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Case Report

THE USE OF MODIFIED HIGH FLOW NASAL CANNULA (HFNC) IN PRETERM INFANTS WITH NEONATAL RESPIRATORY DISTRESS SYNDROME (NRSD) IN PRIMARY ICU SERVICES

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ABSTRACT

Introduction: NRSD (Neonatal Respiratory Distress Syndrome) is one of the most frequent causes of newborns in intensive care (NICU). Several NICU centers are now using the High Flow Nasal Cannula (HFNC) recent years. With the use of HFNC as a breath aid in preterm infants, HFNC had the same efficacy ratio as nasal Continuous Positive Airway Pressure (CPAP) (continuous or intermittent). **Case Report:** A three-day-old baby boy was admitted to anesthesia with respiratory failure due to grade II HMD with suspicion of congenital heart failure. The initial condition showed that a respiratory rate of 70-80x / minute, breathing of the nostrils and retractions in the intercostals and abdomen with 85% post ductal SpO2 with the help of a CPAP mask (Pinsp 10, Fio2 70%). There was a Ronchi sound in the right and left basal lungs, and hemodynamics obtained a pulse of 180-195x / minute, non-invasive blood pressure 95/34 mmHg (54), heart murmurs were not found. During day 1 - day three, the patient uses a CPAP mask until the patient vomits and being consulted to an Anesthesiologist. On day 3 - day seven, the patient uses HFNC; after day seven until day 10, the patient uses neonatal nasal canularis oxygen. Until day 10, the patient is still being treated at the NICU by administering oxygen 0.5 liters/minute with SpO2 ranging from 93-96% with stable conditions but still needing oxygen. **Conclusion:** The use of Modified High Flow Nasal Cannula (HFNC) in preterm infants with Neonatal Respiratory Distress Syndrome (NRSD) is more effective and efficient than CPAP. The use of HFNC was associated with a lower incidence of nasal trauma and pneumothorax than nasal CPAP.

Keywords: Continous Positive Airway Pressure (CPAP); Childbirth Complications; Modified High Flow Nasal Cannula (HFNC); Neonatal Respiratory Distress Syndrome (NRSD); Preterm infants

ABSTRAK

Pendahuluan: NRSD (Neonatal Respiratory Distress Syndrome) merupakan salah satu penyebab bayi baru lahir yang paling sering dirawat di ruang perawatan intensif (NICU) hingga saat ini. Beberapa pusat NICU sekarang mulai menggunakan *High Flow Nasal Canula* (HFNC) dalam beberapa tahun terakhir. Dengan penggunaan HFNC sebagai alat bantu napas pada bayi prematur, ditemukan bahwa HFNC memiliki rasio efikasi yang sama dengan CPAP *(Continuous Positive Airway Pressure)* nasal (kontinu atau intermiten). **Laporan Kasus:** Bayi laki-laki usia tiga hari dirawat di anestesi dengan gagal napas karena HMD *grade* II dengan kecurigaan gagal jantung bawaan. Kondisi awal menunjukkan *respiratory rate* 70-80x/menit, pernafasan dari lubang hidung dan retraksi pada interkostal dan abdomen dengan 85% post ductal SpO2 dengan bantuan CPAP *mask* (Pinsp 10, Fio2 70%). Pada pemeriksaan fisik didapatkan suara ronchi pada basal paru kanan dan kiri, hemodinamik didapatkan *heart rate* 180-195x/menit, tekanan darah non invasif 95/34 mmHg (54), tidak ditemukan bising jantung. Selama hari ke-1 hingga hari ke-3 pasien menggunakan masker CPAP sampai pasien muntah dan dikonsultasikan ke Dokter Spesialis Anestesi, pada hari ke-3 hingga hari ke-7 pasien menggunakan HFNC, setelah hari ke-7 hingga hari ke-10 pasien menggunakan oksigen nasal canular neonatus. Sampai hari ke 10 pasien masih dirawat di NICU dengan pemberian oksigen 0,5 liter/menit dengan SpO2 berkisar 93-96% dengan kondisi stabil namun masih membutuhkan oksigen. **Kesimpulan:** Penggunaan *Modified High Flow Nasal Cannula* (HFNC) pada bayi prematur dengan *Neonatal Respiratory Distress Syndrome* (NRSD) lebih efektif dan efisien

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dibandingkan penggunaan CPAP. Penggunaan HFNC dikaitkan dengan insiden trauma hidung dan pneumotoraks yang lebih rendah daripada masker CPAP.

