CASE REPORT

Nimodipine Prevent Vasospasm Complication in Anesthesia Management of Cerebral Aneurysm Clipping

SATRIO ADI WICAKSONO[1], TAUFIK EKO NUGROHO[1], HIMAWAN SASONGKO[1], MOHAMAD SOFYAN HARAHAP[1], SULISTIYATI BAYU UTAMI [2]

[1]*Dept of Anesthesiology& Intensive Therapy, F*aculty of *M*edicine. *D*iponegoro *U*niversity / *Dr. K*ariadi *G*eneral *H*ospital, *Semarang, Indonesia*

[2]*Dept of Cardiology and Vascular Medicine.Faculty of Medicine. Diponegoro University / Dr. Kariadi General Hospital,Semarang, Indonesia*

Correspondence to: Satrio Adi Wicaksono, Email : *drsaw11@yahoo.com*, Phone/Fax : +62 24 – 76928010,

ABSTRACT

Background: Subarachnoid haemorrhage (SAH) can be defined as a process of blood vessel rupture into the subarachnoid space in which the most common cause of SAHiscerebral aneurysm.The management of SAH since the initial diagnosis, emergency,surgical,and intensive care management, including calcium channel blocker (CCB) nimodipine therapy, mayaffect the outcomes and prevent SAH complications, such as vasospasm.

Case Illustration: This case report reported three patients with aneurysmalSAH.Patient 1 was a 67-year-old woman with a chief complaint of acute severe headache accompanied withright-sided hemiparesis and motoric aphasia. Patient 2 was a 68-year-old woman with a chief complaint of loss of consciousness since 1 day before admissionaccompanied with right-sided hemiparesis. Patient 3 was a 65-year-old man with a chief complaint of loss of consciousness since 4 hours before admission. All patients have a history of hypertension. Acraniotomy aneurysm clipping surgery was performedtoall patients, by placing a clip along the neck of the aneurysm, maintaining the main arteries and adjacent arteries, especially in cases of difficult intracranial aneurysms.

Conclusion: Administration of nimodipine in anaesthesia management of cerebral aneurysm clipping showedexcellent results. The earlier administration of CCB nimodipin might resultin shorter length of stay.

Keywords: Aneurysm clipping; calcium channel blocker; nimodipine; SAH; vasospasm

INTRODUCTION

Subarachnoid hemmorage(SAH) can be defined as a proses of blood vessel rupture into the subarachnoid space.Its prevalence may reach up to 33,000 people per year in the United States.The overall incidence of SAH is approximately 9 per 100,000 person-years. Rates are higher inJapan and Finland and increase with age.Incidences per 100,000 person-years were 22.7 in Japan, 19.7 in Finland, 4.2 in South and Central America, and 9.1 in the other regions[1]. However, there is only limited data in the incidence of SAH in Indonesia.

Subarachnoid haemorrhages have a peak incidence at around 55 years for men and 60 years for women.The incidence in women was 1.24 times higher than in men; with a ratio of 3:2.With age category 45–55 years as the reference, incidence ratios was 0.10 for age groups younger than 25 years and 1.61 for age groups older than 85 years[1].

The most common causes of subarachnoid bleeding are rupture of aneurysm in one of the basal cerebral arteries or the presence of an arterivenous malformation (AVM)(10%). Several types of aneurysms that can form in the brain arteries include saccular aneurysms (“berries”) (80%), fusiform aneurysms, and mycotic aneurysms[2,3,4].

About 10–25% of patients with SAH die immediately after the bleed orbefore arriving at the hospital and 40% die in hospital without being able to improve. The mortality rate in the first year is around 60% and in the first 5 years is around 70%. If there is no surgical intervention, about 30% of patients die within the first 2 days, 50% in the first 2 weeks, and 60% in the first 2 months[4,5].

Complications of SAH are distinguished between the acute phase (day 0 to 3), subacute phase (between day 3 and day 30) and late phase (after day 30).Vasospasm and re-bleeding are the most frequent complications in subarachnoid haemorrhage[6,7]. Re-bleeding is the most serious acute complicationand generally occurs in the first three days after the initial bleed[7,8]. The risk of vasospasm occurslater than the risk of rebleeding, classically between day 4 and day 15[9].

Degradation and lysis of extravascular blood clots within the cerebral fluid lead tothe release of vasoactive mediators. These mediators cause cerebralvasoconstriction leading to a fall in cerebral blood flow[6,10]. Although an inconsistent finding, it may be followedby the development of a cerebral hypoperfusion area with a risk of cerebral infarction, which may be fatal[6].

Warning clinical signsand symptoms of vasospasm can be a decrease in mental status anda focal neurological deficit on day 3 after a subarachnoid haemorrhage[6]. Vasospasm will cause delayed cerebral ischemia (DCI), i.e., the complexsyndrome of delayed cerebral hypoperfusion and neurological decompensation,with two main patterns, namely single cortical infarction and extensive multiple lesions.(4)Mortality is reported to be as high as 70–80% inpatients who re-bleed from their SAH[11].

To reduce the risk of re-bleedingbefore repairing the aneurysm, blood pressure must be carefully managed with the administration of phenylephrine, norepinephrine, and dopamine (for patients with hypotension), labetalol, esmolol, nicardipine,and nimodipine (for patients with hypertension).While specific pharmacotherapy for DCI consists mainlyof the administration of dihydropyridine L-type calcium channel blockers[4].

This case report discusses 3 patients diagnosed with SAH and performed an aneurysm clipping craniotomy surgery. Aneurysmclipping is a method in which the aneurysm is closed off from its parent vesselby the

placement of a metal clip to occlude itsneck[4]. In this case report, the role of nimodipine in the management of patients with SAH and the outcome of these patients will be discussed.

CASE ILLUSTRATION

Patient 1 was a 67-year-old woman. She came to emergency departmentwith a chief complaint of acute severe headacheaccompanied by motoric aphasia. Meanwhile, she was used to have headachesperiodically since 1 year that were controlled with medications, however the last one was different and much more severe. She took medication but it did not relieve the headache. She had photophobia. She had right-sidedhemiparesis.Patient 2 was a 68-year-old woman, She came to emergency department with a chief complaint of loss of consciousness since 1 day before admission accompanied withright-sided hemiparesis. Patient 3 was a 65-year-old man. He came to emergency department with a chief complaint of loss of consciousness since 4 hours before admission. Allpatientshave a history of hypertension. The history of all patients are presented in table 1.

