Epidural and general anesthesia versus general anesthesia in radical prostatectomy

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Key words: *epidural anesthesia; general anesthesia; radical prostatectomy; intraoperative blood loss.*

Summary. *Induced hypotension with epidural anesthesia influences the intraoperative blood loss in prostate cancer patients undergoing radical prostatectomy. The aim of this study was to evaluate intraoperative blood loss and need of blood transfusions in patients who underwent radical prostatectomy under epidural/general anesthesia and general anesthesia.*

Two groups were selected: epidural/general anesthesia group (study group, 27 patients) received epidural anesthesia in association with general anesthesia, and general anesthesia group (control group, 27 patients) received general anesthesia alone. Epidural/general anesthesia was performed using 0.5% solution of bupivacaine and maintained by volatile anesthetic sevoflurane. General anesthesia was performed with endotracheal ventilation using sevoflurane and intravenous fentanyl.

The present study showed that the mean blood loss in epidural/general anesthesia group was significantly lower in comparison with that of general anesthesia group (740±210 mL versus 1150±290 mL, P<0.001). In addition, less allogeneic blood was transfused in epidural/general anesthesia group: 0.19 blood units transfused versus 0.52 blood units in general anesthesia group (P=0.007).

Our study proved that induced hypotension with epidural/general anesthesia reduced intraoperative blood loss and need of allogeneic blood transfusions in cancer patient undergoing open radical prostatectomy.

Introduction

Open radical prostatectomy (RP) is an effective surgical method in cancer patients. This procedure is aggressive and associated with the risk of troublesome intraoperative bleeding from plexuses of the dorsal vein complex.

RP is associated with substantial blood loss frequently requiring allogenic blood transfusion. Allogenic blood transfusion has immunomodulatory effects that may increase the risk of nosocomial infections and cancer recurrence, and the possible development of autoimmune diseases later in life (1).

Different attempts are made to reduce bleeding. Improvement of anesthetic techniques and use of new anesthetic agents contribute to better outcome of RP (2–4). Regional anesthetic techniques may reduce this risk. Several studies suggest that anesthesia procedures might impact the intraoperative blood loss and prognosis in patients undergoing RP. Spinal/epidural anesthesia combined with general anesthesia is an attractive method to induce hypotension with significantly reduced blood loss and blood transfusions (5–8).

The aim of the study was to compare intraoperative blood loss and need of blood transfusions using epidural/general anesthesia vs general anesthesia alone in patients undergoing radical prostatectomy. Epidural anesthesia was used not only to induce hypotension, but also for analgesia during surgery and after operation.

Patients and methods

It was a prospective randomized trial comparing two methods of anesthesia. Fifty-four patients took part in this trial. Patients were randomly assigned to two groups by picking out an envelope with indicated method of anesthesia. All patients were informed about this trial and signed informed consent. Twenty-seven patients who underwent radical prostatectomy (RP) under epidural/general anesthesia were considered as study group. They were compared with 27

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patients who underwent RP under general anesthesia (control group).

Patients with a history of myocardial infarction within a year preoperatively, previous cerebrovascular accident, transient ischemic attack, extensive spinal surgery, bleeding diathesis, aortic or mitral stenosis, uncontrolled hypertension were excluded from the study. Preoperative investigations included a complete blood count, serum electrolytes, creatinine, and electrocardiogram (ECG). The patients with creatinine level of >115 μmol/L were excluded from the study too.

Methods of general anesthesia were the same in both groups of patients. Fentanyl (1 μg/kg) was used for premedication, induction was performed with 3 mg/kg of propofol, and 5 mg/kg rocuronium was used for neuromuscular blockade. General anesthesia was maintained by mixture of sevoflurane (Fex=0.7–1.6%), air and oxygen (FiO2=60%). Infusion of rocuronium (0.6 mg/kg/h) was used to achieve muscle relaxation.

Intraoperative monitoring for all patients included recording a continuous five-lead electrocardiogram with special attention to ST segment, oxygen saturation by pulse oximetry, and invasive blood pressure, airway gas analysis, and nasopharyngeal temperature.

