Frenotomy with breastfeeding support versus breastfeeding support alone for infants with tongue-tie and breastfeeding difficulties: the FROSTTIE RCT

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Scientific summary

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Scientific summary

Background

Breastfeeding difficulties have been associated with many factors, from a societal to an individual level. Tongue-tie can be diagnosed in 3–11% of babies, with the variation in reported prevalence thought to relate to the use of different diagnostic or severity criteria. Up to half of babies with tongue-tie are reported to have breastfeeding difficulties, but the reported proportion is highly variable. Some studies report almost universal difficulties, and others report very few feeding difficulties that relate to the tongue-tie itself, instead noting that incorrect positioning and attachment are the primary reasons behind the observed breastfeeding difficulties and not the tongue-tie itself. In a UK survey, it was noted that management of tongue-tie in infants with breastfeeding difficulties was therefore highly variable across the country. This is coupled with highly variable provision of breastfeeding support, which can range from minimal to expert and intensive, and using a variety of different models including peer supporter, midwife and health visitor.

A Cochrane review identified five prior randomised controlled trials (RCTs) of frenotomy including a total of only 302 infants. The trials are small and underpowered and/or include only very short-term or subjective outcomes, suggesting further robust evidence is needed. Hence there is considerable controversy regarding, not only the diagnosis and clinical significance, but also the management of tongue-tie. Current National Institute for Health and Care Excellence (NICE) guidance allows for the procedure, based on lack of safety concerns, but notes very limited evidence of efficacy. There is therefore a clear need for an assessment of the clinical- and cost-effectiveness of frenotomy for babies diagnosed with tongue-tie in the form of an adequately powered, pragmatic RCT, taking into account the diagnostic controversy and variation in practice.

Objective

To investigate whether frenotomy is clinically- and cost-effective to promote continuation of breastfeeding at 3 months in infants with breastfeeding difficulties diagnosed with tongue-tie.

Methods

Study design

The FROSTTIE trial was a multicentre, RCT conducted in 12 infant feeding services in England.

Participants

Inclusion criteria

- Any infant aged <10 weeks referred (by parent or other breastfeeding support service) to an infant feeding service with breastfeeding difficulties and judged to have tongue-tie, whose parent has given informed consent for participation.

Exclusion criteria

Infants were not eligible to enter the study if ANY of the following applied:

- Infant was older than 10 weeks.
- Infant had breastfeeding difficulties but was not judged to have tongue-tie.
- Infant was born at <34 weeks' gestation.
- Infant had a congenital anomaly known to interfere with breastfeeding, for example cleft palate, Down syndrome.
- Infant had a known bleeding diathesis.
- Infant had a frenotomy prior to recruitment.

Interventions

Infants were randomised to receive either a frenotomy with standard breastfeeding support or standard breastfeeding support without frenotomy.

Outcomes

Primary outcome

Any breastmilk feeding at 3 months according to maternal self-report, defined as follows:

- any breastmilk feeding in the 24 hours prior to the infant reaching 3 months of age.

Secondary outcomes

Mother's breastfeeding self-efficacy: measured using the Breastfeeding Self-Efficacy Scale – Short Form

Mother's pain while feeding during the previous 24 hours: measured using visual analogue scale of the Short Form McGill Pain Questionnaire, modified into a Likert-type scale

Amount of breastfeeding support used: measured by total number of contacts (whether face-to-face or virtual) with any breastfeeding supporter since the FROSTTIE procedure

Infant weight gain: measured as difference in weight for age *z*-scores between birth and 3 months of age

Infant postrandomisation weight gain: measured as difference in weight for age *z*-scores between baseline and 3 months of age

Exclusive breastmilk feeding: exclusive breastmilk feeding in the previous 24 hours

Exclusive direct breastfeeding: exclusive breastfeeding directly from the breast with no bottle feeds of expressed milk in the previous 24 hours

Age of child when s/he last received breastmilk: age when child last received breastmilk, to determine when and whether switch to exclusive formula feeding has occurred

Time spent breastfeeding in previous 24 hours: time in minutes/hours spent breastfeeding in previous 24 hours

Frenotomy in comparator group/repeat frenotomy/bleeding following frenotomy or frenulum tear/postprocedure adverse events (tongue cut, salivary duct damage)/maternal and infant NHS health-care resource use): measured by specific questions

Maternal anxiety and depression: dimension of EuroQol-5 Dimensions, five-level version (EQ-5D-5L)

Maternal health-related quality of life: as elicited by the EQ-5D-5L

Any breastmilk feeding at 6 months: according to maternal self-report: defined as any breastmilk feeding in the 24 hours prior to the infant reaching 6 months of age.

Process outcomes

The process outcomes for all infants included the Bristol Tongue Assessment Tool (BTAT) score by adherence status, reasons for non-adherence, and type of breastfeeding support.

Statistics and analysis plan

Sample size

It was assumed that a 10% absolute increase in the rate of breastfeeding represented the minimal clinically important difference that should be detectable by the trial; and breastfeeding rates will remain high in this motivated population. Thus assuming a breastfeeding rate of 70% in the control group and 80% in the intervention group, at 90% power with a 5% level of significance, and allowing for 5% loss to follow-up, with a further 5% increase to account for between-group contamination required a sample size of 870. Given the final sample size achieved with primary outcome data (n = 163), the study had 31% power to detect this difference, assuming the same control group rate.

