peritonealisation until the end of closure of the vaginal apex.

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Table 1. — The mean measurement for one surgery in all three groups.

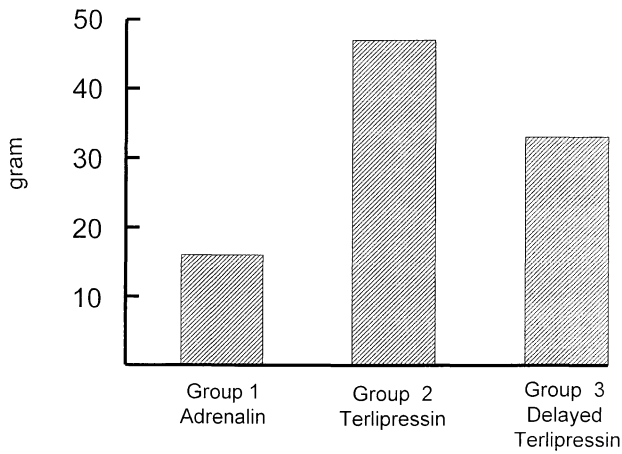


Table 2. — The mean blood loss for one surgery in 1<sup>st</sup> and 2<sup>nd</sup> stages of evaluation in all three groups.

	1 <sup>st</sup> phase	2 <sup>nd</sup> phase	Total
Adrenalin group	5.8 g	10.8 g	16.6 g
Terlipressin group	25.5 g	21.7 g	47.2 g
Delayed Terlipressin group	14.5 g	19.6 g	39.0 g

Table 3. — Values of blood pressure after application of Adrenalin or Terlipressin.

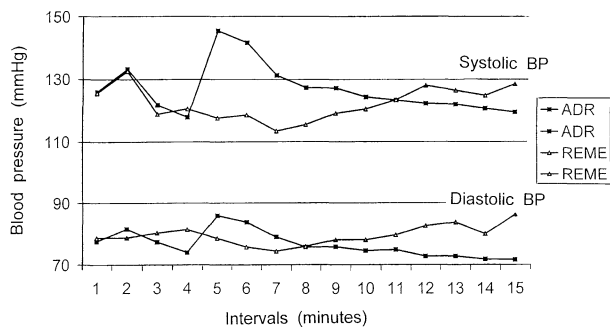


Table 4. — MAP values after application of Adrenalin or Terlipressin.

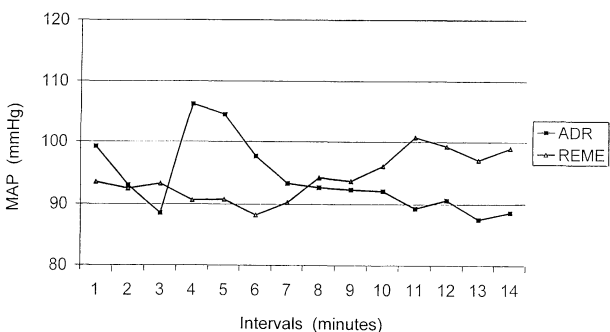


Table 5. — Comparison of pulse frequency after application of Adrenalin or Terlipressin.

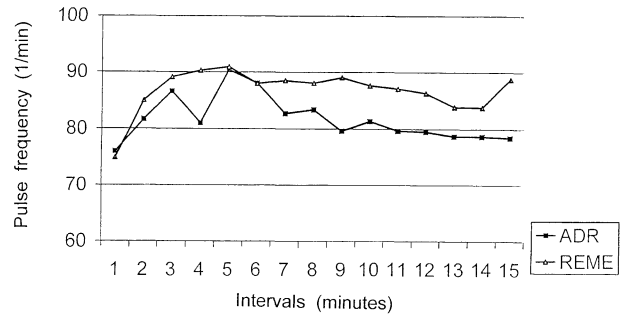
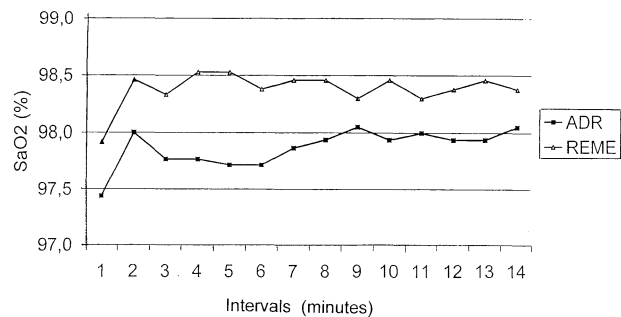


Table 6. — Comparison of SaO<sub>2</sub> after application of Adrenalin or Terlipressin.



The measurement of blood loss was performed evaluating the weight of the tampons and swabs used in cleaning the operative field. Digital scales with a maximum error of 0.1 g were used.

