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ADVANCES IN MANAGEMENT OF ACUTE HYPERTENSION: A CONCISE REVIEW

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ABSTARCT

Ongoing hypertension influences >1 billion individuals worldwide and >70 million individuals in the US. Intense hypertensive scenes (AHE) are characterized as extreme spikes in pulse that may bring about end-organ harm. Despite the fact that AHE may emerge freely as again occasions, they are bound to happen in patients with prior hypertension. One of the debates with respect to the clinical way to deal with AHE is the choice of antihypertensive medicine. Contingent upon the clinical introduction of the patient and the danger of end-organ harm coming about because of circulatory strain rise, suitable and brief treatment is justified. There are various specialists accessible for the administration of hypertension. Be that as it may, the best test lies in the intense consideration setting where the need exists for better introductory and supported control of circulatory strain spikes. Numerous enemies of hypertensive specialists successfully lower pulse, yet just few have the ability to accomplish severe control of hypertension in the intense setting. Clevidipine butyrate is a ultra short-acting intravenous dihydropyridine calcium-channel blocker. Clevidipine has remarkable pharmacodynamics and pharmacokinetic properties that empower the quick, safe, and satisfactory decrease of circulatory strain in hypertensive crises, with the capacity to give profoundly exact titration important to keep a barely characterized target pulse range. A few as of late distributed stage I, II, and III clinical investigations have demonstrated Clevidipine to be a successful circulatory strain modulator in such limit.

KEYWORDS:- hypertension, antihypertensive medicine, Clevidipine and High Blood Pressure.

INTRODUCTION

Acute episodes of hypertension may arise in a variety of clinical settings due to the exacerbation of a pre-existing chronic hypertensive condition or as de novo phenomena (*Varon, 2008; Vuylsteke et al., 2000).* Emergency, intensive care, anesthesia, and surgery are among the clinical settings where prompt recognition and treatment of acute hypertensive episodes (AHE) is of paramount importance. A variety of surgical and medical events may trigger intense sympathetic activity, resulting in sudden elevations in blood pressure (BP) (*Awad and Goldberg, 2010*). If not recognized and treated immediately, AHE leave the patient at risk for end-organ damage and preoperative complications (*Vaughan and Delanty, 2000*). Consequently, it is important that practitioners be aware of current diagnostic and therapeutic approaches involved with management of hypertensive crises. Better utilization of existing therapies and the development of newer agents have improved the overall state of affairs, but the best treatment strategy for AHE is still a topic for debate. The aim of this article is to provide a concise review of therapeutic options for the management of AHE, with a focus on newer therapeutic options including intravenous Clevidipine.

Hypertension: Differentiation and Classification and Epidemiology

Chronic hypertension affects approximately one billion people worldwide and an estimated 72 million people in the United States (*Chobanian et al., 2003*). Despite significant efforts to increase awareness and promote preventive and early interventions, 30% of adults are still unaware of their hypertensive condition (*Smithburger et al., 2010*). Several clinical classifications for chronic hypertension are currently utilized (Table 1).

Table 1: Classification of Blood Pressure for Adults Aged ≥18.

Category	Systolic Blood Pressure	Diastolic Blood Pressure
Normal	<120	<80
Pre- Hypertension	120-139	80-89
Hypertension- Stage I	140-159	90-99
Hypertension- Stage II	≥ 160	≥ 100
Hypertension Urgency	>180	>120
Hypertension Emergency	>180	>120 and target organ damage.

Patients with chronic hypertension are more likely to experience AHE, including the possibility of associated end-organ damage. Overall, approximately 1% of hypertensive patients will experience an episode of AHE, known as hypertensive crisis (*Kuppasani and Reddi, 2010; Owens, 2011*). An AHE may also be the initial presentation in patients without a

prior diagnosis of hypertension, signaling the new onset of hypertension as co-morbid condition. A hypertensive crisis is defined as an elevation in systolic blood pressure (SBP) >180 mmHg and diastolic blood pressure (DBP) >120 mmHg. It is imperative to distinguish between the two types of hypertensive crises — hypertensive emergency versus urgency. A *hypertensive emergency* is an elevation of BP >180/120 mmHg with evidence of end-organ damage to heart, kidneys, eyes, or brain (*Chobanian* et al., *2003; Kuppasani and Reddi, 2010*). *Hypertensive urgency* is defined as the same rise in BP, however with no concurrent evidence of end-organ damage (*Chobanian* et al., *2003; Kuppasani and Reddi, 2010*). The differences between these two entities are summarized in Table 2.

