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REVIEW ARTICLE

Application of tactile/kinesthetic stimulation in preterm infants: a systematic review☆,☆☆

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Abstract
Objective: To verify the methods used by the clinical trials that assessed the effect of tactile/kinesthetic stimulation on weight gain in preterm infants and highlight the similarities and differences among such studies.
Sources: This review collected studies from two databases, PEDro and PubMed, in July of 2014, in addition to bibliographies. Two researchers assessed the relevant titles independently, and then chose which studies to read in full and include in this review by consensus. Clinical trials that studied tactile stimulation or massage therapy whether or not associated with kinesthetic stimulation of preterm infants; that assessed weight gain after the intervention; that had a control group and were composed in English, Portuguese, or Spanish were included.
Summary of the findings: A total of 520 titles were found and 108 were selected for manuscript reading. Repeated studies were excluded, resulting in 40 different studies. Of these, 31 met all the inclusion criteria. There were many differences in the application of tactile/kinesthetic stimulation techniques among studies, which hindered the accurate reproduction of the procedure. Also, many studies did not describe the adverse events that occurred during stimulation, the course of action taken when such events occurred, and their effect on the outcome.
Conclusions: These studies made a relevant contribution towards indicating tactile/kinesthetic stimulation as a promising tool. Nevertheless, there was no standard for application among them. Future studies should raise the level of methodological rigor and describe the adverse events. This may permit other researchers to be more aware of expected outcomes, and a standard technique could be established.

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PALAVRAS-CHAVE
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Ganho de peso;
Estimulação tátil-cinestésica

Aplicação da estimulação tátil-cinestésica em neonatos prematuros: análise sistemática

Resumo
Objetivo: Verificar quais metodologias foram utilizadas por ensaios clínicos que avaliaram o efeito da estimulação tátil-cinestésica sobre o ganho de peso de neonatos prematuros e destacar as diferenças e semelhanças entre esses estudos.
Fontes dos dados: Esta análise coletou estudos de duas bases de dados, PEDro e PubMed, em julho de 2014, além de bibliografias. Dois pesquisadores avaliaram os títulos relevantes independentemente e, então, escolheram consensualmente quais estudos seriam lidos completamente e incluídos nesta análise. Foram incluídos os ensaios clínicos que estudaram a estimulação tátil ou a massagem terapêutica associada ou não à estimulação cinestésica em neonatos prematuros e avaliaram o ganho de peso após a intervenção, tiveram um grupo de controle e foram escritos em inglês, português ou espanhol.
Síntese dos dados: Foram encontrados 520 títulos no total, e foram selecionados 108 para leitura. Os estudos repetidos foram excluídos, resultando em 40 estudos diferentes. Destes, 31 atenderam a todos os critérios de inclusão. Há muitas diferenças na aplicação das técnicas de estimulação tátil-cinestésica entre os estudos, o que prejudica a reprodução precisa do procedimento. Além disso, muitos estudos não descreviam os eventos adversos ocorridos durante a estimulação, o procedimento realizado quando esses eventos ocorriam e seu efeito sobre o resultado.
Conclusões: Esses estudos fizeram uma contribuição relevante ao incluir a estimulação tátil-cinestésica como uma ferramenta promissora. Contudo, não houve padrão de aplicação entre eles. Estudos futuros podem aumentar o nível do rigor metodológicos e descrever os eventos adversos. Isso pode permitir que outros pesquisadores tenham mais ciência do que esperar e assim estabelecer uma técnica padrão.

Introduction

Preterm infants (PI) are exposed daily to many stressors in the neonatal intensive care unit (NICU) inherent to the critical care they need to survive. The manner and intensity of exposure vary according to the individual PI condition and response. It has already been shown that such exposure leads to structural and functional changes in specific areas of the brain, affecting its development,[1] language, and social-emotional and adaptive behavior.[2]

Tactile stimulation (TS) or massage therapy (MT), sometimes associated with kinesthetic stimulation (KS), is used in PI along with the standard clinical treatment. TS have been the object of clinical studies since the 1960s,[3] when it was proposed as a means of encouraging PI growth and development.[3–10] Additionally, recent studies have shown that interventions such as tactile/kinesthetic stimulation (TKS) have the added benefit of reducing behavioral manifestations of stress.[11]

The objective of this systematic review was to verify which methodologies were used by clinical trials that study the effects of some types of TS/MT, whether or not associated with KS, on weight gain of PI. Clinical trials were selected that studied the effects on weight gain, as this is a determinant variable for discharge from the NICU. The differences and similarities between the methods used by the reviewed clinical trials were highlighted in an attempt to improve the methodological quality of future trials.

Methods

Two databases were searched for this systematic review: the Physiotherapy Evidence Database (PEDro)[12] and the United States National Library of Medicine of the National Institutes of Health (PubMed).[13] All studies listed on the date of search were accessed.

The PEDro database was searched by specifying the following fields in the advanced search option: therapy (stretching, mobilization, manipulation, massage); subdiscipline (pediatrics), and method (clinical trial).

PubMed was searched using six keyword combinations, as follows:

- Search 1: massage premature newborn
- Search 2: tactile kinesthetic stimulation premature
- Search 3: tactile stimulation premature
- Search 4: massage premature growth
- Search 5: kinesthetic stimulation premature growth
- Search 6: tactile kinesthetic stimulation premature growth

In addition to these searches, the references of the chosen articles were also checked, and another 12 relevant articles were selected for evaluation.

Inclusion criteria

Two independent researchers preselected the articles according to their titles. In case of doubt, the article was included in the selection process by consensus. The preselected titles were then stored in a file according to the database they were found, and their abstracts or texts were downloaded for assessment. Once downloaded, the articles were thoroughly read to select those that met the inclusion criteria detailed below.

The present review included all clinical trials that studied the provision of TS or MT, whether or not associated with KS, for PI in the NICU, assessed PI weight gain after the intervention, had a control group that did not receive any intervention in addition to the standard treatment provided by the NICU, and were composed in English, Portuguese, or Spanish.

Results

A total of 508 articles were found in the two abovementioned databases. Seventeen articles were fully read among the 206 articles found in the PEDro database, of which eight met the inclusion criteria. The first search on PubMed resulted in 126 titles, of which 30 were selected and 18 met the inclusion criteria. The second search on PubMed resulted in 16 titles, of which ten were selected and eight met the inclusion criteria. The third search on PubMed resulted in 86 titles, of which 14 were selected and ten met the inclusion criteria. The fourth search on PubMed resulted in 49 titles, of which 23 were selected and 16 met the inclusion criteria. The fifth search on PubMed resulted in 14 titles, of which nine were selected and six met the inclusion criteria. The sixth search on PubMed resulted in 11 titles, of which eight were selected and five met the inclusion criteria.

