

RESEARCH ARTICLE

Transient tachypnea of the newborn – need for supplemental oxygen and possible complications

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Summary

Transient tachypnea of the newborn, which is a self-limiting condition, in some cases requires invasive respiratory support. This study aimed to investigate the influence of gestational age and mode of delivery on oxygen therapy, and the occurrence of complications.

This retrospective study covered data about children diagnosed with transient tachypnea who were born during the period of one year. The duration of oxygen therapy and the assessment of complications were analyzed according to the mode of delivery and gestational age. In 77,3% of cases transient tachypnea was well-managed with the use of oxygen therapy in incubator. In relation to the mode of delivery and gestational age, no significant differences in the duration of different oxygen therapy types were observed. Two newborns developed persistent pulmonary hypertension, and one newborn had pneumothorax.

Invasive respiratory support is not frequently used in transient tachypnea. Persistent pulmonary hypertension and air leak syndrome are possible but very rare complications of this condition.

Keywords: Transient Tachypnea of the Newborn; Gestational Age; Cesarean Section; Oxygen Inhalation Therapy;

INTRODUCTION

Respiratory distress (RD) represents a group of pathological conditions with the incidence of about 7% in all neonates, and 0.5-2.8% for transient tachypnea of the newborn (TTN) as one of its leading causes (19). TTN or “wet lung” syndrome, is self-limiting RD disorder occurring within the first few hours after birth, and lasting between two and four days. In most cases, TTN occurs in late preterm (34–36+6 weeks’ gestation), and term neonates born between 37 and 39 weeks (6). Insufficient evacuation of fetal lung fluid is an underlying condition, leading to compliance decrease, a reduction of functional residual capacity and tidal volume, and finally inadequate minute ventilation, the state responsible for breathing acceleration and development of other TTN’s clinical features (23). Tachypnea and distinctive radiological findings are the most representative clinical signs, sufficient for diagnosis of TTN. Recognized risk factors for TTN are: cesarean section (CS), male gender, macrosomia, preterm delivery, maternal sedation, perinatal asphyxia, meconium amniotic fluid, chorioamnionitis, and oligoamnion (17, 21, 22). In full-term newborns, additionally proposed risk factors are the following: assisted reproductive technologies, operative vaginal delivery (forceps or vacuum extraction), and the 5th minute Apgar score (AS) < 8 (22). Further on, previous investigations reported that maternal asthma and gestational diabetes were independent risk factors for developing TTN (3, 15). Although the treatment of TTN mostly requires the use of conventional non-invasive oxygen (O₂) therapy, sometimes invasive types of respiratory support, including nasal continuous positive airway pressure (nCPAP) and mechanical ventilation (MV) are beneficial to patient care. Maintenance of tachypnea and the need of prolonged use of supplemental O₂ may be responsible for the development of TTN complications, such as persistent pulmonary hypertension (PPHN) and air leak syndrome (10).

THE AIM

Since there is a lack of relevant data about the incidence and clinical characteristics of TTN in our population, this study aimed to investigate the influence of gestational age and mode of delivery on TTN incidence, possible appearance of TTN complications (PPHN and air leak syndrome), as well as the need for different types of respiratory support, and duration of oxygen therapy.

MATERIALS AND METHODS

This observational retrospective study was carried out at the Department of Neonatology, The Clinic of Gynecology and Obstetrics “Narodni Front”, Belgrade, Serbia, in

accordance with the ethical standards laid down in 1964 Declaration of Helsinki and its later amendments, and after the approval of the institutional ethics review committee. The research included the data between January 1st and December 31st, 2016. During this period, 7380 newborns were born at the clinic.

All relevant data were gathered from medical records. Clinical findings for the newborns with TTN were: 1. tachypnea (> 60 breaths per minute), within 6 hours after delivery; 2. chest radiography – lung hyperinflation evidenced by flattening and depression of the diaphragmatic domes or increased anteroposterior diameter, or both, prominent perihilar vascular marking and enlarged interlobar fissures containing pleural fluid; 3. need for respiratory support – (O₂ in incubator, nCPAP and MV).

Exclusion criteria were clinical, laboratory, bacteriological, and radiological findings for other conditions leading to respiratory distress (1, 9). Additional exclusion criteria were multifetal pregnancies, operative vaginal deliveries (forceps or vacuum), 5th minute AS < 8, birth weight (BW) < 2500 or > 4000 grams, and delivery before 34 weeks gestation.

Newborns included in this study were compared according to the mode of delivery (vaginal vs. CS) and gestational age (late preterm (34-36+6 weeks) and full-term neonates (37-42 weeks’)). Frequency and duration of different types of O₂ therapy (O₂ in incubator, nCPAP, MV) were analyzed depending on the mode of delivery and gestational age. The assessment of possible development of TTN complications was conducted through consecutive ultrasonography heart examination (PPHN) and chest radiography (air leak syndrome).