Table 2: Characteristics of hypertensive emergency versus hypertensive urgency.

	Hypertensive Emergency	Hypertensive Urgency
Significant elevation in B.P.	Yes	Yes
BP> 180/120	Yes	No
Target organ damage	Yes	No
IV Medications Required	Yes	No
Associated Conditions	Heart Attack, aortic bleeding, Optic swelling, hypertensive encephalopathy, excess circulatory fluid.	Nose Bleeding, and Severe hypertension.

A number of recently published studies explored the clinical-epidemiological profile of patients presenting with hypertensive crises (*Saguner* et al., *2010; Vilela-Martin* et al., *2011*). One prospective study of risk factors showed that patients presenting with hypertensive crises were more likely to have morbidities including somatoform disorders, thyroid disease, and stroke (*Saguner* et al., *2010*). These patients also had greater prevalence of hypertensive heart disease and/or coronary artery disease (Saguner *et al*., 2010). Non-compliance with anti-hypertensive regimens plays a significant role in hypertensive crises, and has been shown to be more prevalent in patients who experienced hypertensive crises than those who had not (*Saguner* et al., *2010*). A greater incidence of non-compliance in women could potentially account for the increased prevalence of hypertensive crises observed in that group (*Vilela-Martin* et al., *2011*). However, men have a greater prevalence of hypertensive emergencies specifically, as well as complications attributable to AHE (*Vilela-Martin* et al., *2011*).found that patients with hypertensive emergencies were more likely to lead sedentary lifestyles and were older than those who presented with hypertensive urgencies. Furthermore, Caucasian patients were more likely to manifest hypertensive emergencies as opposed to hypertensive urgencies *(Vilela-Martin* et al., *2011*). In addition, more patients with hypertensive urgencies

had a history of using antihypertensive medications (*Saguner* et al., *2010; Vilela-Martin* et al., *2011*). The epidemiology of hypertensive crises is similar to that of chronic hypertension, with African Americans and the elderly have higher rates of such crises (*Varon, 2008*).

Pathophysiology of acute hypertension

Although hypertension is among the most prevalent chronic medical conditions, the Pathophysiology of hypertensive crises is still poorly understood (*Kuppasani and Reddi, 2010; Smithburger et al., 2010; Varon, 2008; Varon and Marik, 2003*). Two processes thought to precipitate a hypertensive crisis are a sudden increase in systemic vascular resistance (SVR) and a failure of cerebral blood flow auto regulation, the mechanism that maintains blood flow at an appropriate level during changes in blood pressure (*Smithburger et al., 2010; Varon, 2008*). While a hypertensive crisis can present without a documented history of hypertension, the acute nature of these events suggests an underlying hypertensive condition coupled with the presence of an additional inciting factor or event (*Varon, 2008*). For example, in the preoperative setting, stimuli such as elevated BP during anesthesia induction, tracheal intubation, and emergence from anesthesia can be the initiating event for the hypertensive crisis (*Awad and Goldberg, 2010*). Anesthesia induction alone can cause an increase of 20 mmHg in normotensive patients, and up to 90 mmHg in patients with a pre-existing hypertensive condition (*Ahuja and Charap, 2010*).Vascular endothelial injury may result from repeated instances of acute hypertension, associated with elevated systemic vascular resistance. As blood pressure increases, vessel walls are subjected to stress, which leads to the release of vasoconstrictors resulting in further endothelial damage (*Kuppasani and Reddi, 2010; Smithburger* et al., *2010; Vaughan and Delanty, 2000*). If not promptly treated, a cycle of clotting cascade activation, arteriole tissue death and accumulation, neurohormonal system upregulation, induction of oxidative stress, and inflammatory cytokines develops (*Kuppasani and Reddi, 2010*). Deposition of platelets and fibrin, vasoconstriction, and thrombosis, as a result of vascular injury, result in decreased blood flow and supply to and from organs (hypoperfusion and ischemia) (*Kuppasani and Reddi, 2010; Smithburger* et al., *2010*). If this vicious cycle is not terminated, autoregulatory dysfunction becomes imminent (*Polly* et al., *2011).* Autoregulation is crucial to maintenance of adequate perfusion of the kidney, heart, and brain. These organs require specific amounts of oxygen to function, and reduced blood flow can lead to ischemia and organ injury.