Analgesia method of study group patients

In the study group, all epidurals were performed with appropriate monitoring using a standard midline approach with patients in the sitting position. Catheters were placed at the lower thoracic level (Th10–12) and were tested for intravascular or subarachnoid placement using 40 mg lidocaine with 5 μg/mL epinephrine.

Epidural catheter was used not only for analgesia purposes, but also to reduce blood pressure to 50–60 mm Hg. Algorithm of this procedure is shown in Fig. 1. The first bupivacaine infusion was calculated for 8 segments according to the principle: bupivacaine 0.5%–1 mL/1 segment, when height is 150 cm + 0.1 mL / 5 cm above 150 cm. If mean arterial blood pressure decreased to 50–60 mm Hg after the first bupivacaine infusion, bupivacaine (0.25%) infusion was continued at a rate of 3–5 mL/h. If after the first infusion of bupivacaine mean arterial blood pressure was >60 mm Hg, an additional injection of bupivacaine (0.5%–1/3 of initial volume) was given. If mean arterial blood pressure was <50 mm Hg, we started intravenous epinephrine infusion at a rate of 0.01–0.07 μg/kg/min. Surgeons began operation when the mean arterial blood pressure was 50–60 mm Hg.

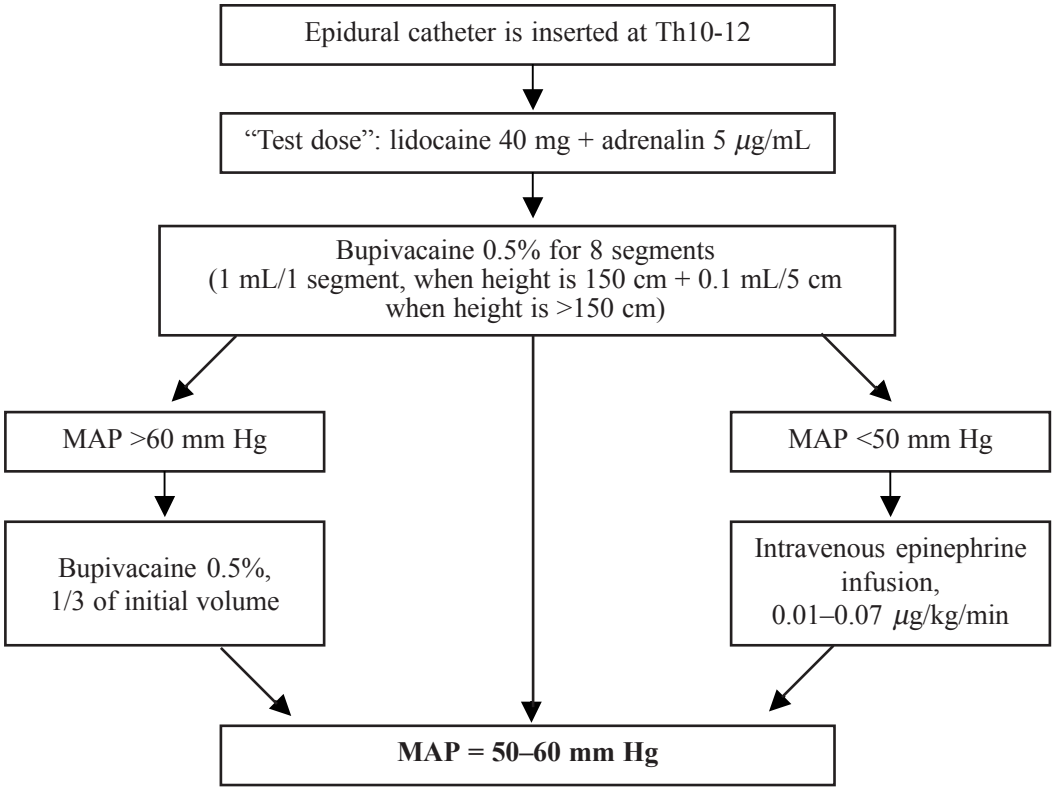

Fig. 1. **Algorithm of hypotensive epidural anesthesia**

MAP – mean arterial blood pressure.

