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Prophylactic use of anticoagulation and hemodilution for the prevention of venous thromboembolic events following meningioma surgery

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ABSTRACT

Objectives: Brain tumors may be associated with postoperative venous thromboembolic (VTE) events with possible devastating consequences. Meningioma has the highest incidence of postoperative VTE events among all brain tumors. Hemodilution and anticoagulation both proved efficacy in deep venous thrombosis (DVT) prophylaxis that is why we theorized that this regimen would be beneficial for VTE prophylaxis in operated intracranial meningioma patients without added risk to the patients.
Patients and methods: A retrospective double-blinded study, where the records of consecutive intracranial meningioma patients were revised comparing the efficacy of two regimens of postoperative VTE prophylaxis. Patients were divided into 2 groups; group A was submitted to the use of compressive stockings, low-molecular weight heparin (LMWH) administration and hemodilution, while group B was submitted only to the use of compressive stockings.
Results: The study included 194 patients. Mean age of patients was 55 years (range from 27 to 78 years). VTE events were diagnosed in 16 patients (8.2%) all of them belonged to group B. The median time for VTE events was 12 days. Older age ($P = .0001$), larger size tumor ($p = 0.0438$), delayed ambulation postoperatively ($p = 0.0351$) as well as skull base location of meningioma ($p = 0.0163$) were associated with higher incidence of postoperative VTE. Overall, group A patients showed more favorable outcome as compared to group B.
Conclusion: In addition to the use of elastic stockings, we recommend starting hemodilution at the outset of surgery, LMWH administration starting 12 h postoperatively as well as refraining from the use of diuretics during and after intracranial meningioma surgery till the patient became fully ambulatory to reduce the incidence of postoperative VTE events.

1. Introduction

Meningiomas represent the second most common primary intracranial tumor in adults with a prevalence of 70.7/100,000 and an incidence of 6.0/100,000 per year [1]. Brain tumors in general are known to increase the risk of venous thromboembolism (VTE), with the incidence in meningiomas being three times higher than other brain tumors. Published research reported an association of 20–30% of postoperative VTE with glioma, whereas it approaches 70% in meningioma [1–4]. A plausible explanation of the increased incidence of hypercoagulability in brain tumors in general could be the release of brain-derived thromboplastin, the associated inevitable damage of vascular endothelium encountered during surgery, prolonged operative time, using muscle relaxants impeding the venous return or due to decreased postoperative mobilization [5]. The occurrence of VTE, which comprises deep vein thrombosis (DVT) and pulmonary embolism (PE), can impose grave consequences exceeding those of the tumor itself or the surgical intervention with an estimated mortality rate of 34% [6,7].

Several strategies were suggested to decrease the incidence of postoperative VTE; the most common of which are the use of elastic stockings, pneumatic calf compression and early mobilization [8]. Implementation of prophylactic postoperative anticoagulation in brain tumor surgery, the onset of anticoagulant administration as well as the recommended dosage is still debatable Some studies advocate its use while others report an unacceptably high incidence of postoperative intracranial hemorrhage [9,10]. Keeping the

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Table 1
Comparing both groups as regards to baseline data, postoperative VTE occurrence and postoperative complications.

Variable	Group A	Group B	*P*-value
Mean age (years)	57.1	53.7	0.11
Female (%)	66 (73)	78 (75)	0.87
Mean duration of surgery (minutes)	332	312	1
Estimated intraoperative blood loss (ml)	290	330	0.91
Mean tumor maximal diameter (cm)	6.1	5.8	0.861
Venous thromboembolic event:			
• Deep vein thrombosis (%)	N/A	12 (12)	0.00048
• Pulmonary thromboembolism (%)	N/A	6 (6)	0.0312
Important intracranial complications related to treatment regimen			
Significant intracranial hemorrhage (%)	2 (2.2)	N/A	0.214
Mean duration of postoperative follow-up (days)	143	165	0.815

patient well hydrated is of utmost importance for vascular surgeons to prevent or treat DVT [11,12]. In this study, we theorized that a new scheme of combined hemodilution and postoperative prophylactic anticoagulation could further minimize the incidence of postoperative VTE complications after meningioma surgery when combined with other traditional management schemes.

