

<b>Table I: The Premature Infant Pain Profile: Revised (PIPP-R)</b>					
Infant indicator					Infant indicator score
	0	+1	+2	+3	
Change in heart rate(bpm) Baseline: .....	0 - 4	5 - 14	15 - 24	>24	
Decrease in oxygen saturation (%) Baseline: .....	0 - 2	3 - 5	6 - 8	>8 or increase in O <sub>2</sub>	
Brow bulge(sec)	None (<3)	Minimal (3-10)	Moderate (11-20)	Maximal (>20)	
Eye squeeze(sec)	None (<3)	Minimal (3-10)	Moderate (11-20)	Maximal (>20)	
Naso-labial furrow(sec)	None (<3)	Minimal (3-10)	Moderate (11-20)	Maximal (>20)	
# Sub-total score					
Gestational age (Wks+days)	>36 wks	32 – 35 wks, 6d	28 - 31 wks, 6d	< 28 wks	
Baseline behavioural state	Active and awake	Quiet and awake	Active and asleep	Quiet and asleep	
## Total score					
# Subtotal for physiological and facial indicators. If subtotal score>0, add GA and BS indicator scores ## Total score: Subtotal score + GA score + BS score Scoring instructions  <b>Step 1:</b> Observe infant for <b>15 seconds at rest</b> and assess vital sign indicators [highest heart rate (HR) and lowest O <sub>2</sub> saturation(O <sub>2</sub> SAT) and behavioural state  <b>Step 2:</b> Observe infant for <b>30 seconds after procedure</b> and assess <b>change</b> in vital sign indicators (maximal HR, lowest O <sub>2</sub> SAT and duration of facial actions observed)  # If infant requires an increase in oxygen at any point before or during procedure, they receive a score of 3 for the O <sub>2</sub> SAT indicator  <b>Step 3:</b> Score for corrected gestational age (GA) and behavioural state (BS) if the subtotal score>0  <b>Step 4:</b> Calculate total score by adding <b>Sub-total score + BS score</b>					

**Table II: Cardiorespiratory stability scoring system**

Score	Designation	Criteria
<b>0</b>	Improved from baseline	Decreased oxygen requirement (>20% relative change in FiO <sub>2</sub> )
<b>1</b>	No change from baseline	
<b>2</b>	Mild instability	Increased oxygen requirement (20%-50%) relative change in FiO <sub>2</sub> ), more apnea' and/or bradycardias responding to gentle stimulation (100% increase or 5 if none before)
<b>3</b>	Marked instability	Increased oxygen requirement (>50% relative change in FiO <sub>2</sub> ), more apnoea's and/or bradycardias responding to vigorous stimulation (100% increase or 5 if none before), higher ventilation requirement
<b>4</b>	Life threatening event	Requiring emergency resuscitation (for example, intubation, suction/bag and mask oxygen, cardiac massage)

**Table III: Method adopted for assigning PIPP-R scores**

<b>Step 1</b>	<b><i>Creation of standard videos</i></b>  Standard videos for each score (0-3) of the behavioural and physiological indicators of PIPP-R score were made by the primary investigator which were used as the ‘reference’.
<b>Step 2</b>	<b><i>Analysis of study video recordings</i></b>  Two independent assessors <sup>1</sup> blinded to the group allocation then analyzed all the recorded videos by referring to the ‘reference’ videos.
<b>Step 3</b>	<b><i>Assigning final score</i></b>  If the scores given by two were the same, that score was recorded as the final score. However, if it was different, the two assessors reviewed the videos together to reach a consensus score
<sup>1</sup> Outcome assessment team included senior resident (SR) pediatrics with at least three year experience in pediatrics and having prior experience and competency in managing neonates.	

