neurocritical care society Neurocrit Care (2012) 16:399–405
DOI 10.1007/s12028-011-9569-9

ORIGINAL ARTICLE

Drainage Efficiency with Dual Versus Single Catheters in Severe Intraventricular Hemorrhage

Holly E. Hinson · Eric Melnychuk · John Muschelli · Daniel F. Hanley · Issam A. Awad · Wendy C. Ziai

Published online: 17 June 2011

Abstract
Background Little is known about the efficacy of single versus dual extraventricular drain (EVD) use in intraventricular hemorrhage (IVH), with and without thrombolytic therapy.
Methods Post-hoc analysis of seven patients with dual bilateral EVDs from two multicenter trials involving 100 patients with IVH, and spontaneous intracerebral hemorrhage (ICH) volume <30 ml requiring emergency external ventricular drainage. Seven "control" patients with single catheters were matched by IVH volume and distribution and treatment assignment. Head CT scans were obtained daily during intraventricular injections for quantitative determination of IVH volume.
Results Median [min–max] age of the 14 subjects was 56 [40–73] years. Median duration of EVD was 7.9 days (single catheter group) versus 12.2 days (dual catheter group) ($P = 0.34$). Baseline median IVH volume was not significantly different between groups (75.4 ml [22.4–105.1]—single EVD vs. 84.5 ml [42.0–132.0]—dual EVD; $P = 0.28$). Comparing the change in IVH volume on time-matched CT scans during dual EVD use, the median decrease in IVH volume in dual catheter patients was significantly larger (52.1 [31.7–81.1] ml) versus single catheter patients (34.5 [13.1–73.9] ml) ($P = 0.004$). There was a trend to greater decrease in IVH volume during dual EVD use in both rt-PA ($P = 0.9$) and placebo-treated ($P = 0.11$) subgroups.
Conclusion The decision to place dual EVDs is generally reserved for large IVH (>40 ml) with casting and mass effect. The use of dual simultaneous catheters may increase clot resolution with or without adjunctive thrombolytic therapy.

Keywords External ventricular drain · Intraventricular hemorrhage · Thrombolysis

Introduction

Intraventricular thrombolytic therapy has been increasingly investigated as a method to accelerate clearance of intraventricular hemorrhage (IVH) [1–5]. An initial external ventricular drain (EVD) is more commonly placed in the least involved lateral ventricle in order to minimize the risk of early obstruction and optimize intracranial pressure (ICP) control. When IVH volume contralateral to the side of EVD is substantial, a single catheter may be ineffective in reducing hematoma volume significantly especially if the foramina of Monro are obstructed.

Placement of a second contralateral catheter has emerged as a strategy to manage specific situations such as trapped ventricles, bilateral-casted ventricles, and EVD obstruction especially if mass effect and potential ischemia are present. It may also improve the efficacy of thrombolytic therapy by ensuring drug delivery close to the greatest clot burden. Currently, accepted practice guidelines regarding catheter

H. E. Hinson (✉) · W. C. Ziai
Division of Neurosciences Critical Care, Johns Hopkins University School of Medicine, Meyer 8-140, 600 N. Wolfe St., Baltimore, MD, USA
e-mail: hhinson1@jhmi.edu

E. Melnychuk · J. Muschelli · D. F. Hanley
Division of Brain Injury Outcomes, Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

I. A. Awad
Section of Neurosurgery, University of Chicago Medical Center, Chicago, IL, USA

location and use of dual catheters in IVH do not exist. One study comparing IVH patients with single and dual intraventricular catheters (IVC) found no difference in clot resolution or 3 month outcome between the 2 groups [6]. The objective of this study was to compare the efficacy of IVH resolution during single and dual EVD use using a case control design to minimize the bias caused by discretionary placement of dual catheters.

