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# Timing of oral feeding changes in premature infants who underwent osteopathic manipulative treatment



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#### ABSTRACT

Background: The delayed transition from gavage-to-nipple feeding is one of the most significant factors that may prolong hospital length of stay (LOS). Osteopathic manipulative treatment (OMT) has been demonstrated to be effective regarding LOS reduction, but no investigations have documented its clinical validity for attaining oral feeding.

Objectives: To assess OMT utility regarding the timing of oral feeding in healthy preterm infants.

Design: Preliminary propensity score-matched retrospective cohort study.

Setting: Data were extrapolated from the neonatal intensive care unit (NICU) of Del Ponte Hospital in Varese, Italy, during the period between March 2012 and December 2013.

*Interventions*: Two propensity score-matched groups of healthy preterm infants aged 28<sup>+0</sup> to 33<sup>+6</sup> were compared, observing those supported with OMT until hospital discharge and control subjects.

Main outcome measures: Days from birth to the attainment of oral feeding was the primary endpoint. Body weight, body length, head circumference and LOS were considered as secondary endpoints.

*Results:* Seventy premature infants were included in the study as the control group (n = 35; body weight (BW) =  $1457.9 \pm 316.2$  g; gestational age (GA) =  $31.5 \pm 1.73$  wk) and the osteopathic group (n = 35; BW =  $1509.6 \pm 250.8$  g; GA =  $31.8 \pm 1.64$  wk). The two groups had analogous characteristics at study entry. In this cohort, we observed a significant reduction in TOF (-5.00 days; p = 0.042) in the osteopathic group with a greater effect in very low birth weight infants.

Conclusions: These data demonstrate the utility and potential efficacy of OMT for the attainment of oral feeding. Further adequately powered clinical trials are recommended.

## 1. Introduction

Prematurity is one of the major factors contributing to neonatal morbidities and represents a substantial problem in perinatal medicine. Despite advances in antenatal care, reports have identified an increase in preterm births in the last few decades. Prematurity might compromise the anatomical and functional development of all organs and apparatuses, further worsened by an earlier gestational age and lower body weight. Cardio-respiratory, neurological and gastrointestinal functions are the most important features in allowing the growth and

viability of preterm babies. <sup>1,2</sup> Because of the high rate of neonatal morbidities, premature infants show a prolonged length of stay (LOS) inside neonatal intensive care units (NICU), with a negative impact on their families and society. LOS is considered one of the major factors contributing to hospitalisation costs. Preterm birth and NICU access annual costs are estimated to be 5.8 billion dollars (US), corresponding to 47% of the overall costs for all infant hospitalisations, and up to 27% of all paediatric stays in the United States. <sup>3</sup>

One of the criteria for hospital discharge is the attainment of oral feeding. In the preterm population, newborns might have difficulties

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with nourishment, due to gastrointestinal disorders that are frequently associated with respiratory pattern alterations. Physiological conditions required for discharge include: maintenance of body heat at room temperature, coordinated sucking-swallowing-respiration while feeding, a sustained pattern of weight gain and stable cardiorespiratory function.<sup>4</sup>

Osteopathic manipulative treatment (OMT) is used to treat the dysfunctions linked with preterm pathological conditions. Osteopathic clinical trials have been conducted to investigate the impact of OMT in the care of preterm infants. A multicentre study and a recent meta-analysis have shown that osteopathic treatment significantly reduced LOS and was cost-effective for a large cohort of preterm infants. LOS reduction has been suggested to have positive emotional, psychological and developmental effects for preterm infants and their families. Notwithstanding this, OMT clinical trials in this field have never investigated clinical outcomes such as the timing of oral feeding (TOF) relative to the duration of NICU residence. The aim of this study was to perform a retrospective observation of the effects of OMT on TOF in a population of very/moderately preterm infants. The secondary outcomes assessed were LOS, body weight, head circumference and body length.

#### 2. Methods

#### 2.1. Subject data

We conducted a preliminary propensity score-matched retrospective cohort study to compare feeding and discharge clinical data of healthy premature infants born between 28 +0 and 33 +6 weeks and with a body weight lower than 2000 g, who underwent routine OMT (OG) compared to non-treated control subjects (CG). All data were extrapolated from the NICU clinical records database of Del Ponte Hospital during the period between March 2012 and December 2013. Key exclusion criteria included: genetic disorders, congenital abnormalities, cardiovascular abnormalities, proven or suspected neurological disorders, abdominal obstruction, pre- and/or post-surgery patients, pneumoperitoneum and/or atelectasis, broncho-pulmonary dysplasia (BPD), patent ductus arteriosus (PDA), respiratory distress syndrome (RDS), neonates born from HIV seropositive and/or drug-addicted mother, infants transferred to/from other hospitals and osteopathic treatment performed more than 14 days after birth.