Autoregulation occurs in many body tissues, but has best been studied in cerebral blood flow.

When blood pressure is severely elevated there is a right shift in the auto regulation curve, resulting in cerebral blood flow at higher mean arterial pressures (*Belsha, 2011; Kessler and Joudeh, 2010; Vaughan and Delanty, 2000*). In order to avoid hyper perfusion of tissues, blood pressure in these patients must be lowered carefully so that hypoperfusion does not occur *(Belsha, 2011; Kessler and Joudeh, 2010*). Therefore caution must be used when selecting an antihypertensive agent to manage AHE. In the blood pressure range between 60 mmHg and 140 mmHg, cerebral blood flow is "auto regulated" extremely well. In hypertensive patients, auto regulation occurs with mean arterial pressure (MAP) up to 180 mmHg (shifted to the right), though the blood flow remains constant. During hypertensive crises, the shift in the autoregulatory curve often fails to occur, putting patients at risk for cerebral hyper perfusion (*Belsha, 2011*). When the corresponding increase in BP crosses the autoregulatory range, compensatory mechanisms cease (*Belsha, 2011*). Vasodilatation and endothelial dysfunction occurs, which may lead to cerebral fluid buildup (edema), ultimately followed by cerebral spasm (eclampsia) and ischemia (*Kuppasani and Reddi, 2010*).

Continuation of this "vicious" cycle results in the severe, acute elevation in BP.

Initial recognition of acute hypertension

Quick determination of a treatment plan for patients experiencing hypertensive crisis is essential. Healthcare providers should focus on obtaining a complete history including any previous diagnosis of hypertension/cardiovascular disorders/endocrine disorders (diabetes for instance), medications, surgeries, and symptoms. Medication history is important to assess compliance (*Kessler and Joudeh, 2010*). Hypertensive emergency patients present with symptoms such as nausea, headache, vomiting, chest pain, dyspnea, vertigo, and neurologic symptoms (*Katz* et al., *2009*). These symptoms are similar to those of hypertensive urgency, so it is necessary to triage patients in order to decide the correct method of treatment. Hypertensive emergency patients present with symptoms of end-organ damage; these symptoms are absent in hypertensive urgencies (*Vaughan and Delanty, 2000*). Blood pressure should be measured on both arms in order to determine if there is a significant difference between the two. A significant difference in the BP could indicate the presence of aortic bleeding, or dissection. Current guidelines suggest that the physical exam should include a fundoscopy, cardiovascular, pulmonary, and neurologic exam. Any evidence of hemorrhaging, excess circulatory fluid, or optic swelling (papilledema) found on the fundoscopy exam indicates a hypertensive emergency (*Vaughan and Delanty, 2000*). Volume

status should be estimated as accurately as possible, because end-organ damage can result from volume overload or depletion. No standardized guidelines for laboratory testing exist; however, a urine analysis, electrolytes, creatinine, and complete blood count should be performed immediately. Additionally, an electrocardiogram and chest x-ray may be necessary to determine the presence of organ damage (*Kessler and Joudeh, 2010; Kuppasani and Reddi, 2010; Vaughan and Delanty, 2000*). A study of the STAT registry found that brain imaging is performed more frequently than other conventional approaches such as urine analysis and fundoscopy (*Katz* et al., *2009*). The organs most susceptible to end-organ damage associated with hypertensive emergencies include the eye, kidney, heart, and brain (*Belsha, 2011; Polly* et al., *2011*). Thus, a physician's clinical evaluation should focus on these organ systems. Common conditions associated with hypertensive emergencies include: acute aortic dissection, acute left ventricular failure with pulmonary edema, acute myocardial infarction (MI), acute renal failure, eclampsia, and ischemic and hemorrhagic stroke (*Kuppasani and Reddi, 2010*). Cerebral edema and neurological dysfunction may result from acute hypertension, a condition known as hypertensive encephalopathy (Strandgaard and Paulson, 1989). Some symptoms of these disorders include chest pain (MI, aortic dissection), back pain (aortic dissection), neurological symptoms, seizures, or altered consciousness (hypertensive encephalopathy), papilledema, hemorrhages, and exudates (eye damage) (*Vaughan and Delanty, 2000*). To prevent end-organ damage, prompt treatment with intravenous anti-hypertensive is often required.