Statistical analyses were performed using IBM SPSS Statistics for Windows Software (Version 25.0; IBM Corp, Armonk, NY, USA). Statistical significance between categorical data was determined by Pearson’s chi-square test (χ^2). Statistical significance between numerical data was determined by Student’s t-test and Mann-Whitney U-test. The logistic regression analysis was used to compare types of O₂ therapy and its duration in relation to the week of gestation and mode of delivery. All P values below 0.05 were considered significant.

Table 1. Distribution of TTN patients according to the gender, mode of delivery and gestational age of birth.

		N	%	P value ^a
Gender	Male	54	72	P < 0.001
	Female	21	28	
Mode of delivery	Vaginal	25	33.3	P < 0.001
	CS	50	66.7	
Gestational age	34-36+6	53	70.7	P < 0.001
	37-40	22	29.3	

^a Chi-square test;

N - number of patients; CS – cesarean section

Table 2. Correlation between gender, mode of delivery and gestational age of birth in TTN patients.

		Gender			P value ^a
			Male	Female	
Delivery	vaginal	N (%)	19 (76)	6 (24)	0.585
	CS	N (%)	35 (70)	15 (30)	
Gestational age	34-36+6	N (%)	37 (69.8)	16 (30.2)	0.512
	37-40	N (%)	17 (77.3)	5 (22.7)	
		Gestational age			P value ^a
			34-36	37-40	
Delivery	Vaginal	N (%)	19 (35.8)	6 (27.3)	0.473
	CS	N (%)	34 (64.2)	16 (72.7)	

^a Chi-square test;

N - number of patients; CS –cesarean section

RESULTS

During the investigated one year period, 75 out of 7380 newborns developed TTN (1,02%). Among newborns with TTN, male gender was significantly more represented than female gender ($P < 0,001$), and CS was performed about twice more frequently compared to vaginal delivery. Median for gestational age at birth was 36, with earliest delivery in 34 and latest in 40 weeks of gestation. More than two thirds of TTN patients were born between 34 and 36+6 weeks, and the rest belonged to the group of full-term newborns (Table 1).

There was no statistically significant difference for gender distribution in relation to the mode of delivery ($P=0,585$), or gestational age at birth ($P=0.512$) (Table 2). Also, the number of SC and vaginal deliveries was not

significantly different in late preterm group compared to the term neonates group ($P=0.473$) (Table 2).

Mostly, TTN was a mild clinical condition and well-managed with the use of O₂ therapy in the incubator (58 cases, 77, 3%). Other types of respiratory support were used in 10 (13, 3%) and 7 (9, 3%) patients (nCPAP and MV). The duration of oxygen therapy shorter than two days was recorded in 34 (45, 3%) newborns with TTN, whereas the need for supplement oxygen > 2 days was present in 41 (54, 7%) patients. The duration of respiratory support did not show a statistical difference in relation to the mode of delivery (Table 3) ($p=0,251$). Further on, after dividing TTN patients according to the type of O₂ therapy used, the difference between the duration of all three types of supplemental oxygen therapy in correlation to the mode of delivery was not statistically significant (Table 3).

Table 3. Frequency of oxygen therapy duration according to the mode of delivery in TTN patients.

Type of O ₂ therapy	Delivery		Therapy duration		P value ^a
			< 2 days	> 2 days	
O ₂ in incubator	Vaginal	N (%)	8 (38.1)	13 (61.9)	0.331
	CS	N (%)	19 (51.4)	18 (48.6)	
nCPAP	Vaginal	N (%)	1 (25)	3 (75)	1.000
	CS	N (%)	2 (33.3)	4 (66.7)	
MV	CS	N (%)	4 (57.1)	3 (42.9)	
Total O ₂ therapy	Vaginal	N (%)	9 (36)	16 (64)	0.251
	CS	N (%)	25 (50)	25 (50)	

^a Chi-square test;

N - number of patients; CS - cesarean section; nCPAP - nasal continuous positive airway pressure; MV - mechanical ventilation;

Table 4. Frequency of oxygen therapy duration according to the gestational week of birth in TTN patients.