**Table IV: Baseline characteristics – revised regimen\***

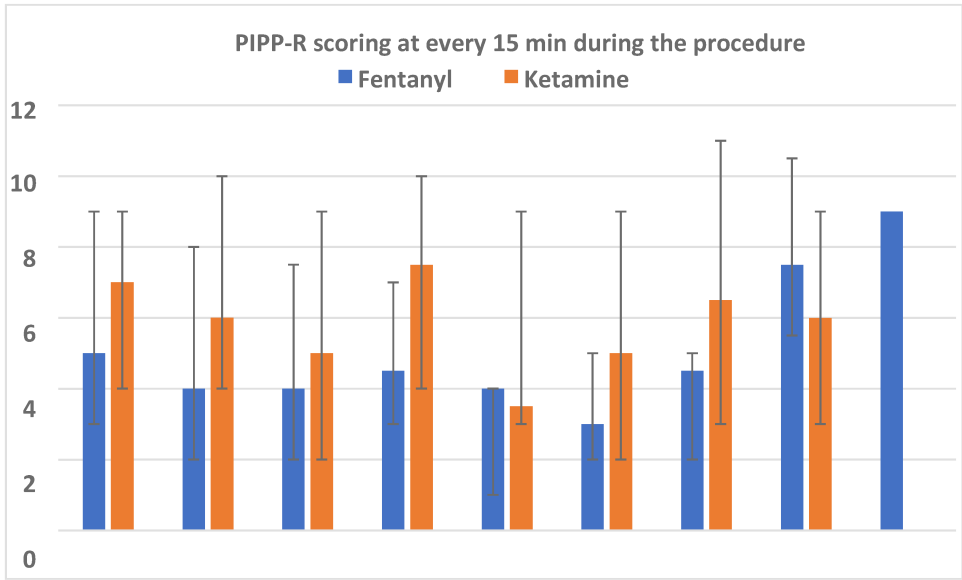
Characteristic	Fentanyl group (N=13)	Ketamine group (N=14)
Gestational age at birth (wk) <sup>#</sup>	30.3 ± 1.3	30.5 ± 2.4
PMA at randomisation (wk) <sup>#</sup>	38.4 ± 3.8	40.6 ± 3.8
Birth weight (g) <sup>#</sup>	1281.6 ± 267	1301.0 ± 338
Weight at randomisation (g) <sup>#</sup>	2061.7 ± 594	2505.2 ± 846
Male gender	9 (69.2)	7 (50)
Antenatal steroid <sup>†</sup>		
Complete	0	0
Incomplete	3 (23.1)	1 (7.1)
None	8 (61.5)	11 (78.6)
Not known	2 (15.4)	2 (14.2)
Cesarean delivery	3 (23.0)	4 (28.5)
Morbidities during neonatal period		
RDS	7 (53.8)	8 (57.1)
Delayed adaptation	2 (15.3)	3 (21.4)
Pneumonia	1 (7.7)	3 (21.4)
AOP	1 (7.7)	2 (14.2)
Any sepsis	12 (92.3)	13 (92.8)
Hypotension requiring inotropes	1 (7.7)	2 (14.2)
Any blood product transfusion	5 (38.4)	6 (42.8)
Stage of ROP <sup>‡</sup>		
APROP	5 (38.4)	4 (28.5)
Stage 2 ± plus	3 (23.0)	1 (7.1)
Stage 3 ± plus	3 (23.0)	6 (42.8)
Stage 4 ± plus	1 (7.7)	2 (14.2)
Stage 5 ± plus	1 (7.7)	1 (7.1)
Eye lasered		
Both	12 (92.3)	12 (85.7)
Right	0	1 (7.1)
Left	1 (7.7)	1 (7.1)
Duration of procedure (min)	48.14 (35-75)	35.5 (32-45.2)
<p>*Data depicted as n (%)</p> <p>#- Indicates data as mean ± SD</p> <p>†- Only in infants with available data</p> <p>‡- Worst stage of ROP was taken in cases where both eyes affected</p> <p>PMA: post menstrual age, RDS: respiratory distress syndrome, AOP: apnoea of prematurity, APROP: aggressive posterior retinopathy of prematurity</p>		

**Table V: Proportion of infants with adequate analgesia with respect to duration of procedure**

<b>Duration of procedure</b>	<b>Fentanyl Initial dose</b>	<b>Ketamine Initial dose</b>	<b>Fentanyl Revised dose</b>	<b>Ketamine Revised dose</b>
<45 min	3/9 (33.3%)	0/11 (0%)	0/5 (0%)	0/10 (0%)
45-60 min	2/8 (25%)	1/10 (10%)	2/2 (100%)	0/2 (0%)
>60 min	3/32 (9.4%)	1/23 (4.3%)	1/6 (16.7%)	1/2 (50%)

*Data represented as n/N (%)*

**Figure 1: PIPP-R score at regular intervals between the two groups (Initial Phase)**



**Figure 2: PIPP-R score every 15 minutes between the two groups (Revised regimen)**