2. Material and methods

2.1. Study design

A retrospective double-blinded study.

2.2. Inclusion criteria

Patients diagnosed and operated for intracranial meningioma from the 1st of February 2010 till the 31st of January 2015 in the Department of Neurosurgery, Alexandria University, Egypt.

2.3. Exclusion criteria

Patients diagnosed with spinal or craniospinal junction meningioma.

Data in the records possibly denoting the regimen used for VTE prophylaxis both physical and pharmacological, including administered intravenous fluids, anticoagulant medications as well as the diuretics, were removed from the files and were given coding numbers to be reintegrated in the original files after data collection was complete. The records were then handed to an independent observer for relevant data collection that included patients' age, gender, history of the complaint, preoperative clinical status as well as radiological findings. Information gained from preoperative radiological investigations included the tumor site and the largest diameter of the tumor in the preoperative magnetic resonance imaging (MRI). Intraoperative information included the duration of surgery, estimated blood loss and extent of tumor excision according to the Simpson's grading system. Postoperative information included general and neurological clinical status, radiological examination, medications given (apart from those removed earlier from the records), frequency and duration of follow-up, histological grade of the tumors, diagnosis of DVT and its complications (including PE), the occurrence of significant intracranial hemorrhage, which was defined as hemorrhage requiring reoperation or causing significant neurological deficit as well as the ambulatory status of the patients postoperatively which was classified as walking unassisted, walking assisted, wheelchair-bound and bed ridden.

The protocol for postoperative VTE prophylaxis in meningioma patients in our institution mainly relied on using elastic stockings and early mobilization. A new protocol was suggested years ago where hemodilution was used during and after surgery in addition to postoperative anticoagulation. An emerging debate concerning whether this new protocol had a superior therapeutic benefit compared to the traditional protocol was thus generated, that is why we conducted this study to obtain a sound conclusion regarding the best management plan. Patients' selection was not biased since surgeons who used the old protocol tended to use it in all their cases, whereas surgeons who used the new protocol employed it in all their cases. Patients submitted to conventional treatment in addition to anticoagulation and hemodilution were included in the treatment group A, while patients submitted only to the conventional protocol were included in the control group B. The primary endpoints of the study were the occurrence of DVT, PE or the concomitant occurrence of both events; while the secondary end points were the occurrence of surgically significant cerebral hemorrhage and/or death.

2.4. Statistical analysis

Using a specially designed sheet on Microsoft Excel, data was entered and thoroughly revised and was transferred to IBM SPSS version 17 format (SPSS Inc., Chicago, IL, USA) and the following statistics were performed.

2.4.1. Descriptive statistics

Mean and standard deviation were calculated.

2.4.2. Comparative statistics

Comparison between the two groups in all variables using *t*-test, Chi square test, Fisher exact test, Wilcoxon rank sum test, ANOVA test and regression analysis tests as appropriate. A 5% alpha error and 80% beta error were adopted. P significance was measured at 0.05. Approval by the ethical committee in the Faculty of Medicine, Alexandria University was taken for this research.

3. Results

The records revealed 214 patients diagnosed with meningioma; 20 (9.3%) of them had spinal or craniospinal junction meningioma and were excluded from the study whereas the remaining 194 (90.7%) patients formed the study cohort.

144 patients (74%) were females. The mean age of patients was 55 years (range from 27 to 78 years, standard deviation [SD] 12 years). The median duration of surgery was 320 min (ranging from 90 to 550 min) with an estimated mean blood loss of 300 cc (ranging from 90 to 900 cc) (Table 1). No significant differences were found between both groups as regards to age, sex, tumor size or location. Correlation was done between different factors possibly predisposing to VTE and the confirmed occurrence of postoperative VTE through a univariate analysis.

Group A included 90 patients who were submitted to the use of compressive stockings, administration of low-molecular weight