Type of O ₂ therapy	Gestational age		Therapy duration		P value ^a
			< 2 days	> 2 days	
O ₂ in incubator	34-36+6	N (%)	22 (50)	22 (50)	0.351
	37-40	N (%)	5 (35.7)	9 (64.3)	
nCPAP	34-36+6	N (%)	22 (50)	22 (50)	0.500
	37-40	N (%)	1 (16.7)	5 (83.3)	
MV	34-36+6	N (%)	4 (80)	1 (20)	0.143
	37-40	N (%)	0 (0)	2 (100)	
Total O ₂ therapy	34-36+6	N (%)	28 (52.8)	25 (47.2)	0.043
	37-40	N (%)	6 (27.3)	16 (72.7)	

^a Chi-square test; N - number of patients; nCPAP - nasal continuous positive airway pressure; MV - mechanical ventilation;

According to the gestational age, the term newborns group significantly more often required supplemental O₂ for more than two days, compared to the late preterm group ($p=0,043$) (Table 4). However, after dividing TTN patients into subgroups according to the type of respiratory support used, we did not find a statistical difference between O₂ therapy duration in relation to the gestational age (incubatory O₂ ($p=0,351$), nCPAP ($p=0,500$), MV ($p=0,143$)) (Table 4).

Complications of TTN were observed in only 3 out of 75 TTN cases (4%). Two newborns developed PPHN, and one had pneumothorax. PPHN patients were born in 35 and 36 weeks of gestation, and gestational age of the patient with pneumothorax was 37 weeks. All 3 cases were delivered with CS and required MV use.

DISCUSSION

Our study has shown that TTN was diagnosed in 1.02% newborns during the period of one year. This is in line with previously reported data demonstrating TTN frequency between 0.5% and 2.8% (19). Today, 3 out of 4 preterm babies are born near term (4). Previous studies have shown significantly higher incidence of respiratory morbidity in the group of newborns delivered before 39 weeks of gestation (16, 20). TTN is a common cause of RD in early neonatal period, especially in the group of neonates born near term (18, 20). Possible explanations for frequent RD occurrence in the group of late preterm newborns are partial surfactant deficiency and cessation in lung development during the transitional phase when vesicles switch to the alveolar stage (10). Even in 37 weeks of gestation the risk of TTN is 3 times higher than in 39 and 40 weeks (12).

Changes in maternal and fetal hormonal milieu during the last few weeks of pregnancy, together with the onset of spontaneous labor are the factors responsible for rapid maturation and fetal preparation for delivery and adaptation to extrauterine life (12). Our study showed 2,5 fold increase of TTN incidence in the group of late preterm neonates (70,7%) compared to the newborns delivered in 37 weeks of gestation and later (29,3%). These results are in accordance with previously reported findings indicating that lungs of preterm fetuses are not ready for transition to extrauterine life, while lungs of term fetuses are physiologically prepared for evacuation of lung fluid stimulated by spontaneous labor (24). Moreover, immaturity of lung epithelial mechanism for Na⁺ transport is described as one of the reasons for TTN development (24). Previous investigation found that alpha-subunit of epithelial Na⁺ channels (ENaC) played a role in disturbance of lung fluid clearance and consequently lead to premature deaths in mice (11).

Lower gestational age, CS and male gender are described as risk factors for TTN (6). Our results are

similar, showing CS frequency to be twice higher than vaginal delivery in newborns with TTN. It is estimated that elective CS is responsible for about 50% of RD cases, with TTN as the most frequent cause (19). A crucial event for normal extrauterine respiratory adaptation is the process of lung fluid evacuation. This is accomplished via compressions on the child's chest by physical forces present during vaginal delivery and with uterine contractions, which are absent in elective CS (23). Numerous studies tried to determine a correlation between the development of TTN and CS performed after signs of spontaneous delivery occurred. One study did not show a decreased risk of TTN development in preterm neonates born after CS with previous signs of spontaneous delivery (6). Nevertheless, researchers described that respiratory symptoms were significantly more frequent after planned Cesarean delivery (16). Fetal increase of catecholamine concentrations provoked by spontaneous labor and rupture of fetal membranes, are additional factors which regulate the absorption of lung fluid and stimulate surfactant release (2). Studies have shown a significantly lower catecholamine levels and changes in lung function in a term infant after an elective CS in comparison to vaginal delivery (14).

We found a similar number of CS and vaginal deliveries in both late preterm and term newborns with TTN. This is in accordance with previous studies describing that preterm neonates are more prone to TTN development, regardless the mode of delivery (6). After 37 weeks of gestation, a significant decrease in incidence of TTN and other RD conditions is observed, regardless the mode of delivery (13).

Beside lower gestational age and CS, our results also showed that male gender was significantly more often present in TTN group. Male gender, as a risk factor for TTN was described and recognized in earlier studies as well (6, 10, 19).