## 2.2. Variables and measures

The variables extrapolated from patient clinical records at discharge were TOF, body weight, body length, head circumference and LOS. TOF is a time measure obtained by counting the days from birth to the achievement of complete oral feeding. LOS was obtained measuring the time passed from birth to hospital discharge.

## 2.3. Ethics

All the infants' families provided signed informed consent for the use of these data for research purposes. The Provincial Ethics Committee of Varese approved the study on 02/14/2017.

## 2.4. Osteopathic manipulative treatment

Osteopathic medicine is a form of drug-free non-invasive manual medicine, designated by WHO as complementary and alternative medicine. It relies on manual contact for the diagnosis and treatment of somatic dysfunction (ICD-10-CM Diagnosis Code M99.00-09).

OMT is a patient-tailored therapy that has been introduced into the routine care of many NICUs, as in Varese. Its diagnostic approach is based on an anatomical, structural and functional analysis. In

newborns, the structural exam is usually performed with the infant lying down on the incubator or table. Somatic dysfunctions can be found in body districts where altered tissue texture, restricted range of motion, tenderness or asymmetry are manifested. This concept must be adapted to the clinical condition of the preterm infant, as OMT is a measured and calibrated application of forces in precise areas and districts. Safety criteria are considered before the delivery of OMT, considering the patient's stable condition, clinically defined with the following parameters:

- absence of apnoea in the preceding 48 hours
- absence of intubation
- presence of adequate blood pressure with respect to gestational age (mean pressure = gestational age)

The palpatory assessment allows the osteopath to identify areas of greater density, tissue impairment and structure resilience. The osteopathic examination is based on the strength of anatomical and physiological evidence, by integrating the manual evaluation with clinical, specialised and instrumental exams. It is performed by a standardised palpatory analysis, which involves a two-hand grip, with the caudal hand on the sacral region and the cranial hand on the occipital region. The main goal is to analyse asymmetry through the palpatory homogeneity and range of motion patterns of the axial myo-fascial system. After that, by exploiting a light compression between the two hands, the osteopath performs a myo-fascial system stimulation, designed to check for tenderness reactions. At the end, a specific palpation of the spine, chest, abdomen and limbs is performed to focus on the examination of mvofascial texture in more restricted areas. Based on this examination, the OMT procedures were designed based on a consensus between at least two osteopaths, and a treatment protocol was trialled, allowing for more reliable and safer OMT.

As mentioned above, osteopathic procedures were focused on the myo-fascial and connective tissues, prevalently in the following areas: cranial (cranial techniques) and occipital, <sup>10</sup> the C1-C2-C3 areas, hyoid, sacrum, diaphragm, upper chest, scapulae, left iliac fossa and the structures connected in anatomical and physiological ways to these structures. A randomised controlled trial from Martelli et al. investigated osteopathic sham therapy and showed that no placebo effect occurs in newborns. <sup>11</sup>

During the investigated period, ten osteopathic practitioners worked synergistically with one another and with NICU specialists; OMT procedures were always under the control of experienced osteopaths. OMT was started in the first two weeks of life, with a frequency of twice a week, in addition to reference standard medical treatment. Every single evaluation and treatment of OG subjects lasted at least 30 min, while CG subjects were treated with standard medical care without OMT.

## 2.5. Statistical analysis

To adjust for potential confounders, a propensity score matching procedure was performed at study entry, matching with a 1:1 ratio. Considering the 35 OMT subjects adherent with inclusion/exclusion criteria, to balance the patient baseline characteristics in the CG, Mahalanobis metric-matching was used, considering as confounders gestational age, gender, ventilatory support and APGAR score, with a calliper of 0.2 of the standard deviation of the logit of propensity score. Imbalance after matching was tested at baseline between groups using the chi-squared test for categorical variables and the Mann-Whitney U test for continuous variables. Variables are reported in terms of mean and standard deviation. A preliminary analysis was performed to determine whether the collected variables were normally distributed. Since this analysis did not show any evidence in this direction and the collected data showed some outliers, it was decided to proceed with a