Physical examination of all patients are presented in table 2. Otherphysical examination findings that were not mentioned, were within normal limits.Patient 1 and 2 showed lateralization, while patient 3did not get the impression of lateralization on motor examination. The laboratory and other supporting examination findings are presented in table 3.

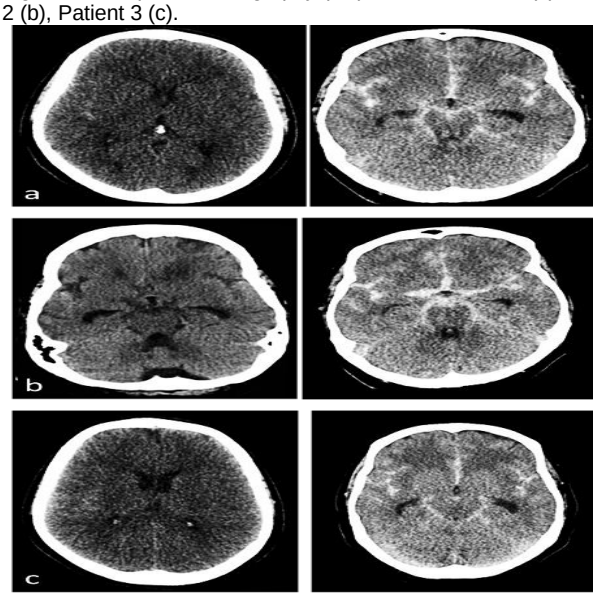
Patient 1 showed inferiorly directed saccular aneurysm at the origin of the right posteriorcommunicating artery with neck (sized 2.7 mm and diameter ±3 mm, length 2.7 cm) to the. There was no visible extravasation of contrast perianeurysm. There were partial stenosis of the right internal carotid artery at the cavernous segment and lacunar infarction of the anterior crus of the right and left internal capsule and the posterior crus of the right internal capsule.The hypodensity in theleft and right sides of the anterior and posterior ventricles and anterior and posterior pericornu of right and left lateral ventricle tends to be gliotic appearance (Figure 1a). Patient 2 also showed a saccular aneurysm in the left posterior communicating artery with a wide neck (size ± 3.3 mmanddiameter ± 4.2 mm, length 8.0 cm) to the inferior direction thatwasruptured. There was still visible active bleeding of subarachnoid haemorrhage with ventricular haemorrhage. Hydrocephalus communicans appeared to be signs of increased intracranial pressure (ICP) (Figure 1b). Patient 3 also showed a saccular aneurysm in the right posterior communicating artery with a wide neck (size ± 3.1 mm and diameter ± 3.5 mm, length 6.0 cm) to the inferior direction that was ruptured. There was still visible active bleeding of subarachnoid haemorrhage with ventricular haemorrhage (Figure 1c).

Anesthesia Management: All patients underwent cerebral aneurysm clipping surgery in Dr. Kariadi General Hospital, Semarang, Indonesia. Patient 1 was given a premedication of atropine(atropine sulfate)0.25 mg. Then she was induced with propofol 200 mg, fentanyl 100 µg, and rocuronium 50 mg. Patient 1was maintained with propofol 30mg/hour, rocuronium 3 mg/hour, fentanyl 25µg/hour, and 0.5 MAC sevoflurane.Patient 1wasadministered withmanitol 250 mg as a neuroprotector.During surgery, her vital sign was stable with an average MAP of 65 mmHgmeasured with arterial lines (pressure) and heart rateof 60 times/minute. Her operating time was 260 minutes in which the total liquid enteredwas a 3500 cc of crystalloid, totalbleeding was100 cc, and urine amount was 1500 cc.

Patient 2 was given a premedication of atropine (atropine sulfate) 0.25 mg. Then she was induced with propofol 150mg-minute. Her operating time was 290 minutes in which the total liquid entered was a 3500 cc of crystalloid, total bleeding was 100 cc, and urine amount was 1540 cc.

Patient 3 was given a premedication of atropine (atropine sulfate) 0.25mg. Then he was induced with propofol 200 mg, fentanyl 100 µg, and rocuronium 50 mg. Patient 3 was maintained with propofol 30 mg/hour, rocuronium 3 mg/hour, fentanyl 25 µg/hour, and 0.5 MAC sevoflurane. Patient 3 was administered with manitol 250 mg as a neuroprotector. During surgery, his vital sign was stable with an average MAP of 65 mmHg measured with arterial lines (pressure) and heart rate of 60 times/minute. His operating time was 280 minutes in which the total liquid entered was a 3500 cc of crystalloid, total bleeding was 100 cc, and urine amount was 1600cc.Systolic (SBP) and diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) during surgery are presented in figure 2–5.

Figure 1. Computed Tomography (CT) scanof Patient 1 (a), Patient 2 (b), Patient 3 (c).



Perioperative Management: Patient 1 was administered withintravenous continous infusion of calcium channel blocker (CCB) nimodipine 2 mg/hour for 6 days followed by nimodipine tablet 60 mg/4 hours preoperatively, as well as CCB amlodipine tablet 10mg/24 hours,intravenous phenytoin 200 mg/24 hours, intravenousmoxifloxacin 400 mg/24 hours,intravenous ranitidine 50mg/12 hours, and intravenous tranexamic acid 1 g/12 hours for supportive therapy. After surgery, patient 1was treated in the intensive care unit (ICU). She receivednimodipine 1.2 mg/hour continous infusionvia syringe pump, intravenous phenytoin

200 mg/24 hours, fentanyl 10 µg/hour continousinfusion, intravenous paracetamol 1g/8 hours, intravenous tranexamic acid 500 mg/8 hours, intravenous vitamin K 10 mg/12 hours,intravenous omeprazole 40 mg/12 hours, and amlodipine tablet 5 mg/24 hours.The total days of ICUtreatment for patient 1was 42 days. The patient was transferred to the ward after 42 days as there were nosigns of deterioration or the appearance of new neurological abnormalities during ICU care.

Patient 2 was administered withnimodipine tablet 60 mg/12 hours, intravenous phenytoin 200 mg/24 hours, intravenous levofloxacin 750 mg/24 hours, and intravenous ranitidin 50 mg/12 hours,preoperatively. Patient 2 was treated at high care unit (HCU) postoperatively. Shereceived amlodipine tablet 10 mg/24 hours, morphine 0.5 mg/hour continous infusion via syringe pump, intravenousketorolac 10 mg/8 hours, paracetamol 1000 mg/8 hoursper oral, ventolin pulmicortnebulisation/8 hours, and intravenous ranitidin 50 mg/12 hours. The total days of ICU treatment for patient 2 was 28 days. Patient 2 was transferred to the ward after 28 days treatment in ICUand without signs of deterioration or the appearance of new neurological abnormalities.