However, another 12 titles found in the references of the articles that met the inclusion criteria were analyzed, and of these, four were included, five were excluded, and three were not found. Table 1 shows the titles and where they were found.

In summary, 520 titles were found; the repeated studies were eliminated, resulting in 31 that met the inclusion criteria of the present review (Table 1).

TS/MT was done in many different ways,[3,9,10,14–18] and the most of the studies did not provide a detailed description of how to proceed during the stimulation if adverse events occur, nor of the possible effects of these events on the outcomes.

Analysis of the techniques used by different studies showed that older studies, such as Solkoff et al.,[6] Kramer et al.,[7] and Solkoff & Matuszak[8] did not specify which parts of the body were stimulated or how often. The pressure used during the intervention and its duration varied greatly between these studies.

White & Labarba[3] were the first to combine TS and KS. In 1981, Rausch[9] divided TKS into three phases of five minutes each and applied TKS only when the PI were awake, without changing their position in the incubator. Both Lee[19] and Ferreira & Bergamasco[20] followed these procedures. Rausch[9] suggested that new studies should provide the intervention for at least ten days, because weight gain increased after this period. Rausch's[9] study was the first to show significantly faster weight gain in PI submitted to TKS and to describe the technique used in detail.

Scafidi et al. [21] standardized the three five-minute phases proposed by Rausch[9] into prone TS + supine KS + prone TS. Fourteen of the 31 studies that met the inclusion criteria for the present review used the technique described by Field et al. [10] in 1986; 11 of the 14 were conducted by Field's team[10,21–30] in the same institution and three were performed by other researchers, namely Lee,[19] Massaro et al.,[31] and Ang et al. [32] The intervention was usually performed after the first feeding in the morning. In 1990, Field & Schanberg[24] provided the intervention at the beginning of three consecutive hours, after the midday feeding.

Mathai et al. [14] introduced a new way of providing TKS, as follows: the intervention was done after the morning, midday, and evening feeding in the prone (TS) + supine (TS) + supine (KS) positions, which was repeated by Arora et al. [33] Like other studies, they also used some type of oil to reduce friction on the PI's skin.[14,17,33–35] In some studies, only the mothers provided KTS.[16,35,36]

Ferber et al. [15] suggested that during the first ten seconds of TS, the caregiver should only rest his hand on the PI, avoiding movements.

Dieter et al. [27] was the first to provide TKS for only five days, showing that this was enough to increase the rate of weight gain significantly compared with the control group.

Diego et al. [28] demonstrated that moderate KTS pressure promoted better outcomes than the placebo group who received light KTS pressure. Also, in another time, trained a few therapists and suggested that the technique was effective, regardless of therapist.[29]

Massaro et al. [31] tested KTS and TS separately in different groups of infants and found that KTS appears to be better, but the difference was not significant.

Fucile & Gisel[18] used the same trained researcher to provide the intervention and introduced oral stimulation (OS) in addition to KTS. They found that OS did not increase the rate of weight gain and attributed this result to the shorter period dedicated to each intervention, suggesting that the duration of the sensoriomotor input is critical for improving defined outcomes.

Ferreira & Bergamasco[20] used gentle techniques with no rigid sequence, only when the PI was awake.

Moyer-Mileur et al. [37] used the Infant Massage USA protocol, but they modified for PI, eliminating massage of the abdomen.

Kumar et al. [34] demonstrated that PI who received oil massage soon after birth had less weight loss in the first week, probably due to undetectable water loss through the skin due to blockage of pores and sweat glands. Also, early oil application probably leads to better temperature regulation and less caloric expenditure due to cold stress.

Abdallah et al. [35] used TS without KS and did not find greater weight gain, but the pain scores on the Premature Infant Pain Profile were favored in the massaged infants, being lower after the intervention and at discharge, in addition to demonstrating better cognitive scores.

Table 1 Descriptions of the included studies.

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Effects of handling on the subsequent developments of premature infants[6] Solkoff et al., 1969 Bibliography of article	Total: 20 MBW = 1360 g MBW = 1369 g	Verify immediate and subsequent effects of handling on the behavior and physical development 12 h after delivery, randomly assigned.	5 min each hour, for 24 h, 10 days. While awake, the infant's neck, back and arms were gently rubbed by a nurse or aide.	1) Activity (polygraph reading, from a recorder) 2) WG 3) Temperature 4) Startle responses 5) Crying 6) Frequency of urination and defecation 7) Physical development	Body weight taken daily with normal nursery routine, approximately the same time.	Not described	Was not performed statistically because of the small sample. It appeared that the TG was more active, cried less, and gained weight faster.
Extra tactile stimulation of the premature infant[7] Kramer et al., 1975 PubMed search 3 and PEDro	Total: 14 TG: 8 GAM = 33 w BWM = 1441 g CG: 6 GAM = 33 w BWM = 1418 g After the random start, subjects were alternately assigned to TG or CG.	Verify if touch such as extra tactile stimulation could result in faster physical and social development and a greater degree of social development of PI. Beginning when the infants were at least 2 weeks in the isolletes.	Gentle, nonrhythmic stroking of the greatest possible skin area of the infant's body, by trained nurse, 48 min/day, 2 min before and 2 min after each feeding (if two in 2 h) or 3 min before and 3 min after (if three in 3 h). Stop watches were used for accurate timing.	1) Daily WG 2) Social (Gesell development schedule) and physical development (Bayley scale) 3) Plasma cortisol level	Body weight take daily with normal nursery routine. Scales used to weigh infants were checked and calibrated once a week by the researchers using Ohaus weights.	Not described	TG appears to have demonstrated a higher degree of motor skill.
Tactile stimulation and behavioral development among low-birth weight infants[8] Solkoff Matuszak, 1975 PubMed search 3	Total: 11 TG: 6 GAM = 31.2 w BWM = 1375.3 g CG: 5 GAM = 31 w BWM = 1564.5 g	To check the effect TS on WG and behavioral by Neonatal behavioral assessment scale. The mean age of start of stimulation was 14 days.	7.5 min of extra-handling, for ten days, in the form of stroking, during each hour of 16 h/day, total of 1,200 min. Applied by two nurses.	1) Temperamental, reflex, and ''early'' social behavior - Neonatal behavioral assessment scale. 2) WG	Not described	Not described	Was not performed statistically because of small sample size.