Keywords: *Continous Positive Airway Pressure* (CPAP); Komplikasi Bayi Baru Lahir; *Modified High Flow Nasal Cannula* (HFNC); *Neonatal Respiratory Distress Syndrome* (NRSD); Bayi Prematur

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INTRODUCTION

NRSD (Neonatal Respiratory Distress Syndrome) is one of the most common causes of the newborns in intensive care (NICU). Until now, the NRSD is one of the causes of mortality in newborns (especially in preterm infants) (1,2). The incidence of NSRD frequently in preterm infants and Low Birth Weight (LBW). Premature babies are prone to shunting and hypoventilation, often due to lack of surfactant and bad lungs. This can lead to pulmonary vasoconstriction and lead to NSRD in premature infants (3). HMD (*Hyaline Membrane Disease*) is one of the most common causes of NSRD in preterm infants and has a reasonably high Case Fatality Ratio (CFR) (4). HMD can be treated by administering artificial surfactants, using a breath aid machine, or administering CPAP (Continuous Positive Airway Pressure). The administration of CPAP proved to reduce the risk of BPD (Bronchopulmonary Dysplasia) and decrease the mortality rate in preterm infants (5).

CPAP as a non-invasive breath aid is the first line of breath assistance in premature infants with respiratory distress. During the last few years, nasal CPAP has been one of the most frequent methods of non-invasive ventilation aid (5,6). The administration of nasal CPAP has several disadvantages, such as there are various modes of CPAP, to work effectively, it must be used by trained nurses, providing discomfort to the baby. The use of nasal CPAP is associated with side effects such as trauma to the nose and pneumothorax. Several NICU centers are now using the High Flow Nasal Cannula (HFNC) in recent years. However, several studies have doubted the efficacy and efficiency of HFNC (6,7). HFNC is a method of supplying high-volume oxygen (flow> 1 liter/minute) with warm air (37ºC) and humidified air (humidification>96%) through the nasal cannula (7). Based on a systematic review, the use of HFNC as a breath aid in preterm infants, HFNC had the same efficacy ratio as nasal CPAP (continuous or intermittent), even though it was associated with a lower incidence of nasal trauma and pneumothorax than nasal CPAP (8).

The case in this journal is the use of HFNC (modification) in premature infants with NRND due to grade II HMD with a suspected congenital heart defect which we treated at Kuala Pembuang Hospital, Seruyan, Central Kalimantan (Type C Hospital in a remote area).

CASE REPORT

A three-day-old baby boy was admitted to anesthesia with respiratory failure due to grade II HMD with suspicion of congenital heart failure. The initial condition of the baby showed signs of respiratory distress, a respiratory rate of 70-80x / minute, breathing of the nostrils, and retractions in the intercostals and

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abdomen with 85% post ductal SpO2 with the help of a CPAP mask (Pinsp 10, Fio2 70%). There was a Ronchi sound in the right and left basal lungs, and hemodynamics obtained a pulse of 180-195x / minute, non-invasive blood pressure 95/34 mmHg (54), heart murmurs were not found. The baby was restless and vomiting (though he had an OGT installed) in black. The initial action we give is oxygen assistance with HFNC-modified (as in Figure 1) with a flow of 4 lpm, and the temperature is warmed 30^{o} - 34^{o}C. After 15-20 minutes after the giving of HFNC, the evaluation obtained that the Respiratory rate decrease to 70-75x/minutes, retraction still obtained SpO2 preductal 99%, Non-invasive Blood Pressure was 75/40 mmHg, clinically the baby was calmed down.