Patient 3 was administered with nimodipine2 mg/hour continous infusion via syringe pump for 1 day,nimodipine tablet 60 mg/12 hours, intravenous phenytoin 200 mg/24 hours, intravenous levofloxacin 750 mg/24 hours, and intravenous ranitidin 50 mg/12 hours, preoperatively. Patient 3 was treated at high care unit (HCU) postoperatively. He received amlodipine tablet 10 mg/24 hours, morphine 0.5 mg/hour continous infusion via syringe pump, intravenous ketorolac 10 mg/8 hours, paracetamol 1000 mg/8 hours per oral, and intravenous ranitidin 50 mg/12 hours. The total days of HCU treatment for patient 3 was 30 days. Patient 3 was transferred to the ward after 30 days treatment in HCU and without signs of deterioration or the appearance of new neurological abnormalities.SBP, DBP, MAP, and HR post surgery in intensive or high care unit are presented in figure 6–9.

Table 1: Baseline History of Subjects

	Patient 1	Patient 2	Patient 3
History of Medication	Paracetamol 500 mg /8 hours Ranitidin 50 mg /12 hours Amlodipin 5 mg/24 hours	Paracetamol 500 mg/8 hours Ranitidin 50 mg /12 hours Amlodipin 10 mg/24 hours	Paracetamol 500 mg/8 hours Vitamin B1, B6, B12 1 mg /8 hours Ranitidin 50 mg / 12 hours Amlodipin 10 mg/ 24 hours
History of Other Illness	History of hypertension. No history of asthma, allergy, fever, diabetes mellitus,heart disease, norprevious surgery. No history of smoking, cocaine use, or marijuana use.	History of hypertension. No history of asthma, allergy, fever, diabetes mellitus,heart disease, norprevious surgery.No history of smoking,cocaine use, or marijuana use.	History of hypertension.No history of asthma, allergy, fever, diabetes mellitus,heart disease, nor previous surgery.No history of smoking,cocaine use, or marijuana use.

Table 2: Baseline Physical Examination

	Patient 1	**Patient 2**	**Patient 3**
	Emergency department	Emergency department	Emergency department
General condition	weak	weak	weak
Vital Sign			
Consciousness (Glasgow Comma Scale)	E4M6Vaphasia	E2M4V2	E3M4V2
Blood Pressure (mmHg)	151/90	190/90	180/90
Mean Arterial Pressure (mmHg)	110	123	120
Heart Rate (/min)	96	120	110
Respiratory rate (/min)	25	28	26
Temperature (^oC)	37.4	37.3	37.2
Body weight (kg)	80	70	75
Body Mass Index (BMI) (kg/m^2)	29.0	26.6	28.5
Eye	Isokor, normal light reflex	Isokor, normal light reflex	Isokor, normal light reflex
Lungs	normal	rough rales in both lungs	normal
Extremities	swollen legs	swollen legs	
Neurological Examination			
Superior Extremities			
Motoric	reduced / +	reduced / +	+ / +
Movement	444/555	444/555	555/555
Power	reduced / normal	reduced / normal	normal / normal
Tonus	++ / +	++ / +	++ / ++
Physiological Reflex	+/-	+/-	-/-
Pathological Reflex	cannot be assessed	cannot be assessed	cannot be assessed
***Sensibility,* Inferior Extremities**			+ / +
Motoric	reduced / +	reduced / +	555/555
Movement	444/555	444/555	normal / normal
Power	reduced / normal	reduced / normal	++ / ++
Tonus	++ / +	++ / +	- / -
Physiological Reflex	+ / -	+ / -	
Pathological Reflex			cannot be assessed

Sensibility	cannot be assessed	cannot be assessed	

Table 3. Baseline Laboratory and Supporting Examination

	Patient 1	**Patient 2**	**Patient 3**
Hemoglobin(g/dL)	11.2	11.8	10.5
Hematocryte (%)	33.4	32.2	30.1
Platelets (/µl)	395,000	287,000	315,000
Leucocyte (/µl)	8,400	12,100	14,200
Electrolyte			
Sodium (mmol/L)	138	138	142
Potassium (mmol/L)	4.5	4.2	4.4
Chloride (mmol/L)	95	100	102
Random Blood Glucose (mg/dL)	132	188	198
Albumin (g/L)	3.5	3.5	3.5
Ureum (mg/dl)	20	29	28
Creatinine (mg/dl)	0.7	0.8	0.6
Prothrombin Time (PT)	12.0 (control = 10.8)	12.6 (control = 14.4)	11.9 (conttrol = 12.3)
Activated Partial Thromboplastin Time (aPTT)	37.4 (control = 31.1)	24.9 (control = 30.5)	26.5 (control = 31.2)
Electrocardiogram	Sinus rhythm, left ventricular hyperthrophy	Sinus rhythm,left ventricular hyperthrophy	Sinus rhythm,left ventricular hyperthrophy
Chest Xray	Left ventricle enlargement, no infiltrate in both lungs	Left ventricle enlargement, infltrate in both lungs	Left ventricle enlargement, no infiltrate in both lungs
Fisher Grade	Grade 2	Grade 2	Grade 2

Figure 2. Systolic Blood Pressure during Surgery (S) (mmHg), 1, Patient 1; 2, Patient 2; 3, Patient 3