**Table 1**Baseline characteristics of the patients.

Variable	Control Group (N = 35)	Osteopathic Group (N = 35)	p-value
Male – n. (%)¥	18 (51.4)	17 (48.5)	0.811
Perinatal characteristics			
Body weight – g <sup>1</sup>	$1457.9 \pm 316.2$	$1509.6 \pm 250.8$	0.477
LBW – n. (%)¥	14 (40.0)	13 (37.1)	0.806
VLBW − n. (%)¥	18 (51.4)	20 (57.1)	0.631
ELBW – n. (%) <sup>¥</sup>	3 (8.6)	2 (5.7)	0.643
Gestational age – wk <sup>1</sup>	$31.5 \pm 1.73$	$31.8 \pm 1.64$	0.196
Body length – cm <sup>1</sup>	$39.9 \pm 3.7$	$40.7 \pm 2.8$	0.446
Head circumference – cm 1	$28.8 \pm 2.0$	$29.3 \pm 1.6$	0.310
APGAR 5 min – pt. 1	$8.26 \pm 0.94$	$8.62 \pm 1.27$	0.285
Clinical characteristics			
IUGR − n. (%) <sup>¥</sup>	6 (17.1)	9 (25.7)	0.382
SGA − n. (%)¥	2 (5.7)	5 (14.3)	0.235
Type of ventilation			
HFNC – n. (%) <sup>¥</sup>	20 (57.1)	17 (48.6)	0.473
$nCPAP - n. (\%)^{*}$	4 (11.4)	6 (17.1)	0.495
BiPAP – n. (%) <sup>¥</sup>	1 (0.3)	1 (0.3)	0.999

Propensity score-matched baseline characteristics, described by type of ventilation, clinical and perinatal features. Variables were tested between groups, according to their proprieties. The Mann-Whitney U test <sup>(1)</sup> and Chi<sup>2</sup>-test <sup>(4)</sup> were used.

non-parametric approach. Hence, the comparison between control group and osteopathic group was performed with the Mann-Whitney U test. Tests were considered significant for *p*-values smaller than 0.05. The statistical analysis was performed using the R environment for statistical computing.

## 3. Results

Out of 136 eligible subjects, 66 infants were excluded due to the occurrence of PDA, RDS, BPD or unmatched propensity scores. A final sample of 70 premature infants was extrapolated and matched: CG (n = 35; body weight (BW) =  $1457.9 \pm 316.2 \,\mathrm{g}$ ; gestational age  $(GA) = 31.5 \pm 1.73 \text{ wk}$ ) and OG  $(n = 35; BW = 1509.6 \pm 250.8 \text{ g};$  $GA = 31.8 \pm 1.64$  wk). An analysis of the perinatal characteristics of each group was performed, comparing gestational age, body weight, body length, head circumference and the 5-minute APGAR score between the groups. Moreover, a comparison of the infants' clinical characteristics and ventilation support received was performed, comparing the two groups according to the prevalence of intra-uterine growth restriction (IUGR), small for gestational age (SGA), use of respiratory support with high flow nasal cannula (HFNC), nasal continuous positive airway pressure (nCPAP) or bilevel positive airway pressure (BiPAP) (see Table 1). In this cohort, the groups showed similar clinical features, allowing for the comparison of our primary and secondary outcomes. All enrolled subjects were followed from birth to discharge, and no adverse events or side effects emerged during NICU

The primary endpoint was to evaluate the hypothesis that OMT may influence TOF patterns in healthy premature infants. In this cohort, we observed a difference between the OMT group and the control group of -5.00 days, which was found to be statistically significant (p = 0.042). Despite the correlation between TOF and LOS and the clinically significant difference between groups (-5.60 days), LOS showed a quasistatistically significant difference (p = 0.065). Body length, body weight, head circumference did not show significant p-values.

A post-hoc analysis of the primary outcome and the main secondary outcome, stratified by body weight at birth, highlighted a statistically and clinically significant difference in very low birth weight (VLBW) infants underwent OMT, considering both TOF (-7.70 days, p=0.026) and LOS (-11.30 days, p=0.018) (see Table 2).

Table 2
Primary and secondary outcomes.

Variable	Control Group (N = 35)	Osteopathic Group (N = 35)	p-value
Discharge characteristics			
Body weight – g	$2288.1 \pm 553.4$	$2190.4 \pm 470.1$	0.672
Body length - cm.	$45.4 \pm 2.8$	$45.4 \pm 2.3$	0.797
Head circumf cm.	$32.7 \pm 1.9$	$32.5 \pm 1.6$	0.831
Timing oral feeding - d.	$27.0 \pm 19.6$	$22.0 \pm 16.8$	$0.042^{*}$
LBW	$22.2 \pm 8.4$	$16.5 \pm 10.8$	0.096
VLBW	$32.8 \pm 14.0$	$25.1 \pm 14.1$	$0.026^{*}$
Length of stay - d.	$38.4 \pm 19.6$	$32.8 \pm 16.9$	0.065
LBW	$29.6 \pm 15.4$	$27.9 \pm 13.2$	0.240
VLBW	$45.8 \pm 16.8$	$34.5 \pm 17.0$	$0.018^{*}$

Discharge characteristics of the primary and secondary outcomes. TOF and LOS were labelled by group and stratified according to birth weight category.