Methods

Design

This was a post-hoc analysis of patients from two multicenter trials involving 100 randomized adult patients with obstructive hydrocephalus secondary to IVH, and spontaneous intracerebral hemorrhage (ICH) volume <30 ml (by ABC/2 method [7]) requiring urgent external ventricular drainage. Seven cases in the trial were identified as "dual catheter patients", with two EVDs simultaneously in place in opposite hemispheres at any point during treatment. Four had been randomized to receive intraventricular rt-PA at doses 3.0 mg q12h or 1.0 mg q8h, and three cases to receive placebo injections of saline at the same frequency through the EVD. Physicians were blinded to treatment assignment. Patients with dual catheters were given total dose of each injection of study agent through one EVD only. The side of administration was at physician's discretion. Each case was matched to one unique patient enrolled in the trials, who was treated only with a single catheter. Patients were matched according to total IVH volume, IVH location (right lateral ventricle, left lateral ventricle, and bilateral lateral ventricles), treatment assignment and, where possible, similar duration of catheters. IVH volumes were matched between cases and controls within 10 ml of IVH volume in five cases. Two cases had IVH volume more than 10 ml larger than their controls (differences of 38 and 55 ml, respectively). Of the seven matched single catheter control patients, four received thrombolytic, and three placebo. Head CT scans were obtained daily during study agent administration for quantitative determination of IVH volume.

This study was performed under the approval of the institutional review board of each participating center. Written consent was obtained from all participants or their legal representatives.

Patient Selection

Patients with an EVD inserted in the initial 24 h of illness to treat IVH were approached for randomization. Patients were enrolled within 48 h after diagnostic head CT. Exclusion criteria included: posterior fossa hematoma; intraparenchymal hemorrhage volume >30 ml; suspected intracerebral aneurysm or arteriovenous malformation (excluded by appropriate diagnostic studies); any severe complicating illness; active internal bleeding, current use of heparin (but not anti-platelet agents), coagulopathy with prothrombin time (PT) or partial thromboplastin time (PTT) outside of normal range, platelet count <75 IU/mm^3; pregnancy; and age <18 years.

Patient Management

Patients were admitted to an intensive care unit (ICU) with staff experienced in the acute care of patients with IVH and EVDs. EVDs were placed into the frontal horn of the lateral ventricle and tunneled under the scalp by neurosurgical staff. Initial catheters were placed in the least involved ventricle in 9/14 patients (63%) (5 cases; 4 controls). The decision and timing of placement of second EVDs was entirely at the discretion of the treating physician as no guidelines existed for this practice. Intraventricular location of the catheter tip was confirmed by ICP waveform morphology and by CT scan, performed 6 h after placement ("stability" CT scan). After each injection of study agent, the EVD was closed for 1 h to allow time for study agent–clot interaction. After 1 h, the EVD was reopened with a drainage gradient specified by the treating physician (0–20 mmHg). Study agent administration was continued until radiographic clearance of blood from the 3rd and 4th ventricles (ability to visualize a clear pathway of hypodense CSF through the lower ventricular system) had occurred or a maximum of 25 doses had been given.

Imaging

CT scans were performed on admission, 6 h after EVD placement (stability CT scan) and daily. Radiation dose associated with this study was in line with usual care of large volume IVH patients in the acute period during which daily CT scans are common practice in the first few days after onset especially when intraventricular rt-PA may be given to assess for bleeding. The volumes of IVH and ICH were measured independently by a blinded investigator using standard computerized volumetric analysis (Alice 5.1, Perceptive Informatics, Boston MA). The Graeb score [8], absolute IVH volume, and percentage of stability CT IVH volume were reported.

Statistics

Demographic variables, baseline characteristics, average daily CSF volume drained, and change in IVH volume were compared between single and dual EVD-treated

patients. The time was standardized from the "stability" CT to the time-matched CT scan closest after removal of the second EVD in the dual catheter group. "Baseline" refers to data at clinical presentation, "stability" to data at time of stability CT scan. Wilcoxon signed-rank test was used to compare absolute IVH volume reduction, average daily CSF volume drained, and variables with nonnormal distributions. Student's *t*-test was used for continuous variables with normal distributions and Chi-squared or Fisher's exact test was used for categorical data as appropriate. Correlations were performed using the Spearman correlation test. Data are presented as median [range], unless otherwise indicated. Statistical analysis was performed with Stata 10.0 (Stata, College Station, Texas), a value of $P < 0.05$ was considered significant.

Results

Demographics and Baseline Characteristics

Cases and controls were well matched in demographic variables (Table 1). Mean (SD) age of participants was 56 (±11) years and 64% were male ($n = 9$). The most common risk factor precipitating IVH was hypertension (79%; $n = 11$). There were no statistically significant differences in baseline characteristics or IVH severity as assessed by IVH volume and Graeb score (Table 2). Median IVH volume was 75.4 ml [22.4–105.1] in the single catheter group and 84.5 ml [42.0–132.0] in the dual catheter group ($P = 0.28$).

