

MEETING ABSTRACT

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# Pain control in newborn: pharmacological interventions

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## Background

Pharmacological interventions (PIs) are frequently used for pain control in newborn, particularly during respiratory assistance and in the postoperative period. However efficacy and safety of PIs are still not well demonstrated.

## Material and methods

To assess efficacy and safety of PIs for procedural pain in neonate, a literature search covering the period 2000-2015 via Medline and Cochrane Library database, was undertaken. PIs were evaluated in relation to intubation (INT), mechanical ventilation (MV) and postoperative analgesia (POp) in preterm and fullterm infants. Efficacy of PIs in controlling procedural pain and distress was assessed on validated pain scores as PIPP, DAN, CRIES, EDIN etc. Safety of PIs was evaluated in relation to reduced morbidity and on the Adverse Effects (AEs) reported. The authors rated the level of evidence (LOE) and strength of recommendations, according with GRADE system.

## Results

For tracheal intubation the efficacy of PIs in reducing stress and pain has been demonstrated for Remifentanyl 2 mcg/Kg and Remifentanyl 1 mcg/Kg or Fentanyl 1-2 mcg/Kg plus midazolam 100 mcg/Kg. (N. 6 studies and N.344 newborns-LOE +++)[1,2]. In order to improve newborn's stability and reduce the time of intubation, Propofol can be titrated at 1-2,5 mg/Kg in hemodynamically stable patient after the first 24 hours of life, or Fentanyl (F) administered at 2 mcg/Kg plus short half-life curare (N. 18 studies and N.1003 newborns-LOE +/+++ , Recommendation ↑↑) [3]. The use of opioids

(F or Morphine- M) in MV is effective in reducing the pain scores, however they may cause AEs as hypotension (M), prolonged ventilation, long time to reach full enteral feeding (M&F) and adverse effects on neurodevelopmental outcome (M&F) in dose-dependent way; therefore they should be used selectively, when indicated by clinical judgment and evaluation of pain indicators (M 2 RCTs N. 1139 newborns, F 4 RCTs N.228 newborns- LOE+++ , Recommendation ↑↑)[4,5]. In the postoperative period of major surgery, the use of opioids should be guaranteed at least in the first 48 hours (LOE ++ , Recommendation ↑); Tramadol does not appear to offer advantages over F regarding the efficacy, the duration of MV and the time to reach full enteral feeding. (LOE ++ , Recommendation ↑).[6] Intravenous Paracetamol may have an opioids-sparing effect and should be used in association with M or F. (LOE+++ , Recommendation ↑↑)[7] (Table 1)

## Conclusions

PIs are effective in relieving pain and stress from procedural pain in newborn but their use should be individualized and their effects monitored with validated pain scale to reduce the potential AEs.

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**Table 1 Efficacy of Pharmacological Interventions in newborn**

Pharmacological Interventions	Level of evidence		
	Grade of Recommendation		
Opioids	INT	VAM	PostOP
Fentanyl/ Fentanyl+ muscle relaxant	++	+++	+
	↑/↑↑	↑↑	↑
Remifentanyl	+++	++	+
	↑	↓	↑
Morphine	++	+++	+
	↓	↑↑	↑
<b>Anesthetics</b>			
Ketamine	++	Non indication	Non indication
	↑		
Propofol*	++	Non indication	Non indication
	↑		
Tiopental*	++	Non indication	Non indication
	↑		
<b>Sedative</b>			
Midazolam in association with opioids**	++	+	+
	↑	↑	↓
Dexmedetomidine	Non indication	++	+
		↑	↑
<b>Other weak analgesic</b>			
Paracetamol**	Non indication	Non indication	+++
			↑↑
Tramadol	Non indication	Non indication	++
			↑

**Legend.**

INT =tracheal intubation, VAM = mechanical ventilation POp = postoperative pain\* Facilitating the procedure, reducing time required for INT\*\* Only in near term newborn

Level of Evidence (LOE): Very High ++++ (RCT), High +++ (RCT), Low ++ (Case series), Very Low + (Case report). Grade of Recommendation:strong or weak to use or strong or weak

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