Figure 1. Modified HFNC Device (Using A Ventilator Humidifier With Neonatal Nasal Cannula)

From the baby's birth history, it was found that the patient was born immediately on the indication of antepartum bleeding due to placenta previa totalis with signs of pregnancy with 31/32 weeks of gestation; there was no comorbidity in the mother. When the baby was born, it was obtained with an APGAR (Appearance, Pulse, Grimace, Activity, and Respiration) Score of 6-7-7, with a Downe Score of 7. Due to ongoing antepartum inflammation with signs of labor, the mother had no time to get steroids during pregnancy, so immediate termination was performed. In the evaluation of complete physical examination, it was found that there was a sign of breath distress that was better than before, 25ml of urine production was obtained in 8 hours with an excess fluid balance of 220 ml for 72 hours, and there was a hematin of approximately 5ml from OGT. Investigations revealed the presence of leukocytosis 18. 240 and albumin 3,2 on other complete blood counts showed no abnormalities. The results of the baby gram showed that there was white intercourse in both lung fields. Our patient was treated with the antibiotic ceftriaxone 50mg / Kg BW / 24 hours intravenously. We added furosemide and proton pump inhibitor intravenously.

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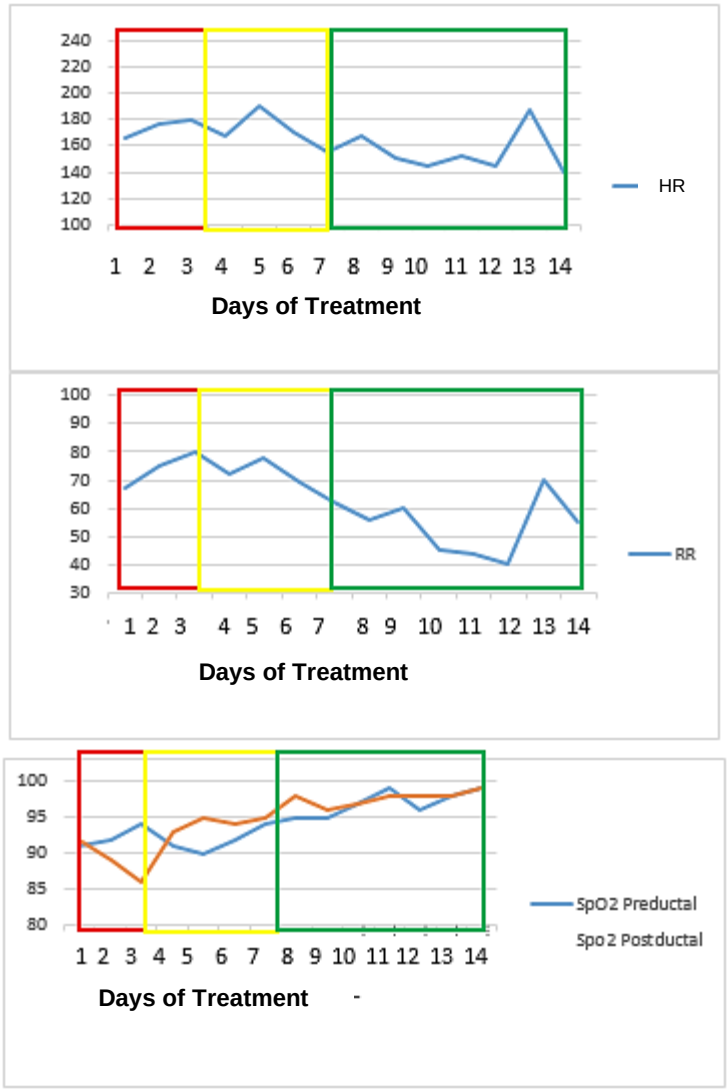

Figure 2. The Patient's Vital Sign During Treatment, Red Box: Using CPAP Mask, Yellow Box: Using HFNC, Green Box Using Neonatal Nasal Cannula Oxygen

