Cost Consequences Analysis of Using Clevidipine in Neurological emergencies from the perspective of a US hospital.

EE579

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INTRODUCTION

Background

- Rapid reduction of blood pressure (BP) with intravenous (IV) anti-hypertensive agents is required in various clinical settings when oral therapy is not feasible or not desirable.
- Clevidipine is an IV dihydropyridine calcium channel blocker indicated for the reduction of BP.
- Clevidipine works by dilating arteries, thus reducing BP. Clevidipine has a fast onset and offset of action making it easily adjustable to achieve desired BP levels.

Objective

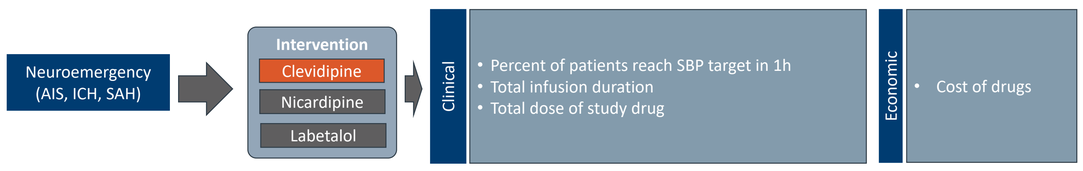
- The aim of this cost consequence analysis was to estimate the economics and consequences of varying clevidipine utilization for BP management in patients experiencing neurological emergencies.

METHODS

Model Summary

- A decision analytic model was developed to simulate the costs and consequences associated with the use of clevidipine, labetalol, and nicardipine in patients experiencing a neurological emergency with acute hypertension. (**Figure 1**).
- The outcomes were quantified from a US hospital perspective over a 3-year time horizon.

Figure 1. Model Structure



Acute Ischemic Stroke (AIS), Intracranial hemorrhage (ICH), Subarachnoid Hemorrhage (SAH), Systolic Blood Pressure (SBP)

Model Inputs

- The model inputs included utilization **(Table 1)**, SBP control **(Table 2)**, dosing information **(Table 2)**, and economic inputs **(Table 3)**.

Utilization

- The utilization of IV anti-hypertensives was calculated based on a retrospective analysis of neurological emergency drug purchase history and Definitive Healthcare claims from 2021.[1]
- Diagnosis Related Group (DRG) codes were used to define neurological emergency claims.
  - Medicare Severity Diagnosis Related Groups (MS-DRGs) included: 20, 21, 22, 25, 26, 27, 34, 35, 36, 37, 38, 39, 61, 62, 63, 64, 65, and 66.
  - Hospitals above 76 neurological emergency claims (median) were included in the IV anti-hypertensive utilization analysis.
  - Low (cohort 1) and high(cohort 2) clevidipine adopter profiles were formed calculating the average utilization for clevidipine, labetalol and nicardipine.
    - Cohort 1 represents the low adopter profile with <10% clevidipine utilization.
    - Cohort 2 represents the high adopter profile with ≥10% clevidipine utilization.
- A change in utilization was modelled starting with cohort 1 as the base year with a linear increase in clevidipine adoption to reach cohort 2 utilization by the third year.**(Table 1)**
- The utilization of nicardipine RTU (0.1 mg/mL) and nicardipine vials are assumed to be equal. Actual use may vary.

Table 1. Projected IV Anti-hypertensive drug market share

Agent	Base Year (Cohort 1)	Year 1	Year 2	Year 3 (Cohort 2)
Clevidipine	1%	14%	27%	39%
Labetalol	32%	30%	27%	24%
Nicardipine	67%	57%	47%	36%
Total	100%	100%	100%	100%