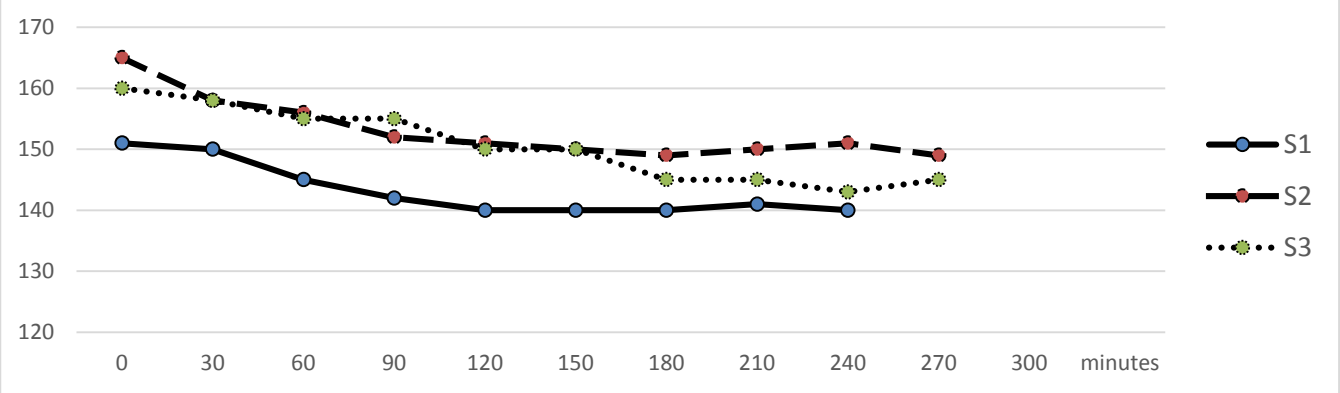


Figure 3. Diastolic Blood Pressure during Surgery (D) (mmHg), 1, Patient 1; 2, Patient 2; 3, Patient 3

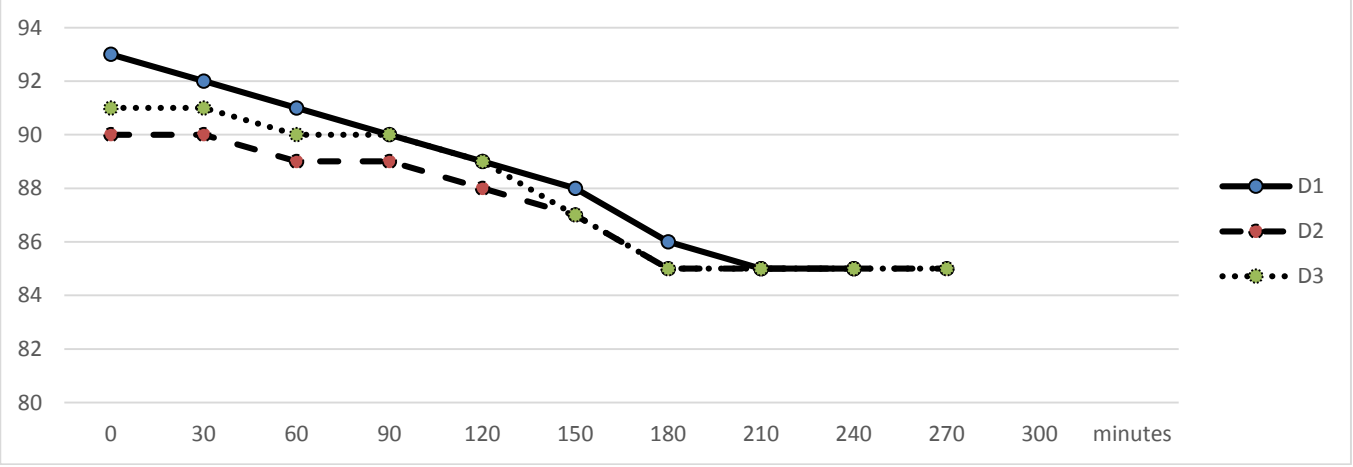


Figure 4. MeanArterial Blood Pressure during Surgery (M) (mmHg), 1, Patient 1; 2, Patient 2; 3, Patient 3

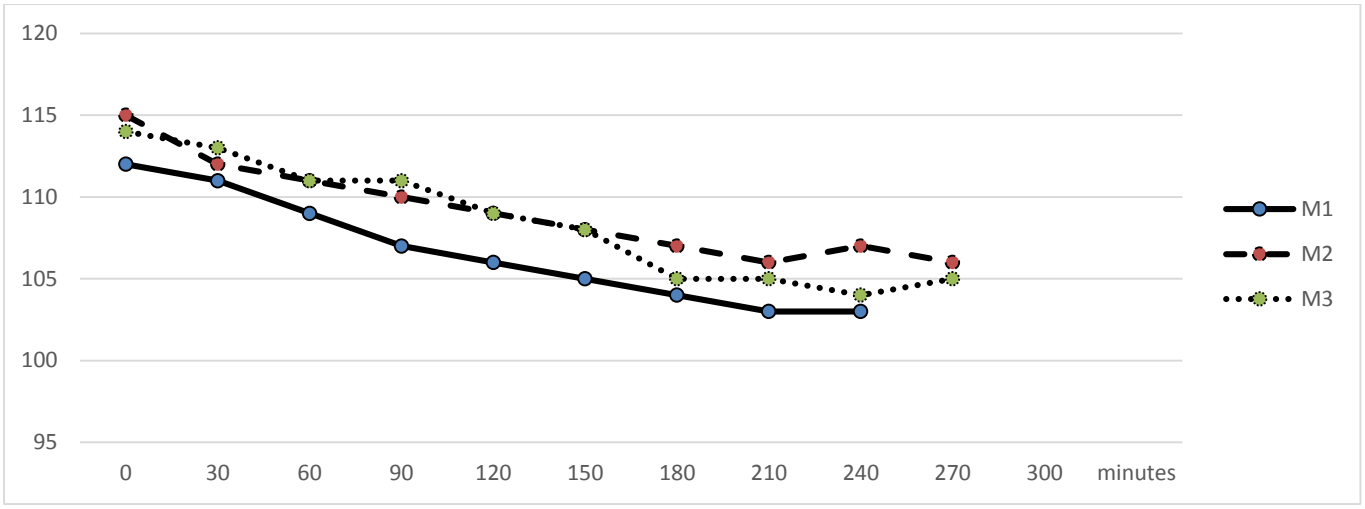


Figure 5. Heart Rate during Surgery (HR) (/minute), 1, Patient 1; 2, Patient 2; 3, Patient 3