On the 5th day of treatment, the patient's body began to turn yellow, so it was decided to do phototherapy (even though without the bilirubin examination because the examination reagent was run out) for 48 hours. Ten hours after the patient was photographed, the patient became restless, and the pulse rose to 190-200 with non-invasive systolic blood pressure ranging from 85 to 95 with a Mean Arterial Pressure (MAP) 65-70, preductal SpO2 decreased 85% and postductal SpO2 88%. At night the patient became increasingly restless until the patient's umbilical infusion was released. Our patient was sedated using ketamine at the time of re-umbilical insertion. If the patient was restless, we sedated the patient using midazolam and fentanyl while observing signs of respiratory depression. On the 7th day of treatment, there was an improvement in clinical and chest X-rays. Patients can be given nasal oxygen 1 liter/minute without giving HFNC, and we stop giving antibiotics after seven days. Figure 2 shows the graph of the patient's vital signs during treatment. During day 1 - day three, the patient uses a CPAP mask until the patient

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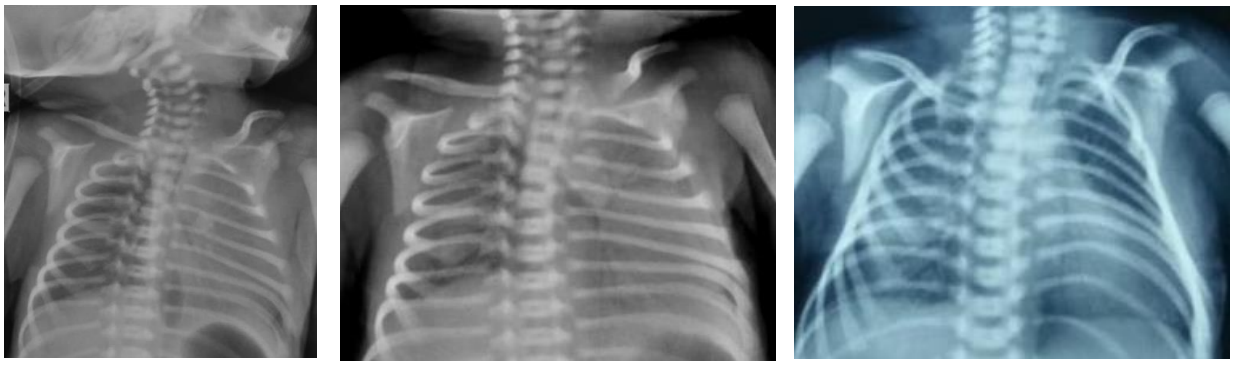
vomits and being consulted to an Anesthesiologist. On day 3 - day seven, the patient uses HFNC; after day seven until day 10, the patient uses neonatal nasal canularis oxygen. Until day 10, the patient is still being treated at the NICU by administering oxygen 0.5 liters/minute with SpO2 ranging from 93-96% with stable conditions but still needing oxygen. On the 13th day of treatment, there was an increase in pulse and breath rate. The patient also started febrile (with axilla temperature 37.4 - 38.0). The patient was suspected of starting a secondary infection, possibly due to the use of umbilical infusion for more than seven days and due to the difficulty of finding peripheral venous access despite attempts. After removing the umbilical infusion and administration of paracetamol, clinical improvement was obtained. The patient, on the 14th day of treatment, decided to be referred to another health facility. Changes in the thorax photo can be seen in Figure 3.