Note: Percentages are rounded and may not add to 100% as shown

Clinical Inputs

- The clinical inputs were based on published literature.[2-7]
- This neurological emergency analysis is based on a naïve indirect comparison of two studies evaluating BP reduction in the stroke population. One single-arm prospective study assessing time to target BP with clevidipine in ICH patients only (ACCELERATE-Graffagnino), and the other being a pseudo-randomized study comparing time to target BP with nicardipine or labetalol (Liu-Deryke). The latter study included hypertensive patients presenting with AIS, ICH, and SAH.
  - ACCELERATE, conducted in 2008-2010, evaluated the efficacy and safety of Clevidipine for BP reduction in 33 patients with ICH presenting with a baseline SBP>160mmHg within 12 hours of symptom onset. Mean baseline SBP was 186 mmHg. Dose was titrated every 90 seconds to target SBP of 140-160 mmHg.
  - Liu-Deryke evaluated continuous infusion nicardipine compared to intermittent bolus IV labetalol in patients presenting with AIS, ICH (54% of patients) or SAH and acute hypertension. 54% of patients were included requiring BP reduction per current practice and AHA guidelines at the time the study was conducted (2005-2009). Baseline initial SBP median was 215 (nicardipine), 208 (labetalol). BP measurements, dose titrations/ administration time intervals were the same for both agents, every 15 minutes. Data were not separated based on stroke subtype.

Table 2. Key Model Assumptions

	Clevidipine	Labetalol	Nicardipine
Average infusion rate (mg/h)[8]	6.3	N/A - bolus dosing	9.6
Infusion duration (h)	24.0	N/A - bolus dosing	24.0
Calculated total dose (mg)	185	140	120
Concentration (mg/mL)[4-6]	0.5	1	0.1
Calculated total volume (mL)	370	140	1200
% Patient using 1 IV anti-hypertensive[2,7]	96.7%	32%	51%
% Patient using 2 IV anti-hypertensive[2,7]	3.3%	42%	28%
% Patient using 3 or more IV anti-hypertensive[2,7]	0.0%	25%	21%
Total (% Patient using 1-3 IV anti-hypertensive)	100%	100%	100%
Calculated weighted average # of IV anti-hypertensive	1.03	1.93	1.70
% Patients reach target SBP in 1 h[2-3]	100%	25%	89%
Median time to achieve BP target (min) [2-3]	5.5	90	30

Note: Clevidipine has not been studied head-to head with any of the comparators

- The infusion duration was chosen to calculate the 24 hr (daily) consumption and cost of infused IV anti-hypertensive medications. The published dose was used for bolus IV anti-hypertensive medications.
- Average infusion rates were based on customer survey data[8]. **(Table 2)**
- The drug concentration[3-5], number of IV anti-hypertensive use[1,6] ,SBP control [1,2] information was derived from literature and the total volume values were based on calculations.**(Table 2)**

Economic Inputs

- The drug acquisition costs were informed by wholesale acquisition costs (WAC) from ProspectoRx.com[9]
- All costs have been adjusted to 2022 USD using Medical Care Consumer Price Index based on Federal Reserve Economic data[10]

Table 3 Acquisition Costs

Agent	NDC code	Utilization	Acquisition price/ml[8]
Nicardipine vial	72572-0470-01	50%	$0.19
Nicardipine RTU	0143-9634-10	50%	$0.51
Clevidipine	10122-0610-01	NA	$1.46
Labetalol	72266-0103-01		$0.06

RESULTS

- For a hypothetical caseload of 100 neurological emergency patients, the use of clevidipine resulted in 9 (10%) more patients reaching BP target in 1 hr.**(Figure 2a)**
- The average time to reach BP target was 14.2 min faster. **(Figure 2b)**
- The average infusion duration of the primary drug increased by 2 hours per patient.
  - The average infusion time increased with reduced use of bolus medications. **(Figure 2c)**
- Additionally, the total infusion volume of primary drug (mL) was reduced by 591 ml per patient **(Figure 2d)**
- The number of IV anti-hypertensives required per patient reduced slightly. **(Figure 2e)**
- The average drug costs decreased by $141 per patient. **(Figure 2f)**

