ORIGINAL ARTICLE

IMPACT OF TOTAL PARENTERAL NUTRITION ON DECIDUOUS TOOTH ERUPTION OF VERY LOW BIRTHWEIGHT PREMATURE INFANTS

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ABSTRACT

Purpose of this study was to investigate the effect of total parenteral nutrition on deciduous teeth eruption of very low birth weight premature infants. It was a prospective study done at Prince Hashim Ben Al-hussein Military Hospital of 85 healthy preterm infants who were born with birthweight of 800-1500grams, and at 27-32 weeks gestational age. They were divided into two main groups ***Group (****40 preterm infants who did not receive total parenteral nutrition) and* ***Group B*** *(45 preterm infants who received total parenteral nutrition (TPN) during stay in the neonatal intensive care unit).* ***Group B*** *was divided into two subgroups* ***B1*** *(20 preterm infants who received only 3.5 grams / Kg / day Amino acids) and* ***B2*** *(25 preterm infants who received amino acids and 3 grams / kg / day intralipids). A first tooth eruption record was completed by the neonatologist and the parents of the enrolled infants during regular clinic appointments. Normal eruption was seen in subjects with birthweight (1001-1500 grams) than those with birth weight of 800-1000 grams and gestational age (30-32 weeks) than (27-29 weeks). There were significant differences between groups for total parenteral nutrition, and they were highly significant when amino acids and intralipids were used together. As far as intubation is concerned the difference was not significant when the delayed group compared to the normal group. Neonatal sepsis were significantly increased when the oral intubation was more than 5 days. The study concluded that the introduction of total parenteral nutrition to very low birth weight premature infants resulted with early first tooth eruption. It is concluded that intralipids component of TPN is responsible for this observation, but further studies to evaluate the role of other TPN components are mandatory.*

Key words: *Premature birth, deciduous tooth eruption, and low birth weight*

INTRODUCTION

The current statistics show that the number of infants born prematurely world wide is about 15%. Although survival rates and outcomes for premature infants have dramatically improved in recent decades due to improvement in medical care. Premature infants may face neurodevelopmental outcomes such as mental retardation, learning and behavioral problems, cerebral palsy, lung problems and vision and hearing loss.[1,2] Most researchers devoted their effort for studying the neurodevelopmental outcomes of prematurity and minimal attention had been given to the impact of prematurity on oral cavity and dentition. There is no agreement on the time of first tooth eruption in prematurely born infants. Viscardi *et al.* 1994 reported that very low birth weight infants had significant retardation of dental eruption compared

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with low birth weight and normal birth weight infants[3]. Lunt 1974, Tanguay *et al.* 1984 and Rose *et al.* 1994 reported that the first tooth erupts at the usual chronologic age in healthy premature infants.[4-6] One of the few studies that addressed the impact of different neonatal factors (e.g., oral intubation, nutrition, infections, and medications) on first tooth eruption of premature infants was a prospective, longitudinal study by Rose *et al.,* 1994, but to our knowledge no single study in the literature addressed the impact of total parenteral nutrition on teething of preterm infants.

Evidence from human and animal research support that lipids influence bone modeling and remodeling.[7] Fat intake found to associate with higher bone density in children.[8] Watkins *et al.* 1996, 1997 reported that dietary lipids modulated ex vivo bone PGE2 production and the concentration of IGF-1 in bone tissue, and led to altered bone formation rates in growing chicks and rats.[9,10] The PGs locally produced in estrogenic cells, regulate both bone formation and bone resorption.[11] PGE2 has a biphasic effect on bone in low concentration PGE2 stimulates bone formation (anabolic effect), while in high concentration it will enhance bone resorption.[12]

Orthodontic tooth movement take place within alveolar bone and PGE2 is a major effector of bone remodeling during tooth movement.[13] Petros *et al.* 1993, and Kokkinos et al.1993 reported that saturated fatty acids associated with increased arachidonic acid and then high PGE2 concentration while n-3 and n-6 polyunsaturated fatty acids associated with low arachidonic acid and then low PGE2 concentrations in the alveolar bone. Petros *et al.,* 1993 reported that the tooth movement was slower in n-6 than n-3 fed rats but still faster than saturated fatty acids fed rats[13].

It was concluded that introduction of total parenteral nutrition mainly intralipid component to preterm infants may cause early first tooth eruption. And to the best of our knowledge this is the first study to evaluate the impact of total parenteral nutrition on teething in preterm infants.