Table 1 Demographic characteristics of single and dual catheter treated patients

	Dual catheter	Single catheter	Overall	*P*
Mean age				
(±SD)	56 (±10)	56 (±12)	56 (±11)	0.96
Gender (*n*)				0.58
Male	5	4	64% (9)	
Female	2	3	36% (5)	
Ethnicity (*n*)				0.55
Caucasian	4	4	57% (8)	
African American	2	3	36% (5)	
Hispanic	1	0	7% (1)	
Risk factors (*n*)				
Hypertension	5	6	79% (11)	NS
Diabetes	1	1	14% (2)	NS
Alcohol use	2	1	21% (3)	NS
Tobacco	1	3	29% (4)	NS
Coccaine use	0	2	14% (2)	NS
Seizure	2	1	21% (3)	NS
Migraine	0	1	7% (1)	NS

Demographics by catheter number

NS not significant

IVC Placement and IVH Clot Resolution

In the dual catheter group, second simultaneous EVDs were placed at a median of 22 [0–80] h after the first. The second catheter was placed for a trapped ventricle in one case, initial catheter obstruction in four cases, and for clot removal without other indication in two cases. In the control group, there was one EVD replacement for obstruction and no case of trapped ventricle. All patients had casted ventricles.

The median EVD duration (any catheter) trended toward a longer duration in the dual EVD group (12.2 vs. 7.9 days; $P = 0.34$). There were two catheters simultaneously present in the dual catheter group for a median of 6 [1–15] days. Of the seven dual catheter patients, three had catheters replaced secondary to catheter obstruction. Of those three patients, two had bilateral replacements and one had a unilateral replacement. Of the single catheter patients, only one catheter was replaced due to obstruction. Otherwise, the original single EVD was in place the entire time. There was no antibiotic protocol for indwelling EVDs.

Change in IVH volume was assessed over intervals of 6 [2–14] days in the single catheter group and 7 [3–16] days in the dual catheter group. The median change in absolute IVH volume was 44.3 [13.1–81.1] ml, representing a 54.5% reduction from stability CT IVH volume. The median decrease in IVH volume in dual catheter patients was significantly larger (52.1 [31.7–81.1] ml) versus single catheter patients (34.5 [13.1–73.9] ml) ($P = 0.004$) (Fig. 1). This represents a 67% (±23.4) reduction in IVH volume (dual EVD group) versus 36% (±21.4) in the single EVD group. Comparing placebo and rt-PA treated group medians separately, there was a trend to greater volume reduction with dual catheters in both rt-PA treated ($P = 0.07$) and placebo-treated patients ($P = 0.11$).

Graeb scores for total and each lateral ventricle decreased in both single and dual EVD groups. No significant differences were found.

CSF Drainage

During the study period, and excluding days on which the EVD was clamped for weaning, average daily CSF drainage was not significantly different between groups although the median was higher in the dual EVD group (142 vs. 68 ml; $P = 0.69$) (Fig. 2).

Table 2 Baseline clinical characteristics of single and dual catheter treated patients

	Dual catheter ($n = 7$)	Single catheter ($n = 7$)	Overall ($n = 14$)	P
ICH volume	10.2 (0–36.8)	0.73 (0–13.4)	2.7 (0–36.8)	0.27
IVH volume	84.5 (42–132)	75.4 (22.4–105.1)	78.8 (22.4–132)	0.28
MAP	127 (110–194)	153 (119–185)	150 (110–194)	0.57
GCS	5 (3–14)	6 (3–13)	6 (3–14)	0.8
CSF drainage	25 (0–85)	53 (0–205)	37 (0–205)	0.14
ICP	14 (4–28)	12 (1–16)	13 (1–28)	0.16
Clot location				0.53
Caudate	2	2	4	
Thalamus	2	0	2	
Putamen	0	1	1	
Globus Paliidus	1	1	2	
Lobar	0	0	0	
Primary IVH	2	3	5	
Graeb score at stability scan				
Total	9 (8–12)	11 (9–12)	10.5 (8–12)	0.51
L lateral vent	3 (0–4)	4 (2–4)	2.5 (0–4)	0.74
R lateral vent	2 (0–4)	4 (3–4)	2 (0–4)	0.19
Graeb score at follow-up scan				
Total	4 (0–10)	6 (4–9)	5.5 (0–10)	0.43
L lateral vent	3 (2–4)	2 (1–4)	2.5 (1–4)	0.46
R lateral vent	2 (0–4)	3 (1–4)	2 (0–4)	0.29
Change in Graeb				
Total	5 (1–9)	5 (2–7)	5 (1–9)	0.84
Study agent				
Time to start (h)	4.8 (1.7–9.3)	5.5 (1.3–22.6)	5.2 (1.3–22.6)	0.57
Total tPA dose (mg)	10.5 (9–51)	7 (3–10)	9.5 (3–51)	0.24
Duration of IVC				
Total days	12.2 (6.5–17.3)	7.9 (1.9–22.3)	8 (1.9–22.3)	0.34
Dual catheters in place		n/a	6 (1–15)	n/a
ICU length of stay				
Total days	15 (10–19)	14 (4–51)	15 (4–51)	0.88
Modified rankin score				
At 30 days	5 (3–6)	5 (4–6)	5 (3–6)	0.95
NIH stroke scale				
At enrollment	25.5 (16–35)	37 (37)	36 (16–37)	0.75
At 30 days	10 (1–20)	18.5 (1–35)	13 (1–35)	0.47
Mortality				
At 30 days	3	3	6	1