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
The effects of tactile and kinesthetic stimulation on neonatal development in the premature infant[3] White Labarba, 1976 PubMed searches 2, 3, 5, 6	Total: 12 TG: 6 GAM = 34.3 w BWM = 1910 g CG: 6 GAM = 34.2 w BWM = 1911 g	Investigate some immediate effects such as WG and the development of low birth weight infants that received T/KS in a typical hospital nursery. Beginning after 48 h of age.	15 min periods every hour for four consecutive hours, for ten days. Rubbing the infant's neck, shoulder, arms, legs, chest, and back; and KS. Performed by researcher.	1) WG, number of feedings, amount of formula intake. 2) Body temperature 3) HR, RR 4) Frequency of voiding and stooling.	All infants were routinely weighed three days each week by the nursery staff.	Not described	1) TG: More WG stimulation effect ($p < 0.05$) and stimulation x days interaction ($p < 0.001$) TG: Greater amount of formula intake ($p < 0.025$) TG: Fewer number of feedings/day ($p < 0.05$)
Effects of tactile and kinesthetic stimulation on premature infants[9] Rausch, 1981 PubMed searches 2, 3, 5, 6	Total: 40 TG: 20 CG: 20 BW = 1000-2000 g Not randomized	To determine the effects of a 10-day regimen of T/KS on caloric intake, stooling, and WG. Beginning at 24-48 h of age.	15 min, 3x/day, at the beginning of three consecutive hours, starting 30 min after the first morning feeding, for ten weekdays; non-treatment on weekend. Performed by researcher. With the infant awake and keeping the baby in position.	1) WG 2) Frequency of stooling 3) Caloric intake	Body weight taken daily with normal nursery routine.	Not described	2)TG: Increase of formula intake on days 6-10 ($p < 0.0001$) 3) TG: Increase stooling frequency ($p < 0.004$)
Effects of tactile/kinesthetic stimulation on the clinical course and sleep/wake behavior of preterm neonates[21] Scafidi et al., 1986 PEDro	Total: 40 TG: 20 GAM = 31 w BWM = 1280 g CG: 20 GAM = 31 w BWM = 1268 g	It was designed to complement the already existing literature of the effects of T/KS in PI. Beginning when clinically stable.	T/KS: 15 min, 3x/day, at the beginning of three consecutive hours, starting 30 min after the first morning feeding, for ten weekdays; non-treatment on weekend. Performed by researcher. Phase 1 and 3 in prone position and phase 2 in supine.	1) Daily WG 2) Formula intake, frequency of voiding, stooling 3) HR, RR, body temperature 4) Number of apneic episodes 5) Parents visiting and touch 6) Brazelton scale 7) Sleep-wake behavioral (Thomas Scale of 1975) 8) Length of hospital stay	Body weight taken daily with normal nursery routine.	Not described	1) TG: Better WG per day (8 g/day more) ($p < 0.0005$) 2) More weight per calories of intake per kg of body weight 6) TG: More mature orientation, motor habituation, and range of state behaviors on Brazelton Scales 7) TG: More time awake ($p < 0.04$) and active ($p < 0.05$) 8) TG: 6 days earlier discharge ($p < 0.05$)

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Tactile/kinesthetic stimulation effects on preterms neonates[10] Field et al., 1986 PubMed search 2,3,5,6	Total: 40 TG: 20 GAM = 31 w BWM = 1280 g 20 GC: GAM = 31 w BWM = 1268 g	Evaluate the effects of T/KS on growth, sleep-wake behavior, and Brazelton scale in PI Beginning when clinically stable	T/KS: 15 min, 3x/day, at the beginning of three consecutive hours, starting 30 min after the first morning feeding, for ten weekdays; non-treatment on weekend. Not clear who applied the technique.	1) Daily WG, formula intake, frequency of voiding and stooling, and parent visits 2) Length of hospital stay 3) Sleep-wake behavior 4) Brazelton scale 5) Physiological parameters	Body weight taken daily with normal nursery routine.	Not described	1) TG: 47% more WG per day ($p < 0.0005$) 2) TG: 6 days earlier discharge ($p < 0.05$) 3) TG: More time awake and active ($p < 0.04$) 4) TG: More mature orientation, motor habituation, and range of state behaviors on Brazelton Scales
Massage of preterm newborns to improve growth and development[22] Field et al., 1987 Bibliography–Touch research institute	Total: 40 TG = 20 CG = 20 Overall average GA = 31 weeks BW = 1274 g	To describe an effective massage procedure for facilitating WG in PI, reviewing data that support it. Beginning when clinically stable and bottle-fed.	T/KS: 15 min, 3x/day, at the beginning of three consecutive hours, starting 30 min after the first morning feeding, for ten weekdays; non-treatment on weekend. Not clear who applied the technique.	1) Daily WG 2) Formula intake and number of feedings 3) Brazelton scale at end of treatment 4) Sleep-wake behavior–recorded for 45 min at end of treatment 5) After six months: half of the sample received rating pediatric (weight, height, and head circumference) and Bayley scales of infant development (1969)	Not described	Not described	1) TG: more daily WG ($p < 0.0005$) 3) Better performance 4) More active 5) Greater WG after six months ($p < 0.05$), better performance ($p < 0.05$)