The anaesthesia for all groups was the same with premedication 30 minutes before the procedure by atropin and promethazin according to the weight of the women. Thiopentone or etomidate in case of allergy to the former was used as the introduction to general anaesthesia with intubation; relaxation by means of succinylcholiniodide.

The anaesthesia was maintained by the mixture of gasses, e.g. N<sub>2</sub>O, O<sub>2</sub> and isofluran, analgesia was managed by sufentanil and long-term relaxation by pancuronium bromide. The monitoring of cardiovascular effects of vasoconstrictive agents included measurement of systolic, diastolic and mean arterial blood pressure (MAR). Pulse arhythmias and O<sub>2</sub> saturation were also observed in each patient. All these parameters were recorded before premedication, before and after introduction to anaesthesia, before application of vasoconstrictive agents and further in one min intervals for a duration of 20 minutes. The parameters were recorded by means of an anaesthetic monitoring unit, Datex Engstrom AS/3, with a written recording.

**Results**

The mean measurements for one surgery of blood loss in all three groups are shown in Table 1. The blood loss in the first and second stages of the evaluation in all three groups is shown in Table 2.

Thus it can be concluded that the mean blood loss per surgery after a terlipressin application is three times higher in comparison to the adrenalin group and two

times higher in the third "delayed" terlipressin group in comparison to adrenalin. This is statistically significant ( $p < 0.01$ ).

On the cardiovascular side, of note is an increase of systolic, diastolic and mean arterial pressure two minutes after the adrenalin application. The mean increase was by 25 mmHg in the case of systolic BP, 10 mmHg in the case of diastolic and 13 mmHg in the case of MAP. During the 4<sup>th</sup> and the 5<sup>th</sup> minutes the values normalised and further remained stabilized. The changes in systolic, diastolic blood pressure and MAP are shown in Tables 3 and 4. The pulse rate values almost always increased, with the mean increase being 15 pulses per minute in the adrenalin group (with a maximum of 35/min). The dynamic changes in pulse rates are shown in Table 5. With the exception of the first four minutes, the adrenalin group was no different from the terlipressin group regarding pulse dynamics. In the adrenalin group we observed three cases of cardiac dysrhythmias with supraventricular extrasystolies, all three complications being easily resolved by application of 10 ml of 1% mesocain intravenously. After correction of cardiac rhythms in these three patients a similar problem did not recur. The differences in O<sub>2</sub> saturation among all three groups were not statistically significant. The results are shown in Table 6.

## Discussion

From a local haemostatic point of view it appears that adrenalin has a significantly superior effect in comparison to terlipressin. Because adrenalin shows faster vessel contraction velocity than any other agent [9] the effect starts immediately with objectively and subjectively obvious vasoconstriction resulting in profound anaemisation of the operating field. The mean blood loss of 16.6 g per surgery in our study enables a practically bloodless operation for the whole duration of the surgery. The haemostatic effect of terlipressin in comparison to adrenalin for the duration of the entire surgery was significantly inferior and the overall blood loss 2-3 times higher regardless of whether the surgeon was waiting or not for its effect to take place. Furthermore, the delayed effect of terlipressin makes this agent unsuitable for a primary vaginal surgery where it is impractical to wait for a delayed effect. The difference in blood loss of immediate surgery and surgery delayed by 20-25 minutes was statistically significant ( $p < 0.01$ ). However, terlipressin might be useful as a systemic agent [10, 11].

From the cardiovascular point of view we should point out that the haemodynamic changes caused by the sympathomimetic effect of adrenalin did require medicamentous corrections in approximately 15% of patients without any further deleterious effects to the patients. We observed these side-effects especially during the adrenalin application into the deeper layers of the cervix, e.g. close to the lateral margin of the cervix and deep under the bladder. If a careful submucous infiltration was used we did not see any significant changes in cardiovascular dynamics with the same haemostatic effect observed. On

the other hand no cardiovascular haemodynamic changes were observed after the terlipressin application. This is in conjunction with its known prolonged biological half-life. This optimal effect in the cardiovascular system correlates with an objective and clinically significant inferior local haemostatic effect in the case of vaginal surgery.

## Conclusions

The study showed significantly lower blood loss when adrenalin was used ( $p < 0.01$ ) in comparison to terlipressin both in the case of immediate or delayed surgery. This correlates with significantly higher surgical comfort and makes vaginal surgery with one surgeon and one assistant easily possible. Adrenalin causes more frequent transient hypertensive reactions and arrhythmias which do not have any clinical sequelae. They could be avoided by a particularly careful application technique. Terlipressin does not appear to be a suitable local vasoconstrictive agent in various types of vaginal surgeries, especially LAVH, VH and conizations. In this study the clinical impression of many surgeons was that terlipressin is not an efficient local haemostatic vaginal agent which can be objectively confirmed. It would appear that terlipressin is close to desmopressin in local effects, as opposed to ornipressin (POR 8) which is closer to adrenalin.

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