(a) **(b)** **(c)**

Figure 3. Chest photo during patient treatment
(a) Chest Photo After Birth, (b) Chest Photo After 3 Days of HFNC Use, (c) Chest Photo After 5 Days of HFNC Use

DISCUSSION

NSRD in premature infants is often caused by Hyaline Membrane Disease (HMD). HMD is caused by a lack of surfactant from the alveoli, which causes an increase in pressure on the alveoli surface, resulting in microatelectation and a decrease in lung volume. Clinically newborn babies will experience an increase in respiratory frequency which usually gets worse on the 3rd day. Worsening of the condition is due to decreased pulmonary compliance, decreased functional residual capacity, decreased alveolar ventilation, presence of R to L shunting, decreased capillary perfusion to a decrease. Oxygen supply (1,5). Figure 2 shows that on the first day of treatment, the patient has shown an increase in the frequency of breaths to get signs of respiratory distress (increased breathing rate and pulse) on the 3rd day.

Management of infants with HMD can be divided into the prenatal and postnatal periods. Steroid administration in the prenatal period has been shown to aid maturation at 24-33 weeks of gestation (5). Giving betamethasone to women at 34-35 weeks of gestation can improve neonates better than a placebo. Betamethasone administration has a Relative Risk (RR) of 0.77 (95% CI 0.63 - 0.95) to infants who are given CPAP or given HFNC (9). Betamethasone 12 mg intramuscular (IM)

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every 12 hours for 24 hours with an alternative dexamethasone 6 mg intravascular (IV) every 6 hours for 48 hours is recommended for pregnant women at 34 weeks of gestation (10). Our patient did not have time to be given prenatal steroids because the termination process had to be done immediately because there was an indication of antepartum hemorrhage with signs of labor (inpartum). The postnatal management given is breath support (from CPAP, HFNC to mechanical ventilation) and administration of exogenous surfactants (5). The provision of surfactants as prophylactic or therapeutic has been shown to reduce the risk of pneumothorax and neonatal death in infant patients at risk of HMD. Surfactants that can be given are synthetic or natural. Synthetic surfactants without protein are less effective than natural surfactants with SP-B and SP-C. Early surfactant administration in the first 2 hours of a newborn significantly reduces the need for mechanical ventilation compared to therapy (11).

The provision of breath assistance to patients with HMD can be differentiated based on non-invasive ventilation support (CPAP, NIPPV, HFNC) and invasive (mechanical ventilation) (5). Based on the results of a meta-analysis on the use of non-invasive ventilation in RDS (Respiratory Distress Syndrome) patients, CPAP is preferred for infants who still have spontaneous breathing, with a recommended pressure of at least six cmH_2O to 9 cmH_2O. Apply higher pressure to PIP (Peak Inspiratory Pressure) of 20-25 cmH_2O in infants with persistent apnea or bradycardia. NIPPV is a non-invasive breath support method that provides intermittent mandatory ventilation at continuous distending pressure. The advantages of giving NIPPV are reducing the risk of asynchronous breathing, increasing TV (Tidal Volume) and MV (Minute Volume), and reduce the effort on patient's inspiration (12). Based on an RCT (Randomized Clinical Trial) in Los Angeles County (LAC), it was found that the use of NIPPV in LBW infants after extubation proved to be more effective in preventing respiratory failure at 48 hours after extubation than nasal CPAP (5% vs. 37%). Complications of using NIPPV and nasal CPAP were found in both cases but were not statistically significant (13). The use of HFNC as a therapy for non-invasive ventilation support is now often carried out in several health centers. Based on a survey in Australia and the United Kingdom (UK), it was noted that there are several advantages to using HFNC, such as fewer incidences of trauma to the nose, more comfort in infants, easier if want to provide enteral nutrition, and make it easier to prepare and use (6). Based on a meta-analysis of the use of HFNC in preterm infants as a means of breath support, it shows that there is no significant difference in the use of HFNC to mortality (with a Risk Ratio (RR) of 0.36 95% CI 0.01 - 8.73) and the possibility of chronic occurrence. Lung Disease (CLD) (with RR 2.07 95% CI 0.64 - 6.64) (8). A study found that there was no significant difference between the use of HFNC and nasal CPAP on the success of therapy at less than 72 hours (nasal CPAP 18% vs. HFNC 20%) and more than 72 hours (nasal CPAP 2% vs. HFNC 6%). Still, on nasal complications, trauma on day 3 showed a significant difference (nasal CPAP 14% vs. HFNC 0%) (7).