METHODOLOGY

A prospective study of 85 preterm infants born at means gestational age of 30.05 weeks and mean birthweight 1147.05 grams was conducted. They were born, nursed, and attended the neonatal follow up clinic at Prince Hashem Ben AI-Hussein Military Hospital Zarqa/ North of Jordan until the age of 18 months. Infants were divided into two main groups; **Group A** (40 preterm infants who did not receive total parenteral nutrition, and **Group B** (45 preterm infants who received total parenteral nutrition during stay at the neonatal intensive care unit . Group B was divided into two subgroups **B1** (20 preterm infants who received 3.5 grams/Kg/day Amino acids only) and **B2 (**25 preterm infants who received amino acids and 3 grams /kg/day intralipids). After the approval of Jordanian Royal Medical Services ethical committee, a first tooth eruption record including the factors(sex, gestational age, birth weight and weight on the time of the first tooth eruption, neonatal sepsis, history of oral intubation, use of total parenteral nutrition, feeding history, use of multivitamins, history of rickets, presence of chronic medical illnesses, recurrent diarrheal episodes and history of recurrent admissions to the hospital) that might have an influence on eruption were completed by the following neonatologist using the medical records and the parents of the enrolled infants, during regular visits to the clinic, and after full explanation of the benefits, risks , procedures and possible discomforts that the infant might face to the infant's parents, and their consent was obtained prior to inclusion in the study. All infants treated with Ampicillin and gentamycin in the intensive neonatal care unit until proved negative blood cultures but none of them given long term Lasix. Infants with congenital orofacial abnormalities (e.g. cleft palate or cleft lip), chronic medical illnesses (such as chronic lung disease, failure to thrive, congenital hypothyroidism, bone defects, malabsorption states, and inadequate body weight gain) and infants with documented rickets were excluded.

Tooth eruption was considered if any part of its crown had penetrated the mucous membrane and confirmed by the dentist who was not aware of the medical history of the infant during the oral examination that was carried out using an artificial light, in the dental clinic at Prince Hashem Ben AI-Hussein Military Hospital. Delayed tooth eruption was considered if the first tooth erupted after the chronological age of 40 weeks since the first tooth in normal infants erupts between 24 and 40 weeks of age.

RESULTS

The premature infant was the unit of analysis in this study. A descriptive statistical study (mean, crosstabulation) was carried out on the measurements of variables collected. All the data collected in this prospective study were nonparametric. The Chi-squire distribution or Fisher's exact test where appropriate were used when concerning proportions. Simple Pearson's correlation was used for the study of the possible association and interrelationships between first tooth eruption and factors that might have an influence on teething (sex, gestational age, birth weight neonatal sepsis, history of oral intubation, use of total parenteral nutrition). The level of significance was set at $P<0.05$.

As shown in Table 1 the study population consisted of 85 premature infants (35 males and 50 females) who were born at mean gestational age of 30.05 weeks and mean birthweight 1147.05 grams. Subjects were arranged into two groups according to gestational age and birthweight.

Eighty five subjects were examined serially until eruption of the first tooth or longer. Since the first tooth erupts between 24 and 40 weeks of age in the normal population. Subjects were considered to be delayed if their first tooth erupted after 40 weeks chronologic age. There were 33 subjects (38.8%) whose first tooth erupted between the 26th and 40th week chronologic age (normal group) and 52 subjects (61.2%) whose first tooth erupted after the 40th week (delayed group). (No tooth erupted in any child before the 26th week.)

Thirty-five patients were males (9 with upper incisors and 26 with lower incisors) compared to 50 patients were females (8 with upper incisors and 42 with lower incisors). However, the difference in proportions was not statistically significant ($P>0.05$, Fisher's exact test).

Comparison between normal and delayed groups

More normal eruption has been seen in subjects with birthweight (1001-1500 grams) than (800-1000 gram) and gestational age (30-32 weeks) than (27-29 weeks). There were no differences in birthweight or gestational age between normal and delayed groups Table 2 and 3.

As far as intubation is concerned the difference was not significant when the delayed group compared to the normal group Table 4. Neonatal sepsis were significantly increased when the oral intubation was more than 5 days Table 5. According to the gestational age premature infants spend long time (several weeks to months) in neonatal intensive care unit (NICU) and are subject to various complications relating to their prematurity. This period of time is critical for development and considered one of most rapid growth. If the infant was in the uterus, he would take essential nutrients carbohydrates amino-acids and fatty acids)for its growth and development. However, outside the womb meeting the nutritional demands of these infants presents challenges. Due to the immaturity of the gut, nutrition is initially provided in a fluid called parenteral nutrition (total or partial) TPN group were started on a modified Vamin-based glucose amino-acid infusion and Intralipid that is given through the veins. Traditionally, the amount of nutrition provided in this way has followed an incremental pattern (starting well below Recommended Daily Intake or RDI of key nutrients) because of concern that babies may not cope with the nutrition.

In this study, premature infants were divided into 3 groups, one group was not given TPN, the second one was given amino acids only and the third group was given amino acids and intralipids

As shown in Table 6, there were significant differences between groups for total parenteral nutrition (TPN), and they were highly significant when amino acids and intralipids were used together.