Baseline clinical characteristics by catheter number. Data are expressed as a median (min–max), except clot location and mortality which are given as an absolute number

ICP Control

Initial opening pressure was not different between groups and was not >20 mmHg in any patient (median 16 mmHg-dual vs. 12-single EVD; $P = 0.13$). Only 1/7 dual EVD patients had any ICP reading >30 mmHg (while EVDs were open to drainage) compared to 2/7 single EVD patients. During clamping of the EVD for injection of study agent, the number of injections associated with ICP $>$ 20 mmHg in the first 10 doses was 4 in the single EVD group versus 6 in the dual EVD group.

Complications

No patients in this cohort developed meningitis or ventriculitis. CSF samples were routinely drawn from the EVD

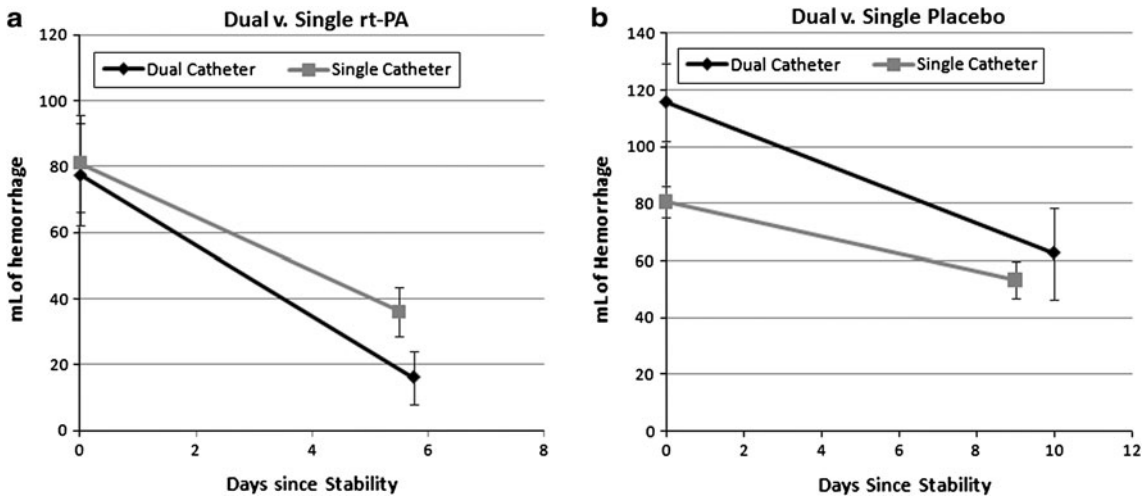

Fig. 1 Intraventricular hemorrhage clearance in dual and single catheter groups by treatment group. **a** rt-PA treated, **b** placebo treated

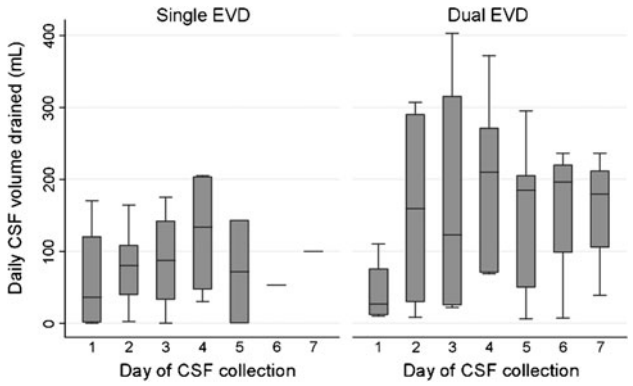

Fig. 2 Box plots of average daily cerebrospinal fluid drainage in dual and single EVD groups for the median duration of dual EVD use

daily while intraventricular injections were performed. In addition, CSF samples were sent per standard of care if there were signs or symptoms of infection.