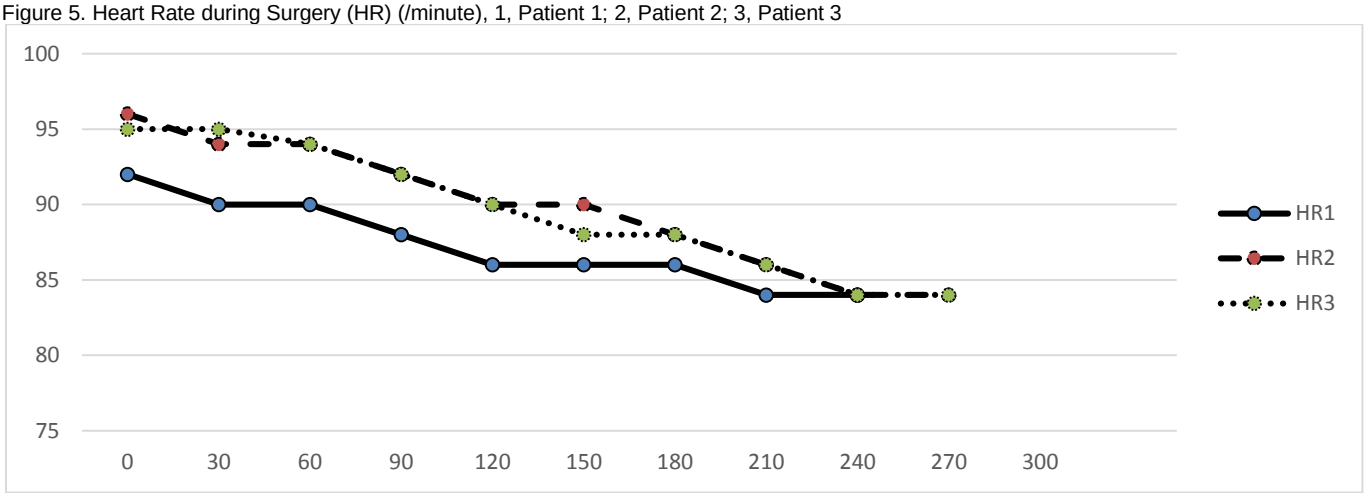


Figure 6. Systolic Blood Pressure Post Surgery in intensive or high care unit (S') (mmHg), 1, Patient 1; 2, Patient 2; 3, Patient 3

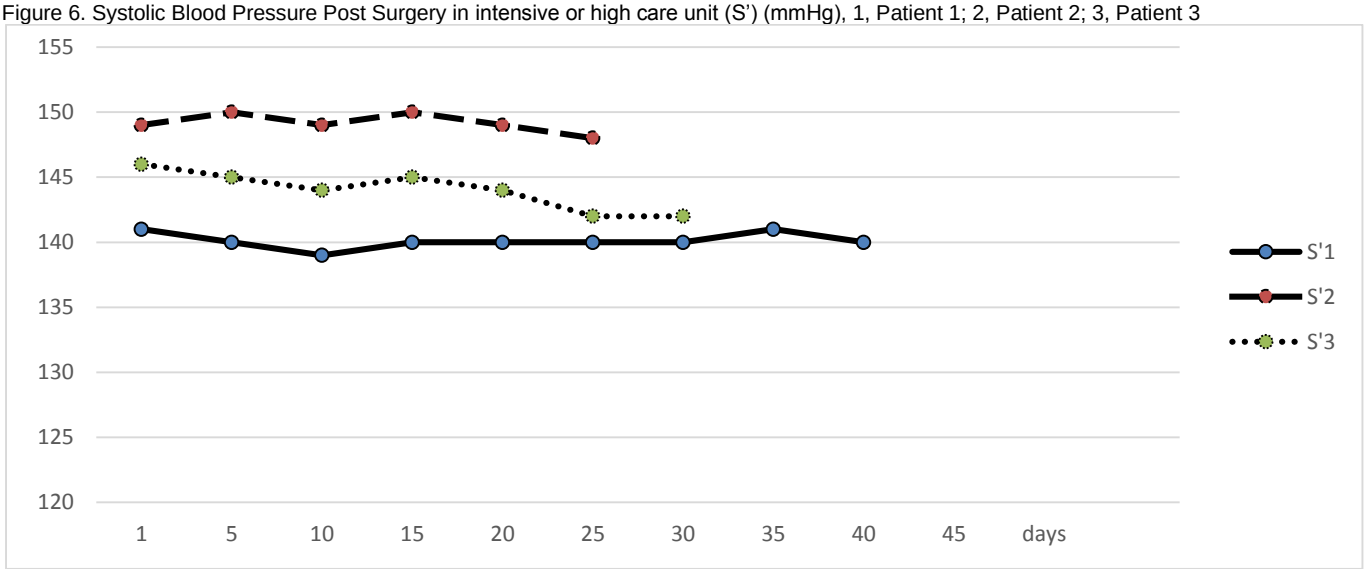


Figure 7. Diastolic Blood Pressure Post Surgery in intensive or high care unit (D') (mmHg), 1, Patient 1; 2, Patient 2; 3, Patient 3

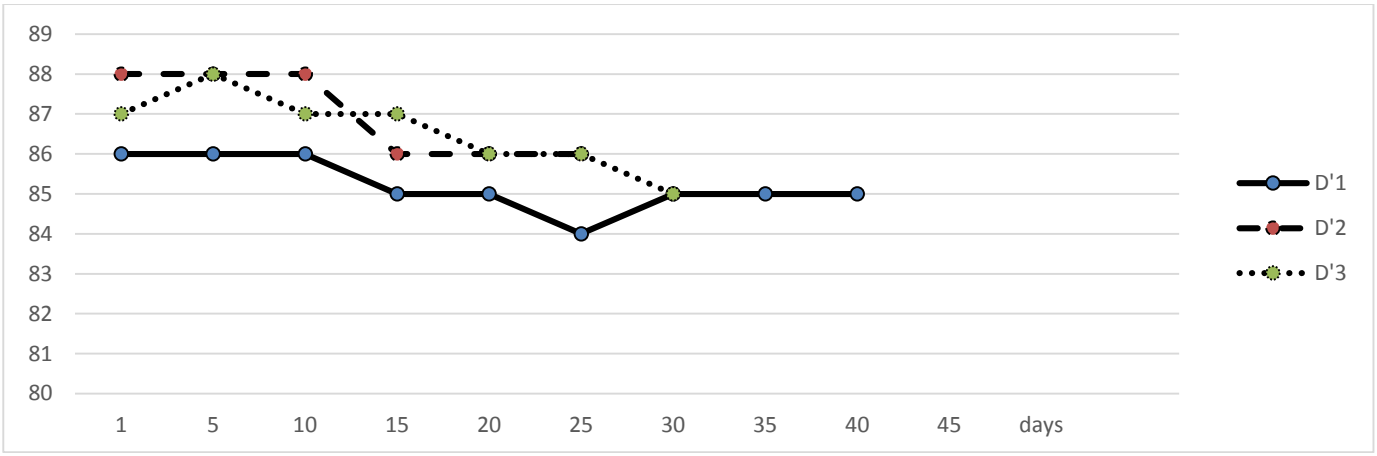


Figure 8. MeanArterial Blood Pressure Post Surgery in intensive or high care unit (M') (mmHg), 1, Patient 1; 2, Patient 2; 3, Patient 3