Analgesia method of control group patients

In the patients of study group, analgesia was achieved by intravenous injection of opiates. An initial dose of fentanyl was 6 μg/kg. Intravenous fentanyl infusion of 100 μg/h was performed subsequently. Study group patients were operated on without suppression of arterial blood pressure. The mean arterial blood pressure was maintained between 80 mm Hg and 110 mm Hg.

Calculation of blood loss

The trigger for allogenic blood transfusion in both groups was a hematocrit value of <0.28.

Blood loss was calculated as follows:

$$ABL=[EBV\times(H_i-H_f)]/[(H_i+H_f)/2]+(500\times T_u) \quad (9),$$

where ABL indicates mean actual blood loss; EBV, estimated blood volume and it was assumed to be 70 mL/kg; H_i, patient's initial hematocrit level; H_f, patient's final hematocrit level; T_u, the sum of autologous whole blood and packed red blood cell units transfused.

None of the patients received hormonal or radiation therapy before RP, none had a known coagulopathy, and none was receiving anticoagulant or antiplatelet therapy at the time of RP.

Statistical analysis

Data analysis was done using SAS. Required number of patients was calculated using unilateral *t* test. Statistical significance was 0.025; test power, 0.9; clinically significant blood loss, 400; standard deviation, 300. It was calculated that there should be 25 patients in every group. In order to compare quantitative characteristics, mean values, standard deviations, minimum and maximum values were calculated. For comparison of qualitative characteristics, frequency of values and percentage were calculated. Differences were considered significant if *P* value was <0.05.

Results

Both groups were similar for age, ASA physical class, body mass index, prostate volume, and tumor stage (Table).

The mean intraoperative blood pressure was significantly higher in the control group as compared with the study group (91 mm Hg and 56 mm Hg, respectively; *P*=0.006) (Fig. 2).

Time in surgery for the study group was 167 min versus 188 min for the control group (*P*=0.01).

Evaluation criteria were intraoperative blood loss and blood transfusions. The present study showed that the mean intraoperative blood loss in the study group was significantly lower in comparison with that of control group (740±210 mL versus 1150±290 mL, respectively; *P*<0.001). In addition, less allogenic blood was transfused in the study group than in the control group (0.19 blood units transfused versus 0.52 blood units; *P*=0.007) (Fig. 3).

Postoperative bleeding was similar in both groups; the mean drainage was 220±95 mL and 250±105 mL, respectively.

The percentage of patients who achieved the threshold trigger for allogenic blood transfusion was significantly lower in the study group than in the control group (8% versus 26%, *P*=0.019).

There were no serious adverse events in either group during the study.

Discussion

Radical prostatectomy is a procedure that is widely used for cancer patients (10). After the first perineal radical prostatectomy for prostate cancer by Hugh Hampton Young in 1904, this surgery was the accepted

***Table*. Characteristics of the patients**

Variable	Study group	Control group	*P* value
Age, years	60.3	60.7	NS
ASA physical class (II/III)	20 / 7	19 / 8	NS
Clinical TNM stage (T1), n	15	16	NS
Clinical TNM stage (T2), n	10	11	NS
Clinical TNM stage (T3), n	4	4	NS
Prostate volume, mL	42.2	40.5	NS
Body mass index, kg/m^2	27.3	28.0	NS
Preoperative Hb, g/L	132.2	137.1	NS
Preoperative Ht	37.0	34.4	NS

NS – not significant.