The designation of bacterial ventriculitis/meningitis required a fever and a positive culture. If there were CSF signs of infection and symptoms but no organism grew in culture, the event was classified as nonbacterial ventriculitis. One single catheter patient treated with rt-PA had an asymptomatic catheter tract hemorrhage. No patients in this cohort required lumbar drainage or permanent shunting for CSF drainage. No patients included in this group demonstrated clinical or radiographic findings indicative of over-drainage such as subdural hematoma (SDH).

Length of ICU Stay

Length of stay in the ICU among survivors was not statistically different between the two groups (Table 2).

Discussion

Our intent was to characterize the use of dual EVDs and potential differences in clot resolution between single and dual catheters in patients with IVH causing obstructive hydrocephalus. Discretionary use of dual EVDs was limited to patients with very large IVH (>40 ml) and in 4/7 patients was performed because of initial EVD obstruction. Our findings suggest dual catheters might improve clot clearance in very severe IVH. Based on these retrospective observations, recommendations for placing a second EVD would include large IVH volume (greater than 40 ml), a trapped ventricle or significant mass effect due to hydrocephalus. The impact of dual EVDs on clot clearance was not significantly different between rt-PA and placebo-treated patients. The high mortality (43%) and poor 30 day morbidity (mRS = 5) of this cohort are consistent with IVH volume as an independent predictor of outcome. This report is hypothesis-generating in the effort to develop guidelines for optimal EVD placement in severe IVH. It does not attempt to assess the impact of dual EVDs on intracranial pressure control or neurologic function.

Our results contrast with recent report by Staykov et al. suggesting no difference in IVH clearance with unilateral versus bilateral EVD in "severe" IVH [6]. Those authors compared 14 patients with bilateral EVDs with 13 single catheter patients and found similar clot resolution between the two groups with no difference in outcome at 3 months. There was a trend toward longer EVD duration and higher infection rates in the bilateral group, causing the authors to conclude that bilateral EVDs provided no advantage over single catheters. Our results likely differ because patients with dual EVDs in this study had larger IVH volumes. The median IVH volume in our group was more than double that of Staykov's study (75.4–84.5 ml vs. 31.6–34.7 ml).

It is possible that dual catheters significantly reduce IVH volume only in patients with very large IVH. There may be a threshold IVH volume at which 2 EVDs improve clot clearance compared to a single EVD.

We restricted our analysis to the period of drainage with two catheters, and a comparble period in single catheter control cases, rather than to the entire duration of CSF drainage. This allowed a rigorous comparison of the efficiency of dual versus single catheter drainage in comparable cases during similar time periods. Daily CSF drainage during this period was nonsignificantly greater in dual EVD patients, which may be the basis for reduced IVH volume, and it suggests that both EVDs were functioning to some degree. We did not have separate CSF volumes for each catheter in order to ascertain whether one or both catheters were nonfunctional at some point during the duration of drainage. It is possible that initially obstructed EVDs became functional with injection of thrombolytic or placebo.

The use of dual EVDs increased total EVD duration in our cohort, similar to observations in the study of Staykov et al. [6]. This is likely related to slower "weaning" of EVD with two catheters, often performed sequentially, weaning and removing one catheter then another. However, EVDs were well tolerated and our cohort suffered few complications, specifically only one asymptomatic catheter tract hemorrhage in a single EVD patient and no instances of CSF infection. Despite the low incidence of complication in this cohort, practitioners must keep in mind the incremental risks of multiple EVD placement, namely increased risk of infection and tract hemorrhage, as well as cost. These risks must be weighed against the possible benefit additional clot clearance.

The impact of single versus dual catheter drainage on clinical outcome was beyond the scope of this paper. Any relationship between drainage efficiency and mortality and functional outcome is being tested in the ongoing CLEAR III trial, and this could not realistically be ascertained in our cohort.

