

Cost-effectiveness of Morphine Versus Fentanyl in Managing Ventilated Neonates with Respiratory Distress Syndrome in the Intensive Care Setting

Dina AbuShanab¹, MSc (Pharm), Omar Alsoukhni¹, PharmD, Fouad Abounahia¹, MD, Daoud AlBadriyeh², PhD
¹Hamad Medical Corporation (HMC), ²College of Pharmacy, Qatar University, Doha, Qatar

Background

- Patients with respiratory distress syndrome (RDS) in the neonatal intensive care unit (NICU) may require mechanical ventilation (MV)
- Analgesics are required to facilitate the MV
- Fentanyl and morphine are widely used in ICUs
- No pharmacoeconomics evaluation of morphine or fentanyl for analgesia in NICU exist in literature

Objective

- To perform a clinical and economic analysis of morphine monotherapy versus fentanyl monotherapy in patients undergoing MV due to RDS in the NICU setting

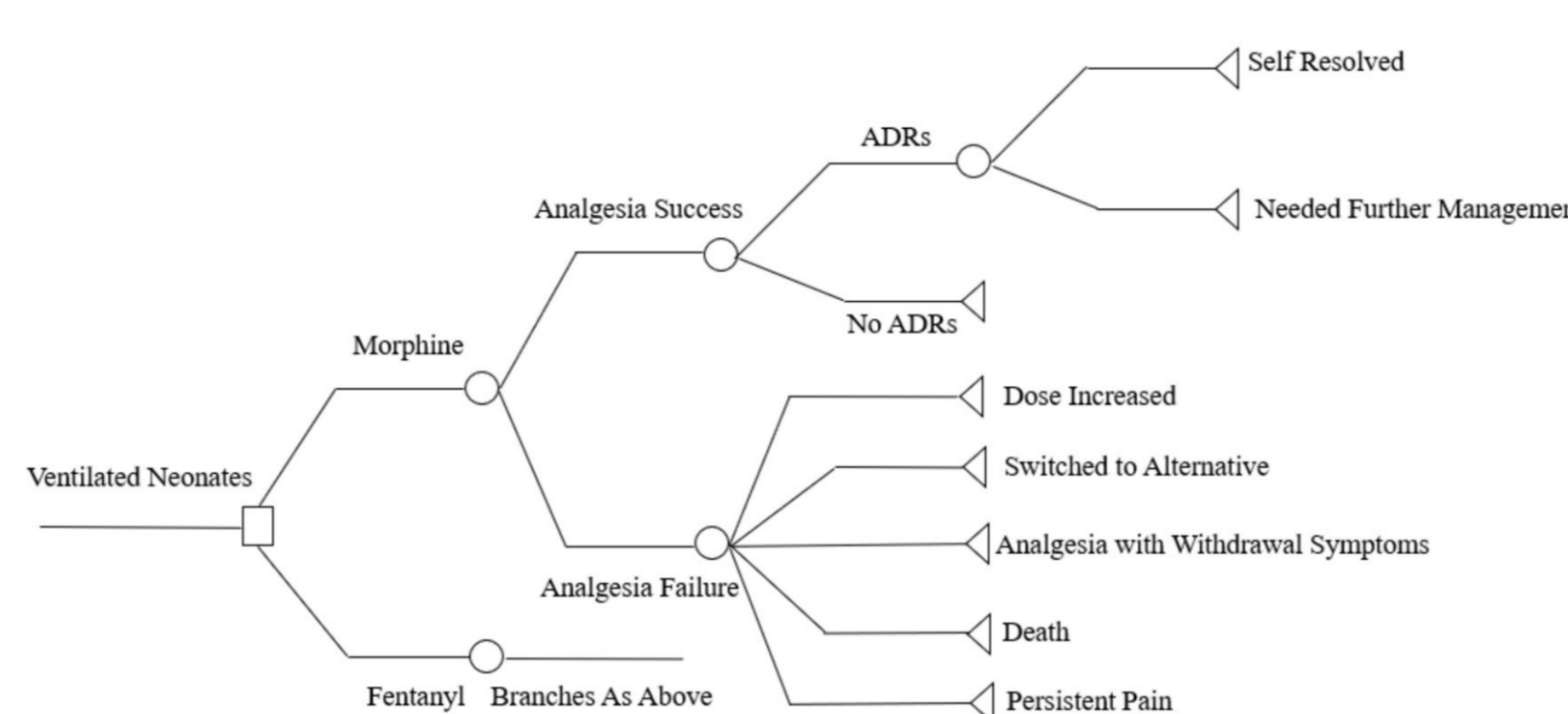
Methods

Table 1. Methods and materials

Design	Comparative retrospective observational cohort study
Type of study	Cost -Effectiveness Analysis (CEA)
Inclusion criteria	<ul style="list-style-type: none"> • All agitated neonates who underwent MV due RDS • All neonates who received initial therapy of morphine or fentanyl
Exclusion criteria	<ul style="list-style-type: none"> • Neonates with congenital anomalies, hypoxic ischemic encephalopathy, pulmonary hypertension , pulmonary hemorrhage • Neonates who received analgesia for other indications
Sample size	N= 126, (morphine=63, fentanyl= 63)
Outcome measures	<p><u>Primary outcome measures:</u></p> <ul style="list-style-type: none"> • Successful analgesia, based on the Premature Infant Pain Profile (PIPP) scale • Overall direct medical costs of managing agitation <p><u>Secondary outcome measures:</u></p> <ul style="list-style-type: none"> • Need for increased medication doses • Need for alternate analgesia • Adverse drug reactions (ADRs) • Total medication doses administered in the NICU • Duration of MV, analgesia, NICU stay • Withdrawal symptoms • Mortality • Persistent pain