Initial treatment of hypertension

Guidelines by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure for treating hypertensive emergencies include immediate intervention with a goal of reducing SBP by 10 to 15%, but no more than 25% within the first hour. Reduction of the absolute BP to 160/110 mmHg should be done gradually over the following two to six hours (*Aggarwal and Khan, 2006; Chobanian* et al., *2003; De Gaudio* et al., *2009; Flanigan and Vitberg, 2006; Hays and Wilkerson, 2010; Pollack and Varon, 2008; Polly* et al., *2011; Smithburger* et al., *2010; Varon, 2008*). In cases of aortic dissection, the SBP should be reduced to less than 120 mmHg within twenty minutes. In hypertensive emergencies associated with ischemic stroke, BP must be decreased to less than 185/110 before thrombolytic therapy may be administered (*De Gaudio* et al., *2009; Hays and Wilkerson, 2010; Pollack and Varon, 2008; Polly* et al., *2011; Varon, 2008*). If BP reduction occurs too quickly, there may be a significant decrease in blood flow to tissues with cell

death as a possible outcome (*De Gaudio* et al., *2009; Polly* et al., *2011; Smithburger* et al., *2010; Varon, 2008*). Since overshooting a target BP (hypoperfusion) is associated with poor results, many treatment protocols require strict arterial BP monitoring (*Pollack and Varon, 2008; Rhoney and Peacock, 2009*). Hypertensive emergency should be treated aggressively, using quick-onset intravenous medications, whereas hypertensive urgency does not always require such aggressive treatment. Longer acting oral medications such as labetolol and celandine may be more appropriate in situations of hypertensive urgency. However, caution should be exercised when using anti-hypertensive agents in the acute setting. An overly aggressive treatment approach may lead to organ hypoperfusion (as mentioned above) (*Rodriguez* et al., *2010*). Therefore, achieving the aforementioned reduction goal timeline decreases the likelihood of organ hypoperfusion and further organ injury. Once the immediate threat of organ damage is diminished, BP should be gradually controlled to the baseline within a period of 24–48 hours (*Peacock* et al., *2009*). Longer acting treatments, such as beta blockers, may be more appropriate during such gradual stabilization situations.

The ideal intervention for management of hypertensive emergency is easily prepared and administered, has a rapid onset of action, is rapidly titratable, has a short duration of action, is well tolerated, has a low incidence of toxicity or adverse side effects, has few contraindications, allows for dosage adjustment, has vascular selectivity, is inexpensive, and had predictable effects (*Aronson* et al., *2008; Awad and Goldberg, 2010; Deeks* et al., *2009; Ndefo* et al., *2010; Owens, 2011; Peacock* et al., *2009; Pollack and Varon, 2008; Polly* et al., *2011; Smithburger* et al., *2010*). Many intravenous and oral anti-hypertensive agents are available, but most treatments do not encompass optimal benefit versus risk profiles for a broad range of hypertensive emergency situations. Therefore the patient's medical conditions as well as the preference of individual prescribers and institutions need to be taken into account when choosing among different agents *(Belsha, 2011; Pollack and Varon, 2008*). Calcium-channel blockers, which inhibit L-type calcium channels, and specifically the subclass of dihydropyridine (nifedipine, nicardipine, Clevidipine, etc.), are commonly considered a first-line treatment of hypertensive emergencies because they are strong vasodilators and have few negative effects on cardiac conduction and contractility when compared to classes such as beta blockers (*Eisenberg* et al., *2004*).