Although in most cases represented as a benign condition, TTN requires the use of respiratory support (10, 19). Our results showed that therapy with O₂ in incubator was used in 77.3% newborns with TTN. This is in line with the fact that TTN is most commonly a benign condition demanding minimal therapeutic measures. This research showed that invasive types of respiratory support were mostly required in the late preterm group, probably due to the lung immaturity which made adaptation to extrauterine life difficult. A previous study described the need for assisted ventilation longer than three days in 9.3% TTN cases (8). The duration of oxygen therapy for more than two days was more frequent in the group of term newborns compared to the late preterm group. However, analyzing the duration of different respiratory support types, this statistical significance was lost. Since TTN is most often a self-limiting process, lasting for 48-72 h, the reason for a prolonged need of oxygen support in term newborns might be additional pathological con-

ditions. One research showed longer use of O₂ therapy, more frequent MV need and longer hospitalization in the group of children delivered after CS without symptoms of spontaneous labor (1). Preterm birth, low AS, and umbilical artery acidosis were described as independent risk factors for a worse TTN outcome (1).

Nasal CPAP is demonstrated as a useful method in TTN treatment, due to a decrease in the occurrence of TTN therapy side effects (9). Researchers described a significantly shorter neonatal intensive care unit stay, the need for minimal O₂ fraction, and similar incidence of air leak syndrome in the nCPAP group in comparison with the oxygen supplementation group (9). Additionally, different MV types were compared with nCPAP in order to define the best TTN treatment option. Nasal high frequency percussive ventilation (NHFPV) was proposed as safe in TTN treatment. Compared to CPAP, NHFPV use was well-tolerated, more effective, with a significantly shorter duration, demanding lower O₂ concentrations, and showing no complications (7). Nasal intermittent mandatory ventilation (NIMV) showed similar efficacy and tolerance, without a significant difference in the duration of respiratory support, hospitalization and the occurrence of TTN complications in comparison with nCPAP (5).

Although TTN is most often a self-limiting condition, lung air leak syndrome and PPHN might occur as a result of hypoxemia (10, 19). A contribution to these conditions might be the immaturity of the system for surfactant production, which has been already recognized as a

mechanism for TTN development (10, 19). Only 3 our patients manifested a TTN complication. Pulmonary hypertension was observed in two preterm neonates, whereas pneumothorax developed in one term newborn. All three were born with the CS.

CONCLUSIONS

TTN is RD disorder, most frequently present among late preterm and term neonates. Our study, in accordance with previously published results, has shown that lower gestational age, Cesarean delivery and male gender are independent risk factors for TTN development. In most cases, TTN did not require invasive respiratory support. As was noticed in our patients, PPHN and air leak syndrome are rare but possible complications of this condition.

This study is the first one performed on our population giving the information about TTN clinical course. There is a need for large, prospective studies that would provide information about other potential TTN causes, and possible long-term complications. Furthermore, in order to clarify the pathophysiological mechanisms responsible for the occurrence of TTN and its clinical course, it is necessary to carry out studies which will examine the possible presence and amount of retained fluid in the lungs of neonates, the maturity of the surfactant production system, and changes in the catecholamine level in the mother's blood during delivery.

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TRANZITORNA TAHIPNEA NOVOROĐENČADI – POTREBA ZA DODATNIM KISEONIKOM I MOGUĆE KOMPLIKACIJE

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Sažetak

Tranzitorna tahipneja novorođenčeta (TTN) predstavlja samoograničavajući proces, koji zahteva primenu invazivne oksigenoterapije. Cilj ovog rada je da se ispita uticaj gestacijske starosti i načina porođaja na incidenciju TTN, pojava komplikacija, potreba za oksigenoterapijom i dužina njene primene.

Ova retrospektivna studija je obuhvatila podatke o deci rođenoj tokom perioda od godinu dana. Na osnovu kriterijuma za uključenje i isključenje iz studije izdvojena su novorođenčad sa TTN. Ispitivana je dužina primenjene oksigenoterapije i procena pojave TTN komplikacija. Kod 77,3% slučajeva, TTN je bila blagog kliničkog toka,

sa potrebom za oksigenoterapijom u inkubatoru. Statističkom analizom je pokazano da ne postoji značajna razlika u dužini primene oksigenoterapije posmatrano u odnosu na način završetka porođaja, kao i u odnosu na gestacijsku nedelju rođenja. Dvoje novorođenčadi je razvilo kliničku sliku perzistentne plućne hipertenzije, a kod jednog je došlo do razvoja pneumotoraksa. TTN u većini slučajeva ne zahteva potrebu za invazivnom respiratornom potporom. Perzistentna plućna hipertenzija i sindrom curenja vazduha su vrlo retke, ali moguće komplikacije TTN.

Ključne reči: tranzitorna tahipneja novorođenčeta, gestaciona starost, carski rez, oksigenoterapija.

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