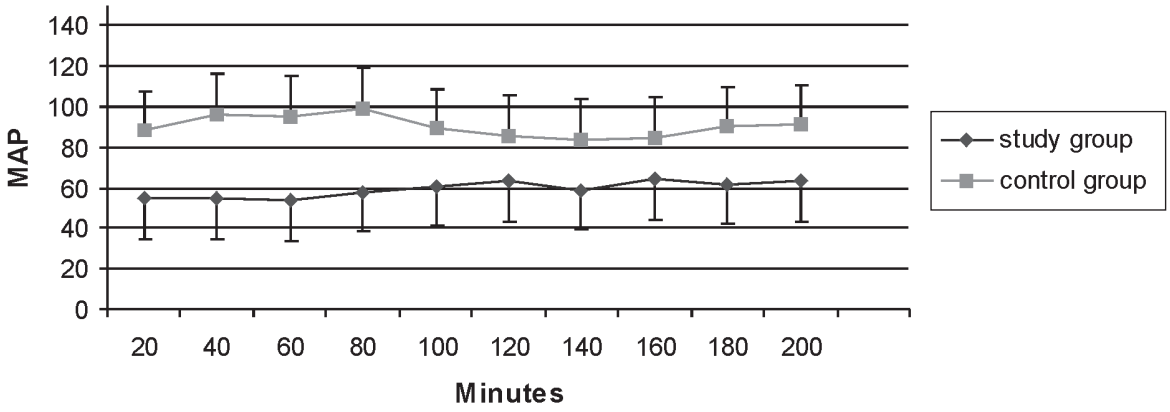

Fig. 2. **Mean intraoperative blood pressure**
MAP – mean arterial blood pressure.

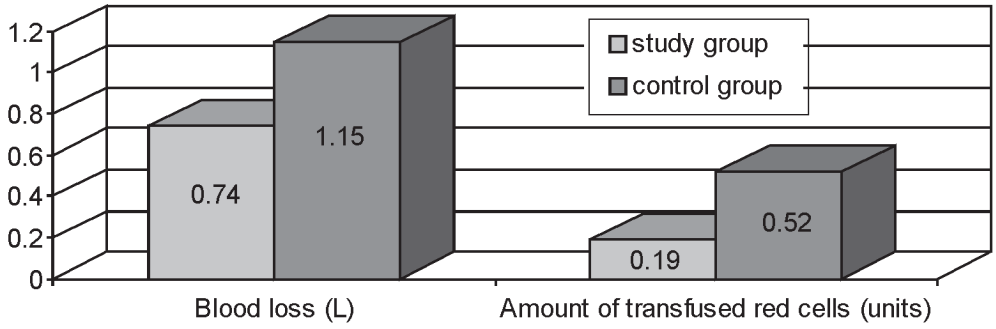

Fig. 3. **Blood loss and amount of transfused blood during operation**

approach for treating patients with localized prostate cancer (11). The most common problem during radical prostatectomy is hemorrhage, usually arising from the periprostatic venous structures.

Lowering mean arterial blood pressure (MAP) is an old method of reducing blood loss, and there is a considerable renewal of interest in this strategy. Controlled hypotension has been proven to be efficacious in decreasing blood loss in many surgical procedures (12, 13). Our study indicated that patients undergoing radical prostatectomy with an intraoperative MAP of 50 mm Hg had significantly lower blood loss than the control group with an intraoperative MAP of >80 mm Hg. The results of our study showed that blood loss while performing in general/epidural anesthesia was reduced to 35% in comparison with that of general anesthesia group.

Hypotension can be achieved by reduction in cardiac output (CO), systemic vascular resistance (SVR), or both. During hypotension, a blood flow sufficient to maintain adequate tissue oxygenation and metabolism must be provided. For this reason, controlled hypotension is usually achieved primarily by decreasing SVR and not by lowering CO.