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Effects of early multimodal stimulation on preterm newborn infants[39] Benavides-González et al., 1989 PubMed searches 2, 5, 6	Total: 18 GAM = 31.5 w BWM = 1296 g GC: GAM = 32.4 w BWM = 1211 g	To study if the supplemental stimulation of PI responses improves neurobehavioral organization, achieving greater WG and a reduction in length of hospital stay.	Intrahospital T/KS: 15 min, 2x/day, for ten days, non-treatment on weekend. Period 1: TS, vestibular and proprioceptive (15 min) Period 2: lateral wedge-shaped crescent (15 min) Performed by three trained people, 30 min before feeding at 7 am and 10 am. Extra-hospital: T/KS + visual, auditory stimulation for 5 min	1) Daily WG 2) Formula intake 3) Length of hospital stay 4) Postural reflexes and neurobehavioral performance were assessed at the time the child left the hospital and one month afterwards.	Body weight taken daily with normal nursery routine. Only one scale was used.	Not described	1)TG: 3.2 g/day more 3) TG: 3 days less 4) Better neurobehavioral performance and postural reflexes
Massage stimulates growth in preterm infants: a replication[23] Scafidi et al., 1990 PEDro	Total: 40 TG: 20 GAM = 30w BWM = 1179 g CG: 20 GAM = 30w BWM = 1180 g Stratification: < or > 30 weeks GA < or >1100 g BW < or >20 days NICU < or > 1300 g at beginning of study	Designed to correct previous methodological weaknesses and provide a replication of the previous study. Not randomized, alternative weeks. Beginning when clinically stable.	T/KS: 15 min, 3x/day, at the beginning of three consecutive hours, starting 60 min after the noon feeding, for 10 weekdays; non-treatment on weekends. Not clear who applied the technique. Never lost contact with the infant's skin during stroking motions.	1) Daily WG 2) Formula intake, frequency of voiding and stooling 3) HR, RR, body temperature 4) Number of apneic episodes 6) Parents visiting and touch 7) Brazelton scale (day 1 and 10) 8) Sleep/wake behavior−videotaped during stimulation/no-stimulation period 9) Length of hospital stay	The infant was weighed daily by the experimenter or research assistant immediately prior to the 3 pm feeding.	Not described	1)TG: Greater daily WG ($p < 0.003$) Greater WG in final period ($p < 0.001$) 2) Frequency of stooling was lower in TG ($p < 0.05$) 7) TG: Better habituation ($p < 0.05$); motor maturity ($p < 0.005$), and number of abnormal reflexes ($p < 0.001$) 8)TG: tactile phase: more active sleep, fewer periods without movement ($p = 0.001$) 9) 5 days less hospitalization ($p < 0.05$)

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Massage alters growth and catecholamine production in preterm newborns[24] Field Schanberg, 1990 Bibliography–Touch research institute	Total: 40 BWM = 1176 g GAM = 30 w NICU = 14 days Randomized	To replicate the stimulation procedure and findings of the earlier study, and to add several under-the-skin variables such as growth hormone, cortisol, and cathecolamine activity that might provide more information on the relationship between TS and WG.	T/KS: 15 min, 3x/day, at the beginning of three consecutive hours, starting 60 min after the noon feeding, for ten weekdays; non-treatment on weekends. Not clear who applied the technique.	1) Formula intake, daily WG 2) Frequency of urination 3) Frequency of stooling 4) HR, RR, body temperature 5) Number of apneic episodes 6) Parents visiting (and if touching, holding, and feeding) 7) Sleep–wake behavior 8) Plasma growth hormone and cortisol 9) Urine-norepinephrine, epinephrine, dopamine, cortisol, and creatinine 10) Length of hospital stay	Not described	Not described	1) TG: 21% greater WG ($p = 0.003$). 3) Better performance on the habituation cluster following the treatment period, less time in active sleep, and less facial grimacing, mouthing/yawning, and clenched fists 10) 5 days less hospitalization
Massage effects on cocaine-exposed preterm neonates[25] Wheeden et al., 1993 PEDro and PubMed searches 1, 4	Total: 30 TG GAM = 29.7w BWM = 1158.3 g CG GAM = 30.8 w BWM = 1265.4 g	To observe the effects of MT in WG of cocaine-exposed PI. Beginning when clinically stable.	T/KS: 15 min, 3x/day, at the beginning of three consecutive hours, for ten days. All performed by the same trained researcher. During TS phase never lost contact with the skin, keeping pressure even if there was some reaction from the infant, such as tickle.	1) Daily WG 2) Formula intake, frequency of voiding and stooling 3) HR, RR, body temperature 4) Number of apneic episodes 5) Parents visiting and touch 6) Brazelton Scale 7) Postnatal complications	Body weight taken daily with normal nursery routine.	Not described	1) TG: 28% greater WG 2) More daily WG, $p < 0.01$ 6) Brazelton scale: better motor maturity ($p < 0.005$), orientation ($p < 0.06$), and stress behaviors ($p < 0.05$)

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Factors that predict which preterm infants benefit most from massage therapy[26] Scafidi et al., 1993 Bibliography–Touch research institute	Total: 93 GAM = 30 w BWM = 1204 g NICU = 15 days Weight at start of study = 1353 g	This study examined individual differences to identify infant and clinical characteristics that would predict maximal WG in control and MT-receiving infants. Beginning when clinically stable.	T/KS: 15 min, 3x/day, at the beginning of three consecutive hours, for ten days; never lost contact with the skin, or lightened the pressure. Trained research assistant or nurse.	1) WG and volumetric and caloric intake 2) Frequency of voiding 3) HR, RR, body temperature 4) Number of apneas 5) Frequency of visiting (including touch, feeding, and holding) 6) Sleep-wake 7) Brazelton scale	Data collected from the nurses notes and daily weighing by a research assistant.	The session was discontinued if behavioral signs of stress or crying persisted for longer than 60 s continuously.	1) TG: Greater daily WG ($p < 0.01$) 2) Separate *t*-test analyses were performed for the low and high weight gainers: 70% of the TG was classified as high weight gain and 40% of the of CG ($p < 0.01$) Low weight gainers of the TG gained more weight ($p < 0.005$)
Effects of tactile-kinesthetic stimulation in preterms: a controlled trial[14] Mathai et al., 2001 PubMed searches 1, 2, 3, 4, 5, 6	Total: 45 TG: 25 GAM = 34.6 w BWM = 1598 g CG: 23 GAM = 34.3 w BWM = 1588 g Not randomized-systematic allocation	Determine the effects of T/KS in PI on physiological parameters, physical growth, and behavioral development (Brazelton Scale). Beginning after two days clinically stable.	T/K: 3x/day, 15 min, for five days, 30-45 min after morning, afternoon, and night feeding, by a trained professional. After this period the mothers performed until 40-42 w post-menstrual age. Prone and supine position. Used talc or mineral oil, excess removed with cotton after finish.	1) Anthropometric data at the beginning and end of the study 2) Physiologic parameters 3) Brazelton scale before and after five days of T/KS and at the end of the study.	Body weight taken daily with normal nursery routine, on an electronic scale (Phillips®, Amsterdam, Netherlands) with an accuracy of $\pm$ 5 g.	If the baby started crying or passed urine or stools during the session, it was temporarily stopped until the baby was comfortable again.	1) TG: Greater WG (21.9%, 4.24 g/day) 2) TG: Higher HR during stimulation ($p < 0.005$) 3) Improved neurobehavior during days 5-7 in orientation, range of state, supplements regulations, and autonomic stability