Perspective	Women's Wellness and Research Center, direct medical cost only
Model structure	Decision analytic tree was structured (Figure 1) Sensitivity analyses were used by Monte Carlo simulation @Risk-7.5® analysis tool
Ethics approval	Obtained from Medical Research Center at HMC

Methods...continued

Figure 1. Decision tree model of morphine vs. fentanyl



Results

Table 2. Baseline patient demographics

Characteristic	Morphine (n= 63) No (%)	Fentanyl (n= 63) No (%)
Gender		
Male	34 (53.97)	38 (60.32)
Female	29 (46.03)	25 (39.68)
p-value 0.59		
Gestational age		
Pre-term (<37)	28.77 ± 4.42	30.49 ± 3.83
Full-term (≥37)	38.88 ± 1.13	39.60 ± 1.26
p-value 0.09		
Birth weight (gram)		
≥ 2500	3069.71 ±368.55	3208 ± 362.47
<2500 and ≥1500	1832.50 ±329.49	1886.33 ± 280.40
<1500 and ≥1000	1175.88 ±160.35	1342.14 ± 202.61
<1000	694.17 ± 139.12	782.14 ± 140.89
p-value 0.07		
Initial PIPP scores		
0-6	3.16 ± 1.47	3.17 ± 1.91
7-12	8.60 ± 1.36	7.91 ± 1.51
>12	NA	NA
p-value 0.32		

Table 3. Clinical outcomes

Study clinical outcome	Morphine P	Fentanyl P
Analgesia success with ADRs	0.68	0.43
Analgesia success without ADRs	0	0
Analgesia failure		
due to increased dose	0.06	0.43
due to need for alternatives (fentanyl or morphine)	0.05	0.1
due to withdrawal symptoms	0.02	0
Due to death	0.17	0.02
Due to persistent pain	0.02	0.03

*P: probability

- Economics of analgesia
- Incremental cost effectiveness ratio (ICER)=

$$\frac{\text{Cost (morphine) - Cost (fentanyl)}}{\text{Effectiveness (morphine) - Effectiveness (fentanyl)}}$$