This study was limited by small sample size and discretionary placement of dual EVDs by treating physicians, which may have introduced a sampling bias. We tried to reduce this possibility with the case–control design. Simultaneous dual catheter placement remains an infrequent treatment approach at most centers, which limits the available data. Cases and controls were carefully matched to minimize differences in the two groups. IVH severity was similar between groups with the exception of two cases in the dual EVD group which had very large IVH volume such that matching to controls within 10 ml was not possible. CT scans on the same day for each case/control pair were not available in all cases, although these were matched within 24 h. Long-term outcome data were unavailable on patients who survived which may be important in this disease where 90 and 180 day outcomes can improve significantly over those at 1 month.

Conclusions

This analysis suggests that dual catheters may be useful in the management of very large volume IVH, for trapped ventricles, or for catheter obstruction. Other possible indications not explored in this analysis are to enhance thrombolytic therapy on the contralateral side, to treat refractory intracranial hypertension or to reduce mass effect from IVH which may precipitate ischemic injury. Experimental studies of IVH suggest that both the volume of IVH and duration of exposure of CSF to clotted blood independent of mass effect or hydrocephalus contribute to altered consciousness and pathological changes within the ventricle [9, 10]. From this viewpoint, therapies that remove more blood clot faster may have clinical benefit. Future investigation should focus on safety, long-term outcomes, and specific indications for use of dual EVDs in IVH.

Acknowledgments CLEAR IVH is sponsored by the FDA orphan drug program, assisted by a donation from Cathflo and a sponsored research agreement with Genentech. Use Patent holder: Johns Hopkins Medical Institutions. Drs. Hanley and Naff hold an Investigator IND for the use of intracerebral rt-PA.

Conflict of interest Dr. Hinson, Mr. Melnychuk, and Mr. Muschelli have nothing to disclose. Dr. Hanley has received research support as PI of the CLEAR IVH trial, which is sponsored by the FDA Orphan Drug Program assisted by a donation from Cathflo and a sponsored research agreement from Genentech. Dr. Ziai has received personal compensation in an editorial capacity for Current Opinion in Neurology.

References

1. Vereecken KK, Van Havenbergh T, De Beuckelaar W, Parizel PM, Jorens PG. Treatment of intraventricular hemorrhage with intraventricular administration of recombinant tissue plasminogen activator. A clinical study of 18 cases. Clin Neurol Neurosurg. 2006;108(5):451–5.
2. Coplin WM, Vinas FC, Agris JM, et al. A cohort study of the safety and feasibility of intraventricular urokinase for nonaneurysmal spontaneous intraventricular hemorrhage. Stroke. 1998;29(8):1573–9.
3. Findlay JM, Grace MG, Weir BK. Treatment of intraventricular hemorrhage with tissue plasminogen activator. Neurosurgery. 1993;32(6):941–7. (discussion 947).
4. Andrews CO, Engelhard HH. Fibrinolytic therapy in intraventricular hemorrhage. Ann Pharmacother. 2001;35(11):1435–48.
5. Naff NJ, Carhuapoma JR, Williams MA, et al. Treatment of intraventricular hemorrhage with urokinase : effects on 30-Day survival. Stroke. 2000;31(4):841–7.

6. Staykov D, Huttner HB, Lunkenheimer J, et al. Single versus bilateral external ventricular drainage for intraventricular fibrinolysis in severe ventricular haemorrhage. J Neurol Neurosurg Psychiatry. 2010;81(1):105–8.
7. Kothari RU, Brott T, Broderick JP, et al. The ABCs of measuring intracerebral hemorrhage volumes. Stroke. 1996;27(8):1304–5.
8. Graeb DA, Robertson WD, Lapointe JS, Nugent RA, Harrison PB. Computed tomographic diagnosis of intraventricular hemorrhage. Etiology and prognosis. Radiology. 1982;143(1):91–6.
9. Pang D, Sclabassi RJ, Horton JA. Lysis of intraventricular blood clot with urokinase in a canine model: Part 1. Canine intraventricular blood cast model. Neurosurgery. 1986;19(4):540–6.
10. Mayfrank L, Kissler J, Raoofi R, et al. Ventricular dilatation in experimental intraventricular hemorrhage in pigs. Characterization of cerebrospinal fluid dynamics and the effects of fibrinolytic treatment. Stroke. 1997;28(1):141–8.