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Massage therapy by mothers and trained professionals enhances weight gain in preterm infants[15] Ferber et al., 2002 PEDro and PubMed searches 1, 4	Total: 57 1) TG mother: 21 GAM = 30.9 w BWM = 1318 g 2) TG prof: 17 GAM = 31.8 w BWM = 1527 g 3) CG: 19 GAM = 31.52 w BWM = 1375 g	Compare the results of MT performed by mothers and by trained professionals on WG in PI. Beginning when clinically stable.	Only TS prone and supine, moderate pressure, 15 min, 3x/daily, early 3hs consecutive for 10 days. One group received from the prof, the other from mothers. Each 7.5 min: Both hands were laid on the baby's head for 10 s without movement, then the infant was stroked slowly by hand movement from the head towards the legs, back and forth. No massages on chest and stomach. Between day 7 and day 9: one day without MT.	1) WG 2) Calorie intake	Not described	Not described	1) TG mother and TG prof: Greater WG ($p = 0.03$) more evident after five days of intervention

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Stable preterm infants gain more weight and sleep less after five days of massage therapy[27] Dieter et al., 2003 PubMed searches 1, 4	Total: 32 TG: 16 GAM = 30.1 w BWM = 1359 g CG: 16 GAM = 31.1 w BWM = 1421 g	To evaluate the effect of five days of MT in WG and sleep-wake behavior in PI. Beginning when clinically stable.	T/KS: 15 min for five days, 3x/day. Performed by a trained therapist.	1) Daily WG 2) Formula intake, kilocalories, stooling 3) Sleep-wake behavior	Daily WG was measured in the early morning by nurses on the preceding night shift.	At the sign of physiologic distress (HR greater than 200 bpm), massage was discontinued for 15 s, or until a return to baseline levels was observed. Massage was then resumed. The occurrence of five periods of physiologic over reactivity was arbitrarily chosen as the criterion for discontinuing an infant from the study. No infant discontinued.	1) TG: 53% greater daily WG ($p = 0.001$) 3) TG: Less sleeping time ($p = 0.04$) and drowsy longer ($p = 0.007$)
Effect of oil massage on growth and neurobehavior in very low birth weight preterm neonates[33] Arora et al., 2005 PEDro and PubMed searches 1, 4	Total: 62 1) TG with oil: 20 GAM = 33.9 w BWM = 1280.2 g 2) TG without oil: 19 GAM = 34.6 w BWM = 1298.6 g 3) CG: 23 GAM = 34.7 w BWM = 1327.1 g	Studying the effect of MT with oil on growth and behavior PI with BW < 1500 g. Beginning as soon as they received enteral feeds of at least 100 mL/kg/day, provided they were less than 10 days of age.	20 gentle strokes in each area, by professionals and mothers. Prone position: both shoulders starting from the neck, upper back to the waist. Supine position: the limbs. 28 days, 4x/day for 10 min. After discharge performed by mothers. Used sunflower oil.	1) WG 2) Anthropometric data 3) Serum triglyceride levels	Body weight taken with normal nursery routine at the time of registration and weekly for the next four weeks.	Temporary interruption in the trial: apnea, sepsis, and IVH. Minor problems: oral thrush, pyoderma, and hyperbilirubine-mia	There were three PI who had more than 20% interruption in their procedure; all were in the oil TG. After exclusion, observed more WG in TG with oil.

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Vagal activity, gastric motility, and weight gain in massaged preterm neonates[28] Diego et al., 2005 PubMed searches 1, 4	Total: 48 1) TG: 16 GAM = 29.8 w BWM = 1091 g 2) Gsham: 16 GAM = 30.3 w BWM = 1184 g 3) CG: 16 GAM = 29.6 w BWM = 1265 g	Assess whether there alteration in VA, GM, and WG in response to MT. Beginning when clinically stable.	T/KS: 15 min 3x/day for five days, 1 h after feeding. Applied by various professionals. The Gsham received the same sequence of T/KS with light pressure.	1) WG 2) Days of hospitalization 3) VA and GM on day 1 (15 min before, during the 15 min of treatment, and 15 min after T/KS)	Data collected by a blinded researcher. Body weight taken with normal nursery routine	Not described	1) GM greater WG ($p < 0.01$), with no greater caloric intake. 3) Increased VA and GM during and shortly after MT.
The effect of infant massage on weight gain, physiological and behavioral responses in premature infants[19] Lee, 2005 PubMed searches 1, 2, 3, 4, 5	Total: 26 TG: 13 GAM = 224.2 days BWM = 1508.5 g CG: 13 GAM = 217.4 days BWM = 1377.7 g	Evaluate the response of infants who received MT in WG, including physiological and behavioral parameters. Beginning when clinically stable, two days after start of enteral feeding.	T/KS: 15 min 2x/day for ten days, 1 h after feeding in the morning and afternoon, with infant's eyes open. Data collected 10 min before and 10 min after the T/KS daily. Use of oil to reduce friction. Performed by nurses.	1) WG 2) Physiological data 3) Behavioral responses: 10 min evaluation pre- and post-MT - videotaped 4) Electrocardiogram	Nurses on the preceding night shift measured daily WG in the early morning.	Study would be discontinued for at least one hour if: HR less than 100 bpm or greater than 200 bpm for 12 s or more, or blood oxygen saturation levels less than 90% for longer than 30 s. Infant showed no signs of stress during the study.	1) Higher in VA in TG: days 1, 2, 6, 7, 8, and 9 2) Increased O_2 Sat on the 9th day in TG 3) Significant increase in alertness and motor activity 4) There was a significant effect for days ($p = 0.001$) both groups increased in WG, on the average, over the ten-day experimental period
Preterm infant massage elicits consistent increases in vagal activity and gastric motility that are associated with greater weight gain[29] Diego et al., 2007 PubMed searches 1, 4	Total: 70 TG: 34 CG: 36	Determine whether the MT in PI is related to the increase in VA and GM and if it interferes with WG. Beginning when clinically stable and gavage-fed.	T/KS: 15 min 3x/day for five days, one hour after feeding, early of 3hs consecutive Performed by professional	1) Daily WG 2) Caloric intake 3) ECGs and EGGs collected on day one and day five, 15 min before, during the 15 min, and 15 min after the procedure. MT was performed at 12 am.	Body weight taken with normal nursery routine.	Not described	1) TG: Increased WG (30% more) 3) TG: Increased VA and GM during MT period, on days one and five ($p < 0.001$)