HFNC therapy in infants is the provision of high flow air (more than 1 liter/minute) that is heated, warmed, and mixed (air and oxygen) through a special nasal cannula. The components of HFNC (can be seen in Figure 4) consist of (a) flow meters, (b) sterile water to be warmed, (c) humidifier chamber and heater, (d) tubing, and (e) specific nasal

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canula6 (14). The recommended airflow for newborns is 4 - 6 liters/minute, depending on the patient's weight. For patients with a bodyweight of 1000 - 1999 grams, the recommended initial flow of 3 liters/minute, bodyweight of 2000-2999 grams, 4 liters/minute, and more than 3000 grams is recommended 5 liters/minute.

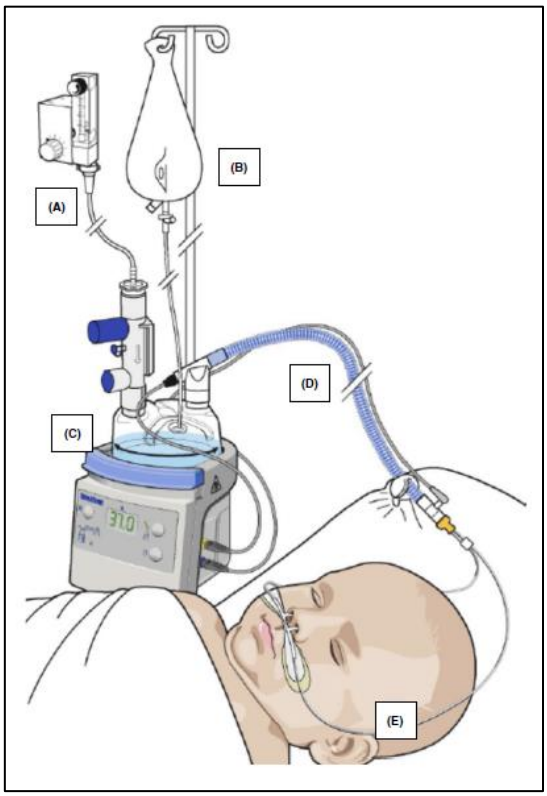

Figure 4. Component Overview of HFNC(14)

The respiratory assist mechanisms provided by HFNC were found to create distending pressure, remove dead space from the nasopharynx, provide sufficient airflow to reduce holding during inspiration, and Work Of Breathing (WOB) and provide adequate hot and humid gas for the baby (15). Physiologically, giving HFNC to preterm infants will increase the pressure from the airway and help wash out from dead space in the airway. Giving HFNC 2 to 8 liters/minute to preterm infants will increase the CO2 pressure in the airway (nasopharyngeal) to decrease the minute volume and reduce breathing effort during inspiration. The baby's weight influences the pressure produced by HFNC, airflow was given, the position of the mouth, and the baby's gestational age when measured. The pressure can be estimated by the formula obtained from Liew's research, HFNC airway pressure = -6,373 + (0.525 x Flow rate (liters/minute) + 1,454 x mouth position (0 when open, 1 when closed) – 1,856 x body weight (kg) + 0.307 x current gestational age (week). The resulting pressure does not differ significantly when compared to the pressure produced by CPAP (16). We use the modified HFNC using heaters and humidifiers used by ventilators to connect using pediatric tubing (as seen in figure 1). We keep the temperature from heater 30^{o} to 34^{o}C; if a lot of steam is obtained, the heater will be turned off 5-10 minutes and restarted. The use of HFNC in these cases can improve SpO2 as

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well as decrease the patient's breath rate and pulse (showing clinical improvement of respiratory distress) as can be seen in figure 2, can be compared at the time of use of CPAP (red box) with HFNC (yellow box).

