COST-EFFECTIVENESS AND BUDGET IMPACT OF CAFFEINE CITRATE VERSUS AMINOPHYLLINE FOR APNEA OF PREMATURITY ACROSS A PUBLIC HEALTHCARE SYSTEM IN MEXICO

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Objectives

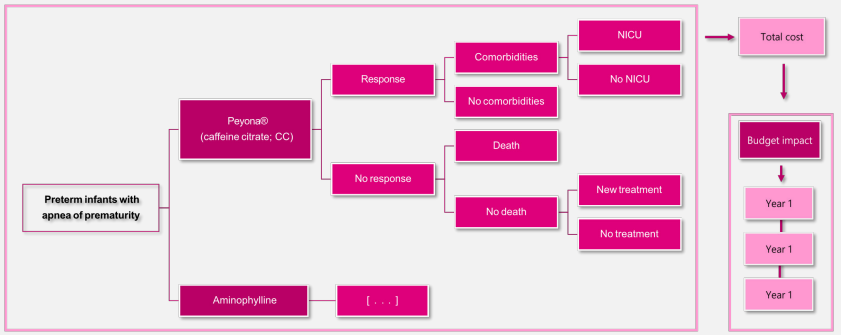
Apnea of prematurity is a frequent complication among preterm neonates and is associated with increased morbidity, prolonged neonatal intensive care unit stay, and high healthcare resource utilization. This study evaluates the cost-effectiveness and budget impact of Peyona® (caffeine citrate; CC) compared with aminophylline for the treatment of apnea of prematurity from the perspective of the ISSSTE in Mexico.

Methods

A cost-effectiveness analysis combined with a budget impact analysis was conducted from the institutional perspective of ISSSTE. Clinical effectiveness in apnea control was assumed to be comparable between treatment alternatives, while economic differences were driven by variations in comorbidity-related resource utilization. CC was assumed to prevent 95% of comorbidities associated with apnea of prematurity compared with aminophylline, resulting in reduced downstream healthcare utilization.

Total per-patient costs were estimated at USD 5,508 for CC and USD 6,152.44 for aminophylline. Comorbidity-related costs accounted for 81.66% of total costs with CC and 99.6% with aminophylline. The budget impact analysis was performed over a three-year time horizon assuming progressive adoption of CC. All costs are expressed in 2026 US dollars.

Illustration 1. CEA and BIM model structure .



Note: model simulates the clinical pathway from treatment response to downstream comorbidities, complications, NICU utilization, and survival. Comorbidities represent a composite endpoint including ROP, PVL, IVH and BPD. NICU utilization reflects length of stay (LOS).

Results

CC was associated with lower total per-patient costs, generating savings of USD 644.44 per treated patient compared with aminophylline. These savings were primarily driven by the prevention of comorbidity-related events, with CC avoiding 95% of comorbidities relative to aminophylline, leading to a substantial reduction in complication-related costs. Within the cost-effectiveness framework, CC was identified as a dominant strategy, offering comparable effectiveness at a lower overall cost. Over the three-year horizon, increasing adoption of CC resulted in cumulative budget savings for ISSSTE, with total savings directly proportional to the substitution rate and number of treated neonates.

Table 1. CEA per patient and BIA year 1-3 results .

Treatment (cost per patient)	Caffeine citrate - early		Aminophylline - late	
	$22.12	(0.40%)	$1,381.68	(18.34%)
Comorbidity	**Caffeine citrate- early**		**Aminophylline - late**	
Retinopathy of prematurity (ROP)	$336.64	(6.09%)	$374.27	(4.97%)
Periventricular leukomalacia (PVL)	$258.72	(4.68%)	$224.60	(2.98%)
Intraventricular hemorrhage (IVH)	$3,830.16	(69.26%)	$4,316.67	(57.30%)
Bronchopulmonary dysplasia (BPD)	$1,082.48	(19.57%)	$1,236.47	(16.41%)
Comorbidity total cost	$5,508.00	(99.60%)	$6,152.00	(81.66%)
Total cost of Apnea of prematurity (per patient)	$5,530.12	(100.00%)	$7,533.68	(100.00%)
Cost-effectiveness analysis	**Caffeine citrate - early**		**Aminophylline - late**	
Total cost of Apnea of prematurity	$5,530.12		$7,533.68	
Incremental cost	Reference		-$2,003.56	
Effectiveness	7.57%		30.25%	
Incremental effectiveness	Reference		22.68%	
Incremental cost-effectiveness ratio			**Dominated**	
Budget Impact Analysis	**Caffeine citrate - early**		**Aminophylline - late**	
Total patients	Year 1 = 10,000 Year 2 = 11,500		Year 3 = 13,225 Average = 11,575	
Current scenario (100% Aminophylline)	$261,606,907			
Year 1 - Total cost	$11,060,241		$60,269,410	
Patients (% / Total)	20%	2,000 patients	80%	8,000 patients
Year 2 - Total cost	$31,798,193		$43,318,638	
Patients (% / Total)	50%	5,750 patients	50%	5,750 patients
Year 3 - Total cost	$30,582,233		$0	
Patients (% / Total)	100%	5,530 patients	0%	0 patients
Year 1-3 - Total cost	$177,028,714			
Budget Impact (new scenario)	-$84,578,192.40		Reference	
Savings associated to Caffeine Citrate	67.7%			

Illustration 2a and 2b. CEA results (PSA).

ICER: Incremental cost-effectiveness ratio. BIA: Budget impact results reflect progressive adoption of caffeine citrate over a 3-year time horizon.
PSA: Probabilistic Sensitivity Analysis (1,000 Monte Carlo simulations). Source: Model-based analysis using clinical and economic inputs described in Methods.

Conclusions

CC represents a cost-effective and cost-saving alternative to aminophylline for the management of apnea of prematurity within ISSSTE, supporting efficient resource allocation and long-term economic sustainability of neonatal care programs.

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References

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