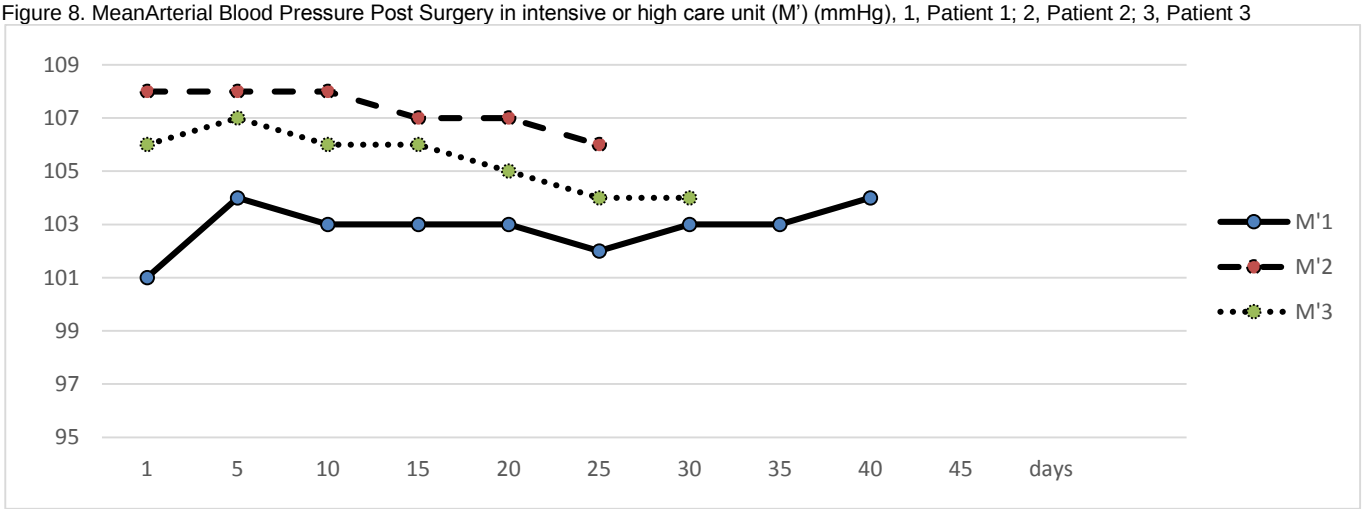
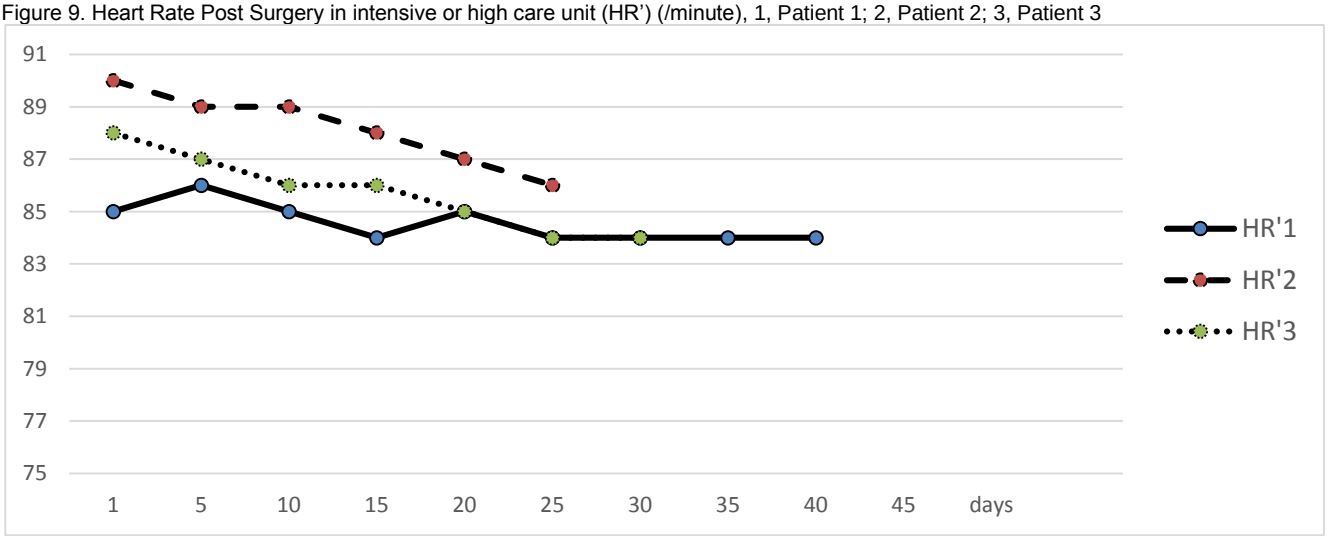


Figure 9. Heart Rate Post Surgery in intensive or high care unit (HR') (/minute), 1, Patient 1; 2, Patient 2; 3, Patient 3



DISCUSSION

Subarachnoid hemorrhage (SAH) is the extravasation of blood into the subarachnoid space between the pial and arachnoid membranes. The most common causes of spontaneous SAH are rupture of a saccular (berry) aneurysm (80%) and rupture of an arteriovenous malformation (AVM) (10%)[1,2]. The management of aneurysmal SAH iscomprehensivethat is aiming to prevent rebleedingfrom the underlying aneurysm, prevent the functional impacts ofvasospasm, prevent seizures, prevent brainedema and swelling, and correct electrolyte abnormalities[3].

Cerebral vasospasm,one of the complications caused by subarachnoid haemorrhage,is the reversible reductionin lumen diameterof a conducting artery in the subarachnoid space.[(12)]Vasospasm usually defines as anangiographic image of a yarn-like of contrast in a larger artery. Vasospasm is vary that depends on degree, extent, and time. If the cerebral vasospasm is severe or widespread, and lasts for a longerduration, it is thought to be responsible for late cerebral hypoperfusion, neurologicaldecompensation, and poor clinical outcomesdue to cerebralinfarction as the compensatory mechanisms fail.[(4)]Itusually takes several daysto be noticeable, such asfrom the third day after the aneurysm event, and reaches its peak near the end of the first week, such ason the fifth to seventh day.[(12)]However, the concept of cerebral vasospasm leading topoor outcomes in patients with SAH isstillchallenged[4].