TABLE 1: STUDY POPULATION ACCORDING TO GESTATIONAL AGE, BIRTHWEIGHT, GENDER AND TYPE OF ERUPTED TOOTH

Upper incisor/Lower incisor	male/female	Gestational age	Birthweight	Total
17/68	35/50	27-29 weeks (27) 30-32 weeks (58)	800-1000 gram (25) 1001-1500 grams (60)	85

TABLE 2: BIRTHWEIGHT (GRAMS) AND NORMAL OR DELAYED ERUPTION

P>0.05, Chi-squire test	Normal or delayed eruption		
	normal	delayed	Total
Birthweight (grams) 800-1000 gram	9	16	25
1001-1500 grams	24	36	60
Total	33	52	85

TABLE 3: GESTATION AGE (WEEKS) AND NORMAL OR DELAYED ERUPTION

P>0.05, Chi-squire test	Normal or delayed eruption		
	normal	delayed	Total
Gestation age 27-29 weeks	11	16	27
30-32 weeks	22	36	58
Total	33	52	85

TABLE 4: ORAL INTUBATION AND NORMAL OR DELAYED ERUPTION

P>0.05, Chi-squire test		Normal or delayed eruption		
		normal	delayed	Total
Oral intubation	No intubation	10	22	32
	<5 days	14	18	32
	>5 days	9	12	21
Total		33	52	85

TABLE 5: ORAL INTUBATION AND NEONATAL SEPSIS

P>0.05, Chi-squire		Neonatal sepsis no	yes	Total
Oral intubation	No intubation	32	0	32
	<5 days	32	0	32
	>5 days	16	5	21
Total		80	5	85

TABLE 6: TYPE OF PARENTERAL NUTRITION AND NORMAL OR DELAYED ERUPTION

P>0.05, Chi-squire test Linear-by-Linear Association		Normal or delayed eruption		
		normal	delayed	Total
Type of parenteral nutrition	No. TPN	12	28	40
	amino acids	7	13	20
	amino acids and intralipid	14	11	25
Total		33	52	85

DISCUSSION

This study is the first study that focuses on the impact of total parenteral nutrition on teething in premature infants. The study confirms that introduction of total parenteral nutrition mainly intralipid component to very low birth preterm infants associates with clinically and statistically earlier first tooth eruption compared to amino acids alone or no TPN groups (p-value <0.05) as shown in Table-6.This finding supports the evidence that lipids influence bone modeling (Hazelwood *et al.,* 2001) [14] and the proposal of Petros *et al.,* 1993, and Kokkinos *et al*.1993[13], that the tooth movement in polyunsaturated fatty acids(n-6 and n-3) fed rats is faster than saturated fatty acids fed rats, that which could be explained by the anabolic effect of PGE2 which in low concentration stimulates bone formation (Cohen *et al.* 2006).[15] Further evaluation of the effect of intralipids on preterm infants in general and teething especially is mandatory.

The study showed that even more normal eruption has been seen in subjects with birth weight > 1000 grams and gestational age >30weeks, there were no statistical differences in birth weight or gestational age between normal and delayed groups (*p*-value > 0.05) Table-2 and3. The finding supports previous studies (Seow1988, Trupkin1974, and Drummond 1992).[16-18]

In this study 38.8% of preterm infants (of them 42.4% preterm infants who received combination of amino acids and intralipids) had their first tooth eruption between the 26th and 40th week chronologic age (normal group) and 61.2% whose first tooth erupted

after the 40th week (delayed group) Table-6, but none of them had delayed first tooth eruption when ages corrected for prematurity. These results support the results of the cross- sectional study of Seow *et al.,* 1988 and the prospective study of Golden *et al.,* 1981.[16-19] That delayed primary teeth eruption in preterm infants was no longer apparent when corrected rather than chronologic ages used.

It was not the aim of the present study to evaluate the prevalence of neonatal sepsis in endotracheally intubated preterm infants but this study showed that there were significant increase when the oral intubation was more than 5 days (Table 5). Present study showed that neonatal sepsis has no significant impact on the time of first tooth eruption in premature infants in all groups.

Previous studies (Seow1984, Pimlott 1985, Johnson 1984, Seow 1987and Moylan 1980)[20-24] showed that local trauma caused by laryngoscope blades or direct pressure from endotracheal tubes disrupted normal dentition development. This study like a study conducted by Fadavi *et al.,*[25] showed that timing of first tooth eruption was not affected by oral intubation or its duration in any study group as the difference was not significant when the delayed group compared to the normal group (Table 4.)

The difference between the results of the present study and the studies by the above mentioned respective authors may be explained by the increase of neonatal complications that associated with prolonged intubation such as bronchopulmonary dysplasia pneumothorax and PDA that affect the general condition of preterm infant and might have influence on teething process like a study conducted by Backstrom *et al.,* 2000.[26]

This study showed that, eruption of the first tooth occurred significantly later in preterm girls than in preterm boys (p-value < 0.05), and the lower incisors erupted earlier than the upper ones in all groups included in the present study, the findings which were not mentioned by other authors.

This study showed that the time of first tooth eruption is significantly affected by total parenteral nutrition introduction mainly the intralipid component and the gender of the preterm infant, other factors have some impact but still clinically and statistically not significant.

CONCLUSION

Introduction of total parenteral nutrition to very low birth weight premature infants is associated with early first tooth eruption. It was concluded that intralipids component of TPN is responsible for this observation, but further studies to evaluate the role of other TPN components are mandatory.

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