Clevidipine for the treatment of acute hypertension

The realm of intravenous anti-hypertensive therapy has remained stagnant for the past decade until the introduction of clevidipine. Clevidipine is a third-generation, intravenous, dihydropyridine calcium-channel antagonist. It was approved by the United States Federal Food and Drug Administration in 2008 for the reduction of blood pressure when oral therapy is not feasible or desirable. The novelty of clevidipine is the ultra short half-life of about 1 minute and its potent arterial vasodilation ability without affecting venous capacitance or myocardial contractility (*Rivera et al., 2010; Smithburger et al., 2010; Varon and Marik, 2008*). Clevidipine reduces the pressure that the heart's ventricles must generate to eject blood, yet has little to no effect on the pressure of blood that fills the heart's chambers prior to contraction (*Varon, 2008*). This results in the same volume of blood being pumped out of the heart, with less resistance to blood ejection, thereby protecting against inadequate blood flow to the heart's muscle and preserving coronary endothelial function. These effects are due to the minimal effects of the agent on stroke volume, cardiac output, or heart rate *(Peacock et al., 2009*). Clevidipine also appears to have no significant adverse effect on heart rate (*Aronson et al., 2008; Polly et al., 2011*). Clevidipine is available as an injectable emulsion and can be administered via a peripheral or a central venous catheter. This product is contraindicated in patients with allergies to soy products, eggs and egg products, or defective lipid metabolism. Clevidipine is rapidly metabolized by blood and tissue esterases into inactive metabolites (*Rivera et al., 2010*). Approximately 99.5% of clevidipine in plasma is protein bound. It is also cleared at a high rate primarily through urine (63–74%) and feces (7–22%) (*Smithburger et al.,2010*). Clevidipine's pattern of metabolism makes it safe for patients with hepatic and renal dysfunction (*Rivera et al., 2010*).

Readmission after treatment

Little is known about the rate of readmission following acute hypertension. A retrospective study using the STAT registry was conducted in order to determine the rate of readmission and the characteristics of readmitted patients (*Gore* et al., *2010*). The highest rate of readmission occurred during the first three weeks following discharge. One third of acute hypertension patients discharged from the hospital were readmitted within 90 days. Approximately 29% of those patients were readmitted for hypertension while 71% were readmitted for other reasons (*Gore* et al., *2010*). Several factors were associated with the readmissions for hypertension, including non-compliance with the hypertensive treatment regimen, substance abuse, dialysis use for chronic kidney disease, prior hospitalizations for

acute hypertension, and presentation to the hospital with shortness of breath or seizures. In addition, these patients were younger than those who were not readmitted or were readmitted for other diagnoses. Lastly, patients with private insurance had fewer re-hospital-izations than those with insurance from the government (*Gore* et al., *2010*). Due to the significant percentage of patients who were re-hospitalized, further research needs to be done in order to determine the effect of patient history and socioeconomic variables on the rate of re-hospitalization (*Gore* et al., *2010*).

CONCLUSION

With regards to the management of hypertensive crises, the debate is still ongoing about the best treatment strategies. First, the medical history of the patient should be taken into consideration when deciding the most effective treatment course. A goal for target blood pressure should be set, including the timing for the gradual lowering of blood pressure. The goal blood pressure should be based on the co-morbidities of the patient as well as the clinical presentation of the patient. This knowledge should factor into the decision as to whether the patient receives longer or shorter acting and oral or intravenous anti-hypertensives Overly aggressive attempts to lower blood pressure may cause unintentional hypotension and associated organ hypoperfusion, especially in patients whose homeostatic mechanisms are dependent on the higher "baseline" blood pressure for adequate tissue oxygen delivery. On the other hand, inadequate lowering of BP may occur, leaving the patient at risk for continued severe hypertension, and a further increase in morbidity and mortality. A "roller coaster" effect of oscillating between overshooting BP (causing hypotension) and using treatments (i.e., vasopressors) to "correct" the blood pressure to normotensive levels may be damaging to end organs and the vasculature. Without precise control of BP in hypertensive crisis situations, the "roller coaster" effect — oscillating between hypertension and hypotension — is a challenge to treating physicians Due to its rapid onset and offset properties, ultra-short half-life, and ease of titration, clevidipine may offer an attractive alternative for patients who stand to benefit from more precise titration and control during anti-hypertensive therapy. However, there is limited data on guidance when tight control of BP is truly indicated. Clinical trial data regarding clevidipine indicate the drug is effective in the treatment of hypertensive crises in patients requiring an initial rapid lowering of blood pressure, without increased risk of over shooting the target BP range, allowed by precise 24–48-hour BP control at the desired level. Current guidelines for treatment of acute hypertension may be too broad. Future studies should focus on the management of acute hypertension in specific

patient populations, with evaluation of the relationship between various anti-hypertensive therapies in the context of patient population and additional focus on safe, rapid, and effective titration. We recommend the following areas of exploration:

- Management of acute hypertension in specific populations (race, sex, obesity, ambulatory patients, critically ill patients).
- Management of interventions in specific co-morbid conditions.
- Advanced techniques (intravenous, transdermal, oral, rectal) for rapid, effective titration and delivery of medications.
- Methods of delivery and pharmacological options in particular patient volume states (renal failure, cardiac disease, dehydration/depletion).
- Better articulation of the definition of end-organ damage in a specific organ system and the limits to which that system may be injured and still achieve functional recovery.
- Use of adjunct medications and techniques to augment the efficacy of the current anti-hypertensive armamentarium.