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Insulin and insulin-like growth factor 1 increased in preterm neonates following massage therapy [30] Field et al., 2008 PubMed searches 1, 4	Total: 42 TG: 95 GAM = 29.3 w BWM = 1178.5 g CG: 42 GAM = 2.8 w BWM = 1292.5 g	Determine if the MT increased serum insulin and insulin-like growth factor 1 (IGF-1) in PI. Beginning when clinically stable.	T/KS: 15 min 3x/day for five days, one hour after the morning feeding (12 am), early of 3hs consecutive. Conducted by a therapist.	1) Daily WG 2) Daily caloric intake 3) Vital signs before, during, and after the MT 4) Serum insulin and IGF-1 on days one and five 5) VA measured at intervals	Body weight taken with normal nursery routine (weighed daily prior to the 8 am feeding)	Not described	1) TG: Greater WG ($p = 0.02$) 4) TG: Increase in insulin ($p = 0.001$) and greater increase in IGF-1 ($p = 0.05$) 5) TG: greater VA ($p < 0.001$)
Massage therapy reduces hospital stay and occurrence of late-onset sepsis in very preterm neonates[16] Mendes Procianoy, 2008 PubMed search 1	Total: 104 TG: 52 GAM = 29.7 w BWM = 1186.8 g CG: 52 GAM = 29.4 w BWM = 1156.7 g	Studying the effects of massage on maternal hospital stay in very low birth weight (VLBW) who were already submitted to skin-to-skin care. Beginning after 48 hours of life.	MT applied only by mothers, 4x/day for 15 min each time, intervals of 6 h. TS: temporal, frontal, periorbital, nasal, and perilabial regions of the face and the external side of the upper and lower limbs + KS (3x each: wrist, elbow, ankle, and knee)	1) Length of hospital stay 2) Growth 3) Age of start of partial or total enteral feeding 4) Age which partial and total oral feeding started 5) Occurrence of late onset sepsis–clinical and blood and or/cerebrospinal fluid 6) Presence of necrotizing enterocolitis and 7) Bronchopulmonary dysplasia	Body weight taken with normal nursery routine, always verified by a blinded researcher, in the afternoon and using the same digital baby scale equipment	Not described	1) TG: Fewer days of hospitalization ($p = 0.084$) 2) TG: Lesser rate of late-onset sepsis ($p < 0.01$)
Weight gain in preterm infants following parent-administered Vimala massage: a randomized controlled trial[17] Gonzalez et al., 2009 PEDro and PubMed searches 1, 4	Total: 60 TG: 30 GAM = 31.4 w BWM = 1235 g CG: 30 GAM = 31.7 w BWM = 1220 g	Evaluate the WG in PI receiving MT, correlate with length of hospital stay and check for other effects. Beginning when clinically stable, with orogastric tube feeding.	Vimala massage 2x/day for ten days, 1 h after feeding. Conducted by the mother or father, trained and supervised: face, upper limbs, chest, abdomen, lower limbs, and back, without ever losing touch, even in cases of PI discomfort. Used oil or cream.	1) Daily WG 2) Daily caloric intake 3) Length of hospitalization	Body weight taken with normal nursery routine with a digital scale, (Seca®, Hamburg, Germany). At 8 am every day, 1 h before the next scheduled feeding. The nurse was blinded.	Not described	1) TG: Greater WG over 10 days and daily WG ($p < 0.001$) 3) TG: Shorter hospital stay ($p = 0.03$)

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Massage with kinesthetic stimulation improves weight gain in preterm infant[31] Massaro et al., 2009 PEDro and PubMed searches 1, 4	Total: 60 TS G: 20 GAM = 29 w BWM = 1097 g T/KSG: 20 GAM = 29 w BWM = 1124 g CG: 20 GAM = 27 w BWM = 959 g	To evaluate the effect of MT with and without kinesthetic phase in WG and in the length of PI hospitalization. Beginning when clinically stable.	TS (only phase 1 and 3) or T/KS 2x/day for 15 min, performed by trained nurses, from the beginning of the study until discharge.	1) Daily WG 2) Daily caloric intake 3) Length of hospitalization	Body weight taken with normal nursery routine.	Not described	T/KS G: with birth weight > 1000 g = higher daily WG (stratification by BW)
Massage therapy improves neurodevelopment outcome at two years corrected age for very low birth weight infants[36] Procianoy et al., 2010 PubMed searches 1, 4	Total: 73 TG: 35 GAM = 30 w BWM = 1192 g CG: 38 GAM = 29.7 w BWM = 1151 g both groups Skin-skin care	Assess the outcome of MT growth and neurodevelopment of PI assessed at 2 years corrected age. Beginning after 48 h of life.	MT applied only by mothers, 4x/day for 15 min, intervals of 6 hours of TS: temporal, frontal, periorbital, nasal, and perilabial regions of the face and the external side of the upper and lower limbs + KS (3x each: wrist, elbow, ankle, and knee)	1) Anthropometric 2) Bayley scales of infant development, second edition (BSID-II). Measured at 2 years of corrected age	Body weight taken with normal nursery routine.	Mothers of the TG were instructed to observe the newborns' tolerance signs, avoiding excessive stimulations.	2) TG: Greater mental development index ($p = 0.035$)

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Sensorimotor interventions improve growth and motor function in preterm infants[18] Fucile & Gisel, 2010 PubMed searches 1, 2, 3, 4, 5, 6	Total: 75 OS G: 19 T/KS G: 18 OS + T/KS G: 18 CG: 20	To evaluate the effect of OS and T/KS alone on WG and motor function in PI and if OS + T/KS have greater influence on these parameters. Beginning when clinically stable, receiving all feedings by tube.	OS: 15 min 2x/day for ten days (7 min: cheek, chin, lips, 5 min on gum and tongue, and 3 min of non-nutritive pacifier sucking). T/KS for 15 min 2x/day. TS: Prone and supine, stroking the body starting from the head, followed by the neck, shoulders, back, legs, and arms + KS. Performed by researcher.	1) Daily WG (g/kg/day) 2) Motor Function. Test of Infant Motor Performance-1969 (TIMP)	Body weight taken with normal nursery routine, nurse was blinded and always used the same scale.	Stop procedure: if fussing, vomiting, growing oxygen demand, frequent episodes of apnea, bradycardia, or desaturation in the 24 h that preceded the intervention; or interventions such as sight or hearing tests performed 30 min before T/KS.	1) OS G and T/KS G: greater WG ($p = 0.014$) 2) T/KS G and OS+ T/KS G: greater TIMP scores ($p < 0.003$)
Behavioral analysis of preterm neonates included in a tactile and kinesthetic stimulation program during hospitalization[20] Ferreira Bergamasco, 2010 PubMed searches 2, 3	Total: 32 TG: 16 GAM = 33.4 w BWM = 1910.3 g CG: 16 GAM = 33.3 w BWM = 1872.8 g Not randomized	To evaluate the effect of T/KS evolution behavioral and clinical newborn PI during hospitalization. Beginning when clinically stable.	8 min/week filming until discharge: behavioral evaluation. TS: performed 4-5x/week for 5-15 min, focusing on alertness. Soft touches, slow and continuous, no rigid sequence, with cerebrospinal flow direction on the trunk, and proximal-distal direction on the limbs, supine or lateral position. KS: flexion and extension of the limbs. Conducted by researcher.	1) Daily WG 2) Length of hospitalization 3) Behavioral evaluation: adapted from the Manual for the Naturalistic Observation of Newborn Behavior (Pre-term and Full-term)	Body weight taken with normal nursery routine.	Not described. Cites some internal events inherent to the nursery that can interfere with behavioral responses, such as time after the last feeding, sleep, pain, noise, light, and temperature.	3) TG: Greater % time with: Regular respiration ($p = 0.002$) State active warning ($p = 0.036$) Postures mixed ($p = 0.013$) Balanced tone ($p < 0.001$) TG: Higher number of movements hand side, suction, grip and support ($p = 0.013$), more coordinated movements and more frequent ($p < 0.001$) CG: More frequent extensor posture ($p = 0.001$) and hypotonia ($p < 0.001$)