Table 1. Criteria for N-PASS (National Pain, Agitation & Sedation Scale)(20)

Assessment criteria	Sedation		Normal	Pain / Agitation	
	- 2	- 1	0	1	2
Cry	Do not cry with pain stimulation	Groaning or crying with pain stimulation	- Cry naturally - No-fuss	- Often fuss or cry - It can be calmed down	- Crying loudly or crying softly but continuously - Fussiness cannot be soothed
Behavior	- Not bothered by any stimulation - No spontaneous movements	- At least disturbed by stimulation - Minimal spontaneous movement	By gestational age	Restless, often wake up when it's time to rest	Likes to kick, gets up during rest or there is no movement (without sedation)
Facial expressions	No expression Saggy mouth	Minimal expression with stimuli	Quiet according to conditions	Frequent expression of pain	Always shows an expression of pain
Extremity tone	- There is no reflex grasp (grasp) - Flaccid tone	- Reflex holding (grasp) is weak - Weak muscle tone	- Hands and feet calm - Normal muscle tone	- Often clenched fists, feet or often spread fingers - Increased muscle tone but not tense	Always clench your fists, feet and spread your fingers - tense body muscle tone
Vital sign	- There is no variation with stimuli - Apnea or hypoventilation	More than 10% of baseline with stimuli	By the baseline or normal according to gestational age	- Increase 10 - 20% from baseline - SaO2 76 - 85% with stimulation	- Increase more than 20% from baseline - SaO2 less than 76% with stimulation

The use of HFNC has the same efficacy as CPAP in providing infant outcomes when used in preterm infants and providing less frequent complications (8). Our patient had gastric distension, which caused reflux of gastric contents when wearing the CPAP mask. CPAP masks make the baby uncomfortable, causing agitation, which will increase Systemic Vascular Resistance (SVR). The patient we treated was suspected of having a Patent Ductus Arteriosus (PDA). An increase in SVR would exacerbate the L to R shunt, leading to increased volume overload from the ventricles and pulmonary pressure (17). According to Figure 2, it can be seen that we use modified HFNC for five days with initial flows ranging from 4 liters/minute to 2 liters/minute.

On the 5th day of treatment, clinically, it was found that the body looked yellowing, possibly due to hyperbilirubinemia. Still, the bilirubin test could not be done because the examination reagent was running out at the hospital, so it was decided to do phototherapy. Icterus in patients may be due to disruption of bilirubin excretion due to neonatal sepsis or because preterm patients may develop neonatal icterus (18). Figure 2 also shows an increase in pulse and breath rate caused by the patient being restless at the time of phototherapy. When the baby was crying and restless, there was a lump in the groin of the thigh, which was suspected of having an inguinal hernia. Agitation and pain in neonatal patients are rarely detected and well treated,

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and in some conditions, the agitation has adverse clinical effects on patients. Patients are suspected of having PDA in their heart defects, so agitation and pain will adversely affect the patient, as previously described (17,19). We use the N-PASS (Neonatal Pain Agitation and Sedation Scale) to determine the use of sedation or analgesia. We provide a clinical combination of midazolam, ketamine, and fentanyl if the N-PASS is more than 219 (20). The N-PASS assessment criteria can be seen in table 1.

On the 13th day of treatment, the patient got an increase in pulse and respiratory rate. The patient also had a fever of up to 38^{o}C. The patient was suspected of having a secondary infection and, after being observed, the use of an umbilical infusion for more than seven days due to difficulty finding venous access. The use of umbilical infusions for more than seven days is at risk of developing CLABSI (Central Line-Associated Bloodstream Infection) (21). After removal, there is a clinical improvement of pulse, breath rate, and decrease in temperature. Due to limited facilities and difficulty collecting blood samples, the patient did not have time to be evaluated in the laboratory for infection markers. The patient was referred to another health facility on day 14.

CONCLUSION

Modified High Flow Nasal Cannula (HFNC) in preterm infants with Neonatal Respiratory Distress Syndrome (NRSD) is more effective and efficient than CPAP. The use of HFNC was associated with a lower incidence of nasal trauma and pneumothorax than nasal CPAP.

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