Dankbaar JW et al categorized vasospasm as: no spasm (0–25%decrease in vessel diameter), moderate spasm (25–50%decrease), and severe spasm (>50% decrease). They showed that vasospasm decreased cerebral perfusion, butcorresponded with the least perfused region in only twothirds of our patients. Furthermore, almost half of patientswith severe vasospasm did not have DCI. Thus, it may be considered that althoughsevere vasospasm can decrease perfusion,it sometimes may not result in DCI[13].

Delayed cerebral ischemia itself can clinicallymanifest asa gradualneurological deterioration over the course of severalhours, or as a decline in the state of consciousness, such as a dropof more than 2 points on the Glasgow Coma scale, oras a focal neurological deficit of acute onset, such as hemiparesis, aphasia, apraxia, or neglect.DCIin aneurysmal SAH was an evidence-based combined clinical and imaging reference standard[4,14].

There are several mechanisms proposed for cerebral vasospasm complication. Blood products released from SAH stimulates the tyrosine kinase pathway causing the release of calcium ions from intracellular storage, resulting in smooth muscle contraction of cerebral arteries. Oxyhaemoglobin in cerebrospinal fluid (CSF) causes vasoconstriction by increasing free radicals, endothelin-1, prostaglandin and reducing the level of nitric oxide and prostacyclin. Besides, the disturbances of autonomic nervous system innervating cerebral arteries is also thought to cause vasospasm.[(15)]Some animal studies described the pathophysiology of DCI post SAH in which the vasospasm could occur since the beginning of brain injury post SAH until the hypoxia occured and trigger the apoptotic cascade[16].

Nimodipine is a Ca2+-channel antagonist of a dihydropyridine type. Its chemical name is 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic acid 2-methoxyethyl-1-methylethylester.[(17)]It has been known that nimodipine could exhibit a degree of selectivity for the cerebral vasculature due to its greater dependence on extracellular calcium for smooth muscle contraction[18,19]. Nimodipine has a cerebral vasodilator action at doses that do not affect systemic arterial pressure and has protective actions in some animal models of cerebral ischemia and hypoxia[20].

In our case report, all patients that received nimodipin therapy before surgery,did not experience worsening and did not get signs and symptoms of cerebral vasospasm either before, during, or after surgery while being treated in intensive care.Our findings are in accordancewith previous studies whichhave shown that a dihydropyridine calcium channel blocker nimodipin therapy significantly prevented major complication of SAH termed cerebral vasospasm as well as resultant cerebral infarction[18,19].

Nimodipine has beneficial effectsdue to thedirect neuroprotective properties inducedbythe prevention of free-radical attacks on intraneuronal mitochondria[21], an improvement ofCO_2 reactivity and cerebral oxygen metabolism[22], ora reduction of tissue damage caused by calcium overload at reperfusion[23,24].

Bele S et al showed that there were better results after 6 months after discharge in nimodipine therapy compared with controlandthere wereno patients in avegetative condition. They showed that the occurrence of cerebral infarctions was significantly lower (42.6%)in the nimodipine group than in the control group (75.0%)[19]. Other studies showed that nimodipine intravenous combination for 10 days followed by oral nimodipine administration for 11 days could decrease DCI[25,26].

Vasospasmcan trigger hypoxia,inflammatory mechanisms,and the apoptotic cascade. This cascade removes activated mitogenactive Ca^{2+}-protein kinases, including p38mitogen-activated protein kinase (p38 MAPK), extracellular signal-regulated kinase 1/2(ERK1/2), and c-Jun N-terminal kinase (JNK), which cause neuronal death and DCI[16]. Therefore, early improvement of hypoxia by increasing cerebral blood flow or reducing vasospasm with nimodipine can contribute to reduce brain injury and protect neurons[27,28]. Therefore, early treatment with intravenous nimodipine might potentially reduce the incidence of vasospasm after SAH and reduce the incidence of DCI[29,30] In our case report, oral administration of nimodipin alone or combination also successfully prevented cerebral vasospasm as indicated that there were no worsening of signs and symptoms and neurological deficits during intensive care.

Furthermore, there were also no rebleeding in all our patients, although Tanno et al showed that rebleeding occured more frequently in the earlier period after the initial SAH than previously believed.They suggested that more aggressivepharmacologically induced systemic arterial hypotension appeared to be important for preventing

rebleeding but ultimate outcome ofmore aggressivehypotension was yet tobe determined[7].

In our cases, we applied aggressive management of high blood pressure as it wascritical because increased blood pressure wastheoretically a risk for aneurysmal re-rupture.All patients were admitted to anICU or HCU, as we needed to perform direct arterial pressuremonitoring with an arterial line, the useof antihypertensive medication drips, and minimizing patienstimulation with so-called subarachnoidprecautions. Subarachnoid precautionsinclude limiting the number of visitors,minimizing room volume, minimizingcoughing by using antitussives if needed, minimizingstrain secondary to pain by usingadequate analgesia, prescribing stool softeners to prevent constipation and unduestrain, and using sedation as necessary tominimize the patient's startle reflex and toprevent acute increases in blood pressure.We also identified and were ready to treat reversiblecauses of active bleeding asneeded, including coagulopathies and platelet disorders, usingfresh frozen plasma, vitamin K, and platelets, respectively[3].

CONCLUSSION

Calcium channel blocker nimodipin could prevent cerebral complications in patients with aneurysmal SAH who would undergo or had been undergoing the aneurysmal clipping surgery. Complications that arised after therapy such as cerebral vasospasm, delayed cerebral ischemic, and re-bleedingcould be prevented. Thus, nimodipin might also help to reduce morbidity andmortality of these patients while treated in intensive care.