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
A randomized placebo-controlled trial of massage therapy on the immune system of preterm infants[32] Ang et al., 2012 PubMed searches 1, 4	Total: 120 TG: 58 GAM = 30 w BWM = 1389 g CG: 62 GAM = 30 w BWM = 1286 g Randomized	To investigate the effects of MT on the immune system of PI. Beginning when clinically stable.	T/KS: 15 min, 3x/day, at the beginning of three consecutive hours, behind two wide screens, for a minimum of five days and maximum of four weeks or until hospital discharge. CG: nurse remained behind the two wide screens the same amount of time.	1) Immunologic evaluation (absolute NK cells, T and B cells, T cell subsets, and NK cytotoxicity 2) WG 3) Number of infections 4) Length of hospital stay	Not described	Not described	1) TG: NK cytotoxicity higher ($p = 0.05$) 2) TG: Greater daily WG ($p = 0.01$) and higher final weight ($p = 0.05$)
Massage improves growth quality by decreasing body fat deposition in male preterm infants[37] Moyer-Mileur et al., 2013 PubMed searches 1, 4	Total: 44 TG: 22 GAM = 31.4 w BWM = 1574 g CG: 22 GAM = 31 w BWM = 1618 g Randomized	To assess the effect of MT on WG and body fat deposition in PI. Beginning when tolerating enteral feeding volumes > 100 mL/kg/day.	20 min 2x/day at 7 am and 7 pm, 6 days/week (except Sunday), performed behind a privacy screen by a licensed massage therapist. The MT was modeled after the Infant Massage USA protocol and modified for PI by eliminating massage of the abdomen.	1) WG 2) Length of hospital stay 3) Ponderal index 4) Body circumferences 5) Skinfold thickness 6) Insulin-like growth factor I, leptin, adiponectin levels 7) Daily dietary intake	Body weight on an electronic infant scale (Air shields-vickers®, Ohio, USA) was recorded to the nearest gram.	All massage therapists were trained to recognize clinical signs of distress.	3) TG: Male infants had smaller ponderal index 5)TG: Male infants had triceps, subscapular, and mid-thigh skinfold thickness increases ($p < 0.05$) TG: Female had larger subscapular ($p < 0.05$) 6) Circulating adiponectin increased over time in GC male infants ($p < 0.01$) and was correlated to ponderal index ($p < 0.01$)

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
Effect of oil massage on growth in preterm neonates less than 1800 g: a randomized control trial[34] Kumar et al., 2013 PubMed searches 1, 4	Total: 48 TG: 25 GAM = 32.9 w BWM = 1466.6 g CG: 23 GAM = 32.6 w BWM = 1416.6 g Randomized	To study the effect of oil massage on growth in preterm babies less than 1800 g. Beginning < 48 h of age and on at least 100 mL/kg/d of feed oral or tube feed.	10 min, 4x/day, 4 w massage was carried out first over both shoulders starting from the neck with the baby in prone position. Then it was carried out from the upper back to the waist. Each of the two upper and lower limbs was separately massaged in the supine position. Twenty gentle strokes in each area. Massage was provided with 2.5 mL/kg (10 mL/kg/day) of sunflower oil, by researcher or mother (if discharged before 4 w)	1) WG after 28 days 2) Length and head circumference after 28 days 3) Loss of weight after 7 days 4) Difference in serum triglyceride levels after 28 days	Were measured using standard techniques, at enrollment and then weekly for next 4 weeks.	Not described	1) TG: Greater WG over 28 days ($p < 0.05$) 3) TG: Less weight loss after 7 days ($p = 0.003$)

Table 1 (*Continued*)

Title/Author/ Year/Database	Sample Size	Objectives and starting conditions	Description of the technique	Main variables	Measured weight gain	Description of adverse events during the procedure	Results achieved statistical significance
The efficacy of massage on short and long term outcomes in preterm infants[35] Abdallah et al., 2013 PubMed searches 1, 3, 4	Total: 66 TG: 32 GAM = 32.2 w BWM = 1747 g CG: 34 GAM = 32.6w BWM = 1684 g The first 34 infants were assigned for the CG and then 32 for the TG	To assess the short and long term benefits of MT on stable PI.	TS, without KS, for 10 min, for at least 10 days, 1x/day, performed by trained mothers, using 2 mL of olive oil (6 drops).	1) PIPP after MT 2) PIPP at discharge 3) Cognitive score (Bayley scales) 4) WG 5) Length of stay 6) Breastfeeding duration 7) Motor score (Bayley scales)	Not described	The infant's reaction to TS was monitored by a research assistant for any adverse physical or behavioral signs, Sat O_2, HR, and RR. At any sign of physiologic distress (HR greater than 200 bpm or Sat O_2 less than 95%), massage was discontinued for 15 s, or until a return to baseline levels then resumed. None of the infants experienced any of the above signs.	1) Lower scores on the PIPP after MT ($p = 0.041$) 2) Lower PIPP scores on discharge ($p = 0.011$) 3) Higher cognitive scores of TG at 12 months corrected age ($p = 0.004$)

TS, tactile stimulation; T/KS, tactile and kinesthetic stimulation; KS, kinesthetic stimulation; HR, heart rate; RR, respiratory rate; BW, birth weight; BWM, birth weight-mean; GAM, gestational age-mean; GA, gestational age; NICU, Neonatal intensive care unit; MT, massage therapy; prof, professional; VA, vagal activity; GM, gastric motility; ECGs, electrocardiograms; EGGs-electrogastrograms; OS, oral stimulation; PIPP, Premature infant pain profile.