Figure 2 : Results per patient

Figure 2a. Patients reaching target SBP in 1h

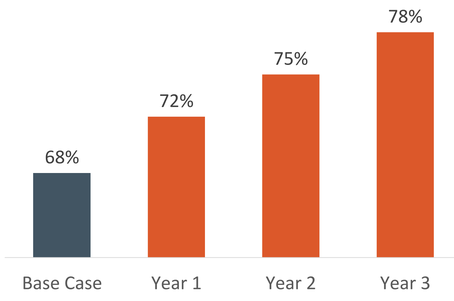


Figure 2b. Median time (minutes) to achieve BP target

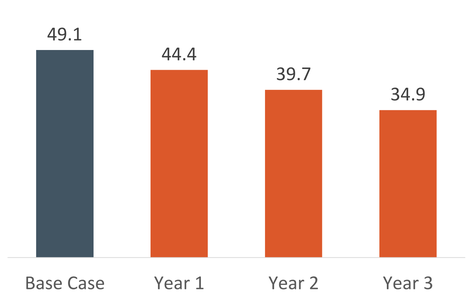


Figure 2c. Infusion duration (hours)

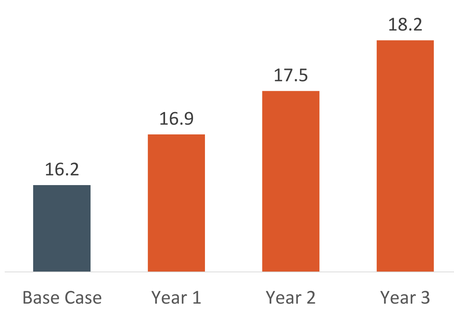


Figure 2d. Total primary drug infusion volume (mL/patient)

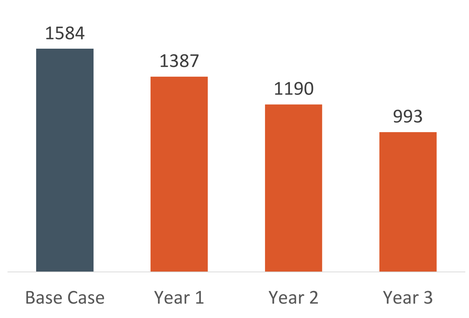


Figure 2e. Number of IV anti-hypertensives per patient

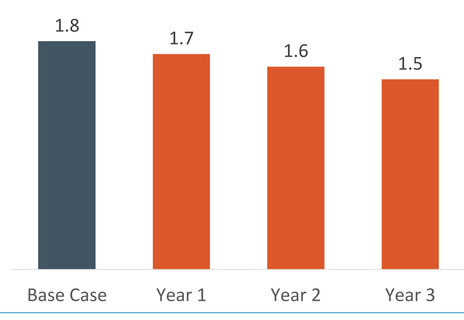
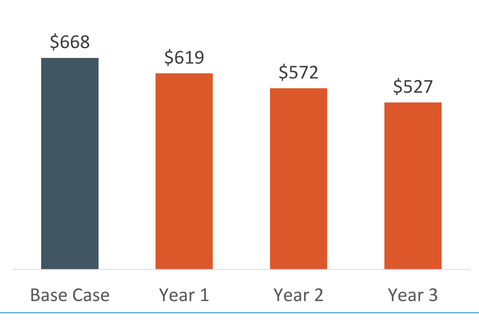


Figure 2f. Total IV anti-hypertensive drug costs per patient



CONCLUSION

- The increased use of clevidipine results in lower IV anti-hypertensive drug cost per patient with a neurological emergency. Additionally, outcomes are improved from more patients reaching BP target in less time and lower infusion volume.

ASSUMPTIONS AND LIMITATIONS

- Clevidipine has not been studied head-to head with any of the comparators. Further prospective research is warranted.
- As a simplifying assumption, only up to 3 IV anti-hypertensives are assumed to be used.
- Vasopressors are excluded from the analysis. Vasopressors may be used in conjunction with IV-antihypertensives which could impact costs and outcomes. The concomitant use of vasopressors and IV anti-hypertensives has not been well-established and requires further prospective research.

DISCLOSURES

IJ, AS, are PRECISIONheor consultants for Chiesi USA, Inc. and received grants/research funding; and MG, SW, AC and EP are employees of Chiesi USA, Inc

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