#### 4. Discussion

Full oral feeding is a crucial aspect for the health of premature infants and clinical management within the NICU. Several studies have documented the efficacy of OMT in the paediatric setting, but very few have investigated the possible benefits of OMT in preterm infants. <sup>12–15</sup> The most relevant studies have demonstrated an effect on LOS, especially in preterm babies born between 24 and 31 weeks. <sup>6,7</sup> However, TOF has never been investigated when associated with OMT delivery. This might be a crucial aspect, since the costs related to NICU permanence are relevant. Interestingly, OG subjects registered a statistically significant reduction in TOF compared to CG subjects (see Fig. 1), outlining a possible influence of OMT over sucking and swallowing functionality. Furthermore, after stratification by body weight, VLBW infants showed a greater TOF reduction compared to the general cohort assessed here.

A comparative study highlighted how a more intensive enteral nutrition can reduce the time of parenteral nutrition and the incidence of sepsis. 16 In addition, oral sensory-motor system stimulation is a very important strategy to decrease the transition time to full oral feeding.<sup>1</sup> Oral feeding requires a complex set of actions and skills, which preterm infants have difficulty with because their neurologic and oral motor systems are functionally immature. In the first weeks of life, preterm infants receive gavage for enteral nutrition until the transition from tube feeding to independent oral feeding. The time needed to develop independent oral feeding is related to gestational age and the acquisition of automatic and coordinated swallowing-sucking skills combined with respiration. 18 This problem is mainly associated with prematurity, enhanced by the occurrence of bronchopulmonary dysplasia and probably worsened by localised somatic dysfunctions. 19,20 Each specific sensorimotor action involved in the suck-swallow-respiration dynamic has a functional convergence in brainstem. In this context, sensory feedbacks are essential for the implementation of the correct feedingrespiratory dynamics and the proper attainment of oral feeding. <sup>21</sup> This neurological pattern might promote a positive feedback on swallowing and breathing synchronisation, which is important for the improvement of nipple feeding mechanics. Furthermore, the occipital and upper cervical areas might have a primary impact on oral feeding mechanics and any related impairment, and they are correlated with the cervical voluntary muscle development. 12-20-22 Interestingly, the chest, neck and upper cervical regions were frequently involved in the somatic dysfunction pathways observed in these patients, and OMT seems to ameliorate oropharynx muscular coordination and the pump load of breathing muscles. Other aspects that should be considered are esophago-gastric positional development and autonomic nervous system functionality.2

The effects of OMT on the autonomic nervous system have been demonstrated by studies on crying frequency, sleep, heart rate variability, interoception and visceral functionality. <sup>15,19,22–24</sup> Administration

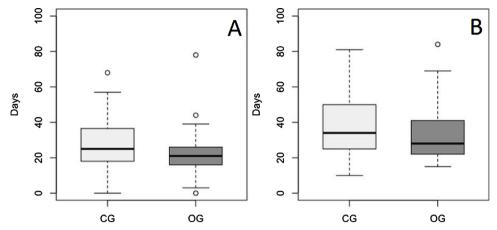


Fig. 1. Time to full oral feeding (A) and hospital discharge (B) for the control group and the osteopathic group. Subjects exposed to OMT showed a significant decrease in TOF.

of OMT has been shown to have parasympathetic effects as well as antiinflammatory action, and is effective on the structures and fascial layers in close relationships with areas involved in swallowing and sucking. <sup>23–25</sup> Nevertheless, the biological effects of OMT remain under active investigation.

Improving the functionality of sucking and swallowing means abbreviating the time needed to reach full oral feeding, allowing the child to reduce nutrition with a nasogastric tube (gavage) and favouring more prolonged contact with the mother. Many reviews have highlighted the key role of mother-child contact, and the positive effects of this on public health. What emerges is that mother-child contact can be increased by working on the transition from gavage to nipple feeding, reducing the risks associated with early discharge. Therefore, the clinical and biological effects of OMT on the neurological development of premature infants should be studied in depth.

The sample size and the absence of randomisation pose some limitations on our pilot observational study. Moreover, all patients enrolled were treated at a single NICU and may not be representative of the general preterm infant population. Furthermore, it is not possible to comment on the placebo effect of OMT on TOF since Martelli et al. investigated the placebo effect on LOS only. Hence, we suggest that future randomised trials should compare the placebo effect in the experimental group using a sham group. In conclusion, the results that emerged from our investigation highlight a significant relationship between OMT administration and a reduction in TOF, with different effects observed in VLBW infants compared to LBW subjects. Further clinical trials should be performed to address the effects of OMT on swallowing and sucking mechanics in correlation with respiratory parameters and the clinical effects on transition patterns of feeding procedures.

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