Ultimately, achieving acute blood pressure control should take into account patient co-morbidities, medications and their usage adherence, clinical presentation, and procedures, if applicable. Clevidipine's characteristics, which include rapid onset of effect, high clearance, and small volume of distribution, make it an ideal agent for the management of acute severe hypertension. Several recent studies have evaluated clevidipine's efficacy in the perioperative setting. Two large randomized, double-blind, placebo controlled trials (ESCAPE1 and ESCAPE 2) have evaluated clevidipine in the pre- and postoperative periods, respectively (*Rivera et al., 2010*). ESCAPE 1 was the first trial to demonstrate the efficacy of clevidipine, showing a decrease in systolic pressure by at least 15% from baseline, achieving this within a mean of 6 minutes post-infusion (*Levy et al., 2007*).

The ECLIPSE trial was the first large randomized controlled trial evaluating the efficacy of clevidipine compared to other anti-hypertensive agents (sodium nitroprusside, nitroglycerin, and nicardipine) for the management of perioperative hypertension (Singla *et al.*, 2008). ECLIPSE consisted of three parallel arms in which adult cardiac surgery patients were randomized to either clevidipine or one of the comparator agents. When comparing clevidipine (n=751) to the pooled comparator groups (n=756), clevidipine demonstrated superior BP control within the predefined ranges of 75 to 145 mmHg pre- and postoperatively and 95 to 135 mmHg intraoperatively. This finding was sustained when the ranges were

tightened to 105 to 145 mmHg pre- and postoperatively and 95 to 135 mmHg intraoperatively in a post-hoc analysis. Compared with clevidipine, nitroprusside was shown to have significantly more excursions both above and below the target range while nitroglycerin resulted in significantly more excursions above the range. Nitroprusside was also associated with a significantly higher 30-day mortality rate compared to clevidipine (4.7 vs. 1.7%, p=0.004).

Unlike the other comparator agents, nicardipine had similar efficacy in maintaining BP within the predetermined range of 75 to 145 mmHg pre- and postoperatively and 95 to 135 mmHg intraoperatively, although clevidipine had fewer excursions when the range was tightened to 105 to 145 mmHg pre- and postoperatively and 95 to 135 mmHg intraoperatively in a post-hoc analysis (*Aronson* et al., *2008*). The data emerging from the ECLIPSE trial also suggest that perioperative BP needs to be more tightly controlled than previously thought, since even a 1 mmHg excursion outside of range, when sustained for 60 minutes or longer, can be prognostically important (*Aronson* et al., *2008*). The data also demonstrate the importance of being able to avoid hypoperfusion when treating acute elevations of BP.

The safety and efficacy of clevidipine specifically for the management of hypertensive crises was evaluated in the VELOCITY study, a phase III, open-label, single-arm, multicenter study (*Pollack* et al., *2009*). This study demonstrated the ability of clevidipine to quickly achieve BP within a target range with minimal episodes of excursion below the target range. Within 30 minutes after initiation of the clevidipine infusion, 104 of 117 (88.9%) patients in the efficacy population achieved SBP within their target range. Only 2 patients of 126 (1.6%) in the safety population experienced a decrease in SBP below the lower limit of their initial target range. Findings from VELOCITY were consistent with the other large trials, further demonstrating clevidipine to be a safe and efficacious drug for treating acute hypertension (*Pollack* et al., *2009*).

The ACCELERATE trial was a recently completed multicenter, single arm study evaluating clevidipine for the management of severe hypertension with intracerebral hemorrhage (ICH) (*Graffagnino* et al., *2009*). Clevidipine, as an anti-hypertensive monotherapy, was shown to be effective at rapid BP lowering with 97% of patients (29 of 30) achieving the target SBP of less than 160 mmHg within 30 minutes. The majority of patients achieved the target goal shorter than 30 minutes with a median time to target SBP of 6.5 minutes (95% CI 3–10). However, three hypotensive episodes were reported in association with clevidipine infusion,

with BP increasing promptly after the clevidipine infusion rate was decreased or discontinued.

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