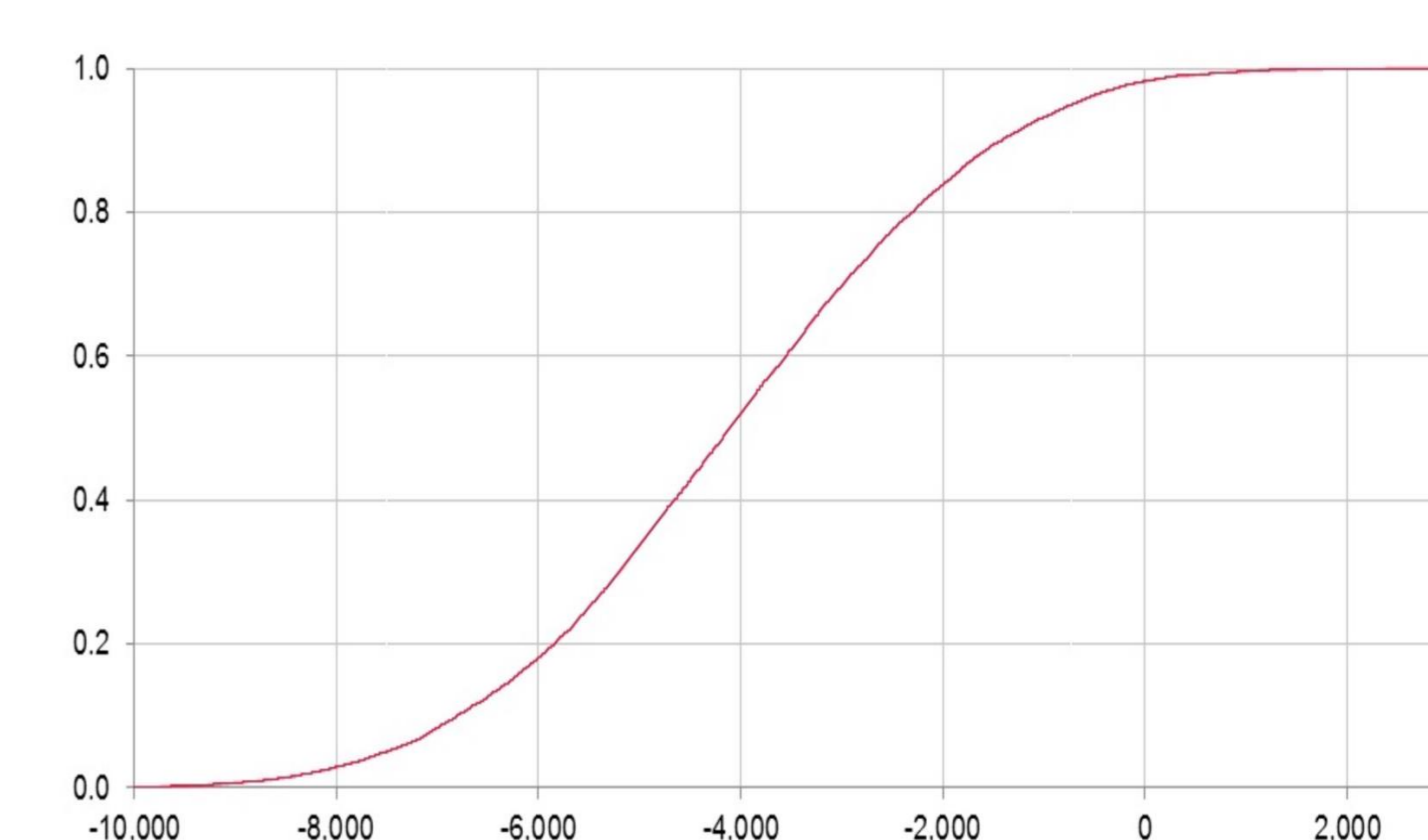
$$\frac{50,637 - 50,512}{68\% - 43\%}$$

$$=490.36 \text{ QAR per additional case of pain relief success with morphine over fentanyl}$$

Results...continued

- Probabilistic sensitivity analysis: morphine had a 98% probability of having an economic advantage over fentanyl (Figure 2)
- A tornado diagram showed that the most impact on the ICER outcome of the study was analgesia with increased doses (fentanyl), whereas analgesia success (fentanyl) had the lowest influence, with none affecting the dominant status of morphine

Figure 2. ICER probability curve, with morphine



Discussion

- The PIPP score was used to reflect the analgesia status of the patient in this study
- There is only one study that compared morphine and fentanyl by Saarenmaa et al., which reported no significant differences between the drugs except in the b-endorphin level in favor of fentanyl
- The study was not purely conducted in neonates with RDS
- The cohort design of the study is appropriate for measuring the effectiveness in practices

Conclusion

- This is the first cost-effectiveness study of morphine versus fentanyl in NICU. Morphine significantly improve the relieve of pain over fentanyl but with higher cost

Acknowledgment

- The authors acknowledge the receipt of grant by Qatar University