Hypotension achieved by epidural anesthesia techniques causes pharmacological sympathectomy, which produces arteriolar dilatation. These effects are enhanced by venous blood pooling that decreases venous return and cardiac output. The unpredictable degree of hypotension and the necessity for large infusions of fluid are the principle drawbacks of this method. Patients who receive more intravenous fluids might have a dilution effect, and this can lead to a misinterpretation of the hematocrit level during radical prostatectomy. William-Russo et al. demonstrated that if hemodynamic stability is maintained by low-dose epinephrine infusion, this technique could be used safely (12). More than 200 elderly adults (mean age, 72 years) with comorbid medical illness were included in a randomized, controlled trial. MAP for the patients was maintained at the levels of either 45–55 mm Hg or 55–70 mm Hg. The overall incidence of major car-

diovascular complications was surprisingly low, despite the high incidence of comorbid vascular risk factors in the study population. The epinephrine infusion used routinely in this study did not affect MAP directly, but maintained normal stroke volume. This was associated with increased cardiac index and might have prevented significant bradycardia. Therefore, we used epinephrine infusion (0.01–0.07 μg/kg/min) in our study to avoid unpredictable degree of hypotension and bradycardia.

The patients in the study group needed fewer hemotransfusions. This factor is very important for oncology patients who were operated on, as it is known that donor's blood suppresses the immune system of a patient (14). Undesirable effects of hemotransfusions are largely reviewed in the literature (14, 15). It is noted that approximately one-third of hemotransfusions caused side reactions. The risk of the transmission of disease and toxicity for a patient are to be mentioned as well. We reduced amount of transfused blood units three times for the patients who received hypotensive epidural anesthesia. Furthermore, 92% of operated patients in the study group needed no hemotransfusions.

The results of our study are similar to data of other investigators who state that while using combined hypotensive anesthesia, operative blood loss is reduced markedly (16–18).

The mean time in surgery was reduced by 21 min in the study group as compared with the control group. This difference, sufficient for performing epidural anesthesia in most patients, may be a result of improved operative conditions in a "drier" surgical field.

Conclusions

The reduction in mean arterial pressure has been associated with reduced blood loss and relatively bloodless operative fields, which may contribute to decreased time in surgery. This makes hypotensive epidural anesthesia an economically attractive concept, and the use of this technique may further promote the trend toward bloodless surgery.

Epidurinės ir bendrosios anestezijos palyginimas su bendrąja anestezija atliekant radikalias prostatektomijas

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Raktažodžiai: epidurinė anestezija, bendroji anestezija, radikali prostatektomija, kraujavimas operacijos metu.

Santrauka. Valdoma hipotenzija padeda sumažinti kraujavimą radikaliai operuojant prostatą. Tyrimo tikslas. Įvertinti kraujo netekimą ir kraujo transfuzijų poreikį onkologinėmis ligomis sergantiems ligoniams, kuriems radikaliai operuojama prostata epidurinės / bendrosios ir bendrosios anestezijos sąlygomis.

Ištirtos dvi ligonių grupės: tiriamoji (T) grupė – 27 ligoniai, kuriems taikyta epidurinė / bendroji anestezija. Į epidurinį tarpą buvo sušvirkščiama bupivakaino 0,5 proc. tirpalo, bendrajai endotrachėjinei anestezijai skirtas sevofluranas. Kontrolinės (K) grupės ligoniams (n=27) buvo taikoma tik bendroji anestezija. Anestezijai palaikyti skirtas inhaliacinis anestetikas sevofluranas kartu su analgetiku fentaniliu.

Tyrimo metu nustatėme, kad T grupės ligonių kraujo netekimas operacijos metu buvo statistiškai reikšmingai mažesnis nei K grupės ligonių: atitinkamai – 740±210 ml ir 1150±290 ml ($p<0,001$). Donorinio kraujo perpilta 0,19 ir 0,52 vieneto, atitinkamai tiriamosios ir kontrolinės grupės ligoniams ($p=0,007$).

Valdoma hipotenzija epidurinės / bendrosios anestezijos metu padeda sumažinti kraujo netekimą ir kraujo transfuzijos kiekį onkologinėmis ligomis sergantiems ligoniams, kuriems atliekamos radikalios prostatos operacijos.

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Received 10 November 2008, accepted 6 October 2009
Straipsnis gautas 2008 11 10, priimtas 2009 10 06