Discussion

Tactile stimulation has the advantages of being noninvasive, inexpensive, and safe, as was demonstrated by Livingston et al. [38] based on physiological stability and no change in agitation/pain scores of the infants receiving massage. The majority of the clinical trials studied herein (20 of the 31 studies)[3,10,14,15,17–19,21–32,34] described a significantly benefit on weight gain in the PI group that received the TS/TKS. This information places TS as a promising adjunctive tool in addressing PI in the NICU. Some of the studies did not assess the data statistically; part of them justified this because of small sample size.[6–8]

Some correlations have been suggested to justify the faster weight gain of PI submitted to TKS, such as greater vagal stimulation and gastric activity,[28,29] relationship with energy intake,[3,10,15,17,22–31,39] sleep-wake behavior and behavioral scales,[6–8,10,14,19–27,36,39] serum insulin and IGF-1 levels,[30,37] and use of oil.[33,40,41] The results found by Diego et al. [28] and Field et al. [42] on the effects of mild and moderate pressure showed that moderate pressure provided greater vagal stimulation. Diego et al. [29] also found greater gastric motility among the PI who were stimulated with moderate pressure and suggested that greater gastric activity may explain their faster weight gain. Field et al. [42] added that the group of PI stimulated with moderate pressure were more relaxed, characterized by their lower heart rates and by the assessment of their wake and sleep status, and behavior, as recommended by the Thomas Scale of 1975.[21] They then suggested that the more relaxed state of the PI resulted in lower energy expenditure, which would then result in faster weight gain. This was confirmed by Lahat et al.,[43] who used indirect calorimetry to show that a group of PI submitted to stimulation had lower energy expenditure.

Regarding energy intake, some studies have shown that stimulated infants have higher daily weight gain.[10,17,22,23,25–28,31,32,39] Other studies recorded stooling frequency and found that it increased significantly, together with an increased formula intake on days 6-10.[9] Rausch[9] suggested that increased stooling was a consequence of higher formula intake. On the other hand, Scafidi et al. [23] found that the frequency of stooling decreased, even when daily weight gain increased. White Labarba[3] reported that the amount of formula consumed per feeding increased while the number of daily feedings decreased, which the authors attributed to the nursery routine: PI who did not consume the entire serving were fed more often. Other studies that reported faster weight gain did not find significant differences in energy intake.

Along with weight gain, other variables, some mentioned above, have been analyzed after application of TKS in premature. All of the following parameters were analyzed by clinical studies in PI who received TS/MT whether or not associated with KS during their NICU stay: weight gain;[3,6–10,14–37,39] length of hospital stay;[10,16,17,20,21,23,24,28,31,32,35,37,39] behavioral responses;[6–8,10,14,19–23,25,26,36,39] sleep/wake stage;[10,21,23,24,26,27] stress behavior;[11] energy expenditure;[43] body temperature;[3,6,21,23–26,44] variations in stimulation pressure;[42] use or non-use of oil;[33,40,41] speed of brain maturation;[38] vagal activity and gastric motility;[28,29] serum insulin and growth factor I levels;[30,37] late-onset sepsis;[16] body fat deposition;[37] effect on the immune system;[32] and bone formation.[45] The studies had very similar objectives; that is, to identify the effects of TKS on these parameters and the possible causes of its benefits.

Some studies using only KS obtained results not only in greater weight gain but also in bone mineralization.[46–48] As for TKS with or without KS for bone weight gain analyzed herein, they found that there was no ideal level of stimulation[47] or optimal duration, frequency, and type of exercise for bone development.[49] Further evaluation of this intervention (KS) was suggested to indicate for this purpose.[50] A more recent study demonstrated a significant improvement in bone formation and decrease of bone resorption, using a more rigorous methodological design.[48]

A few studies have described the adverse situations that could occur during the procedure and the parameters that should encourage the therapist to interrupt the session.[14,18,19,26,33] Certain signs during the application of the TKS, such as stress or uninterrupted crying for more than 60 seconds,[26] defecation or urination,[14] increased heart rate,[19,27] or heart rate < 100 for 12 seconds and desaturation for more than 30 seconds,[19] were some of the causes that led the therapists to interrupt the procedure or discontinue the study. Some therapists considered some signs in the 24 hours that preceded the intervention to suspend the procedure, such as fussing, vomiting, growing oxygen demand, frequent episodes of apnea, bradycardia, desaturation, or interventions conducted within the 30 minutes that preceded TKS, such as sight and hearing tests.[18] Arora et al. [33] separated the adverse situations into temporary interruption and minor problems that neither affected feeding nor required any interruption in the trial.

Despite the information above, the majority of the studies did not mention adverse events and/or did not describe a course of action to deal with adverse events during the intervention. The studies that reported the occurrence of events that required the interruption of the procedure did not indicate how the procedure was resumed; for example, whether it was resumed from the start of the massage routine or whether it was continued from where it had stopped; also, they did not indicate whether the procedure should be resumed on the same day or on the next day, or whether these interruptions could affect weight gain. The clinical trials studied by this review made a relevant contribution to the scope of TS. Nevertheless, adding detailed data highlighted by this review, such as adverse events, would improve methodology and reliability for future studies.

Limitations

This systematic review was performed using two databases, in addition to checking the bibliographic articles of those that met the inclusion criteria; however, the possibility of not having included an article relevant to the topic that could have been found in other databases cannot be ruled out.

Conclusion

Assessment of the methodology of the studies reviewed herein showed that there is no standard for application of

TS technique or recommended course of action if adverse events occur during the procedure. The effect of these adverse events that can occur during the TKS procedure may influence the results.

Generally, some kind of benefit associated with TKS, such as faster weight gain, shorter hospital stay, and better behavior, among others, was reported by all studies that used TS or TKS in PI. Nurseries have many stressors and TKS has been shown to be helpful in this context. Therefore, TKS should be considered as a possible therapy to be associated with the standard medical treatment. Even discrete gains in this population can result in long-term benefits. Future studies may raise the level of methodological rigor and describe the adverse events that can occur during the procedure. This may permit other researchers to be more aware of expect outcomes, and a standard TKS technique could be established.

Conflicts of interest

The authors declare no conflicts of interest.

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