Conflict of interest = none

REFERENCES

1. de Rooij NK, Linn FH, van der Plas JA, Algra A, Rinkel GJ. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. J Neurol Neurosurg Psychiatry. 2007;78(12):1365-72.
2. Caplan LR. Subarachnoid Hemorrhage, Aneurysms, and Vascular Malformations. Caplan's Stroke: A Clinical Approach. 6th ed: Cambridge University Press; 2015. p. 542-86.
3. Pouration N, Dumont AS, Kassell NF. Subarachnoid Hemorrhage. Handbook of Neuroemergency Clinical Trials: Academic Press; 2006. p. 17-44.
4. Petridis AK, Kamp MA, Cornelius JF, Beez T, Beseoglu K, Turowski B, et al. Aneurysmal Subarachnoid Hemorrhage. Dtsch Arztebl Int. 2017;114(13):226-36.
5. Lovelock CE, Rinkel GJE, Rothwell PM. Time trends in outcome of subarachnoid hemorrhage: Population-based study and systematic review. Neurology. 2010;74(19):1494-501.
6. Daniere F, Gascou G, Menjot de Champfleur N, Machi P, Leboucq N, Riquelme C, et al. Complications and follow up of subarachnoid hemorrhages. DiagnInterv Imaging. 2015;96(7-8):677-86.
7. Tanno Y, Homma M, Oinuma M, Kodama N, Ymamoto T. Rebleeding from ruptured intracranial aneurysms in North Eastern Province of Japan. A cooperative study. J Neurol Sci. 2007;258(1-2):11-6.
8. Diringer MN, Bleck TP, Hemphill-III JC, Menon D, Shutter L, Vespa P, et al. Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference. Neurocrit Care. 2011;15(2):211-40.
9. Safain MG, Malek AM. Delayed progressive bilateral supraclinoid internal carotid artery stenosis in a patient with a ruptured basilar artery aneurysm. J Clin Neurosci. 2015;22(2):368-72.
10. Pluta RM, Hansen-Schwartz J, Dreier J, Vajkoczy P, Macdonald RL, Nishizawa S, et al. Cerebral vasospasm following subarachnoid hemorrhage: time for a new world of thought. Neurol Res. 2009;31(2):151-8.
11. Starke RM, Connolly JES. Rebleeding after aneurysmal subarachnoid hemorrhage. Neurocrit Care. 2011;15(2):241-6.
12. Weir B. The pathophysiology of cerebral vasospasm. BrJNeurosurg. 1995;9(3):375-90.
13. Dankbaar JW, Rijsdijk M, Schaaf ICvd, Velthuis BK, Wermer MJH, Rinkel GJE. Relationship between vasospasm, cerebral perfusion, and delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage. Neuroradiology. 2009;51(12):813-9.
14. Sanelli PC, Kishore S, Gupta A, Mangat H, Rosengart A, Kamel H, et al. Delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage: proposal of an evidence-based combined clinical and imaging reference standard. Am J Neuroradiol. 2014;35(12):2209-14.
15. Kolias AG, Sen J, Belli A. Pathogenesis of cerebral vasospasm following aneurysmal subarachnoid hemorrhage: putative mechanisms and novel approaches. J Neurosci Res. 2009;87(1):1-11.
16. Palade C, Ciurea AV, Nica DA, Savu R, Moisa HA. Interference of apoptosis in the pathophysiology of subarachnoid hemorrhage. Asian J Neurosurg. 2013;8(2):106-11.
17. Scriabine A, Battye R, Hoffmeister F, Kazda S, Towart R, Garthoff B, et al. Nimodipine. Nav Drugs Annual: Cardiovascular Drugs. 1985;3:197-218.
18. Wessell A, Kole MJ, Badjatia N, Parikh G, Albrecht JS, Schreibman DL, et al. High Compliance with Scheduled Nimodipine Is Associated with Better Outcome in Aneurysmal Subarachnoid Hemorrhage Patients Cotreated with Heparin Infusion. Front Neurol. 2017;8:268.
19. Bele S, Proescholdt MA, Hochreiter A, Schuierer G, Scheitzach J, ChristinaWendl, et al. Continuous intra-arterial nimodipine infusion in patients with severe refractory cerebral vasospasm after aneurysmal subarachnoid hemorrhage: a feasibility study and outcome results. Acta Neurochir (Wien). 2015;157(12):2041-50.
20. Kazda S, Towart R. Nimodipine: a new calcium antagonistic drug with a preferential cerebrovascular action. Acta Neurochir (Wien). 1982;63(1-4):259-65.
21. Hongo K, Kobayashi S. Calcium antagonists for the treatment of vasospasm following subarachnoid haemorrhage. Neurol Res. 1993;15(4):218-24.
22. Rasmussen G, Bergholdt B, Dalh B, Sunde N, Cold G, Voldby B. Effect of nimodipine on cerebral blood flow and cerebrovascdar reactivity after subarachnoid haemorrhage. Ada Nerirol Scand. 1999;99(3):182-6.
23. Roda JM, Carceller F, Díez-Tejedor E, Avendaño C. Reduction of infarct size by intra-arterial nimodipine administered at reperfusion in a rat model of partially reversible brain focal ischemia. Stroke. 1995;26(10):1888-92.
24. Biondi A, Ricciardi GK, Puybasset L, Abdennour L, Longo M, Chiras J, et al. Intra-Arterial Nimodipine for the Treatment of Symptomatic Cerebral Vasospasm after Aneurysmal Subarachnoid Hemorrhage: Preliminary Results. Am J Neuroradiol. 2004;25(6):1067-76.
25. Karinen P, Koivukangas P, Ohinmaa A, Koivukangas J, Ohman J. Cost-effectiveness analysis of nimodipine treatment after aneurysmal subarachnoid hemorrhage and surgery. Neurosurgery. 1999;45(4):780-4.
26. Wolf S, Martin H, Landscheidt JF, Rodiek SO, Schurer L, Lumenta CB. Continuous selective intraarterial infusion of nimodipine for therapy of refractory cerebral vasospasm. Neurocrit Care. 2010;12(3):346-51.
27. Ott S, Jedlicka S, Wolf S, Peter M, Pudenz C, Merker P, et al. Continuous selective intra-arterial application of nimodipine in refractory cerebral vasospasm due to aneurysmal subarachnoid hemorrhage. Biomed Res Int. 2014;2014:970741.
28. Pickard JD, Murray GD, Illingworth R, Shaw MD, Teasdale GM, Foy PM, et al. Effect of oral nimodipine on cerebral infarction and outcome after subarachnoid haemorrhage: British aneurysm nimodipine trial. BMJ. 1989;298(6674):636-42.
29. Samseethong T, Suansanae T, Veerasarn K, Liengudom A, Suthisisang C. Impact of Early Versus Late Intravenous Followed by Oral Nimodipine Treatment on the Occurrence of Delayed Cerebral Ischemia Among Patients With Aneurysm Subarachnoid Hemorrhage. Ann Pharmacother. 2018;52(11):1061-9.
30. Wainsztein N, Lucci FR. Cortical Spreading Depression and Ischemia in Neurocritical Patients. NeurolClin. 2017;35(4):655-64