Statistical analyses

Statistical analyses were carried out according to a pre-specified Statistical Analysis Plan finalised prior to unblinding. For the primary analysis for all primary and secondary outcomes infants were analysed in the groups to which they were randomly assigned [referred to as the intention-to-treat (ITT) population]. Demographic and clinical data were summarised with counts and percentages for categorical variables, means (standard deviations [SDs]) and medians (with interquartile or simple ranges) for continuous variables. For binary outcomes, risk ratios and confidence intervals (CIs) were calculated using log binomial regression or Poisson regression with a robust variance estimator. Continuous outcomes were analysed using linear and median (quantile) regression for normally distributed and skewed variables, respectively. Analyses were adjusted for stratification factors at randomisation where possible (centre, infant's age at randomisation and mother's parity). Two-sided statistical testing was performed throughout. A 5% level of statistical significance was used, and 95% CIs are presented.

Secondary analyses

Four planned secondary analyses were carried out:

1. A comparison of the characteristics and primary outcome by adherence status in the breastfeeding support arm.
2. An assessment of the impact of non-adherence to the randomised allocation using complier-average causal effect analysis.
3. A restricted per-protocol analysis, excluding participants who did not receive the allocated intervention as randomised.
4. An as-treated analysis, grouping participants according to the allocation they received.

Pre-specified subgroup analyses

Four planned subgroup analyses were carried out, examining the primary outcome in the following groups:

- infants aged <2 weeks versus ≥2 weeks at randomisation
- infants with BTAT score 4 or less versus 5–6 versus 7 or more at randomisation
- prior belief concerning frenotomy: likely to be beneficial versus uncertain versus unlikely
- recruited pre- or posttrial pause during the COVID-19 pandemic.

Economic evaluation

We conducted a within-trial cost-consequence analysis that assessed health-care resource utilisation, costs and benefits associated with frenotomy with breastfeeding support versus breastfeeding support only in mothers and their infants with breastfeeding difficulties and judged to have tongue-tie. In a secondary analysis, a cost-utility investigation was conducted to understand the potential value for money of frenotomy with breastfeeding support compared to no frenotomy.

Site monitoring

A monitoring plan for the trial, including responsibilities, was developed prior to the start of recruitment. In person monitoring of sites was carried out to identify barriers and facilitators to recruitment and the findings of the visits summarised to guide ongoing actions to enhance recruitment.

Results

Between March 2019 and November 2020, 169 infants were randomised, 80 to the frenotomy with breastfeeding support arm and 89 to the breastfeeding support arm from a planned sample size of 870 infants. The trial was stopped in the context of the ongoing COVID-19 pandemic due to withdrawal of breastfeeding support services, slow recruitment and crossover between arms. In the frenotomy with breastfeeding support arm 74/80 infants (93%) received their allocated intervention, compared to 23/89 (26%) in the breastfeeding support arm.

Characteristics of participants were similar between the two trial arms. Infants had a mean age of 3 weeks, 87% were born at ≥38 weeks' gestation, and they had a mean birthweight of 3439g. Overall 33% of infants had a BTAT score of 4 or less, 66% had exclusive breastmilk feeding in the previous 24 hours, and 40% had exclusive direct breastmilk feeding. Thirty-four per cent of infants had also received formula milk in the previous 24 hours.

Mothers were a mean of 32 years old, 94% were of white ethnicity, and 48% had a previous live birth. Only 8% were resident in the most deprived quintile of areas. Mothers reported a mean pain score of 4 out of 10 while feeding during the previous 24 hours and 42% had some anxiety or depression. More than half of women recruited to the trial believed a frenotomy would help their baby.

Primary outcome

Primary outcome data were available for 163/169 infants (96%). There was no evidence of a difference between the arms in the rate of breastmilk feeding at 3 months, which was high in both groups [67/76, 88% vs. 75/87, 86%; adjusted risk ratio (aRR) 1.02, 95% CI 0.90 to 1.16].

Secondary outcomes

As would be anticipated by the small size of the trial, there was no evidence of differences in any secondary outcomes comparing infants in the frenotomy with breastfeeding support arm to the breastfeeding support arm at 3 months.

Mother's breastfeeding self-efficacy: Median Breastfeeding Self-Efficacy Scale score 60.0 versus 56.5, adjusted median difference 0.3 (95% CI 5.2 to 5.8)

Mother's pain while feeding during the previous 24 hours: median 0 out of 10 versus 0, adjusted median difference −0.2 (95% CI 0.6 to 0.3)

Amount of breastfeeding support used: median 3 contacts versus 2, adjusted median difference −0.3 (95% CI −1.5 to 1.0)

Infant weight gain from birth: mean difference in weight for age *z*-score −1.1 versus −1.2, adjusted mean difference 0.17 (95% CI −0.60 to 0.95)

Infant postrandomisation weight gain: mean difference in weight for age *z*-score −1.0 versus −1.1, adjusted mean difference 0.10 (95% CI −0.83 to 1.03)

Exclusive breastmilk feeding: exclusive breastmilk feeding in the previous 24 hours 45/71 (63%) versus 50/75 (67%), aRR 0.92 (95% CI 0.61 to 1.39)

Exclusive direct breastfeeding: 38/71 (54%) versus 39/74 (53%), aRR 1.03 (95% CI 0.65 to 1.62)

Age of child when s/he last received breastmilk: not measurable due to high rates of continued breastfeeding

Time spent breastfeeding in previous 24 hours: median 3 hours versus 3 hours, adjusted median difference 0.1 (95% CI −1.1 to 1.2)

Frenotomy performed: 75/80 (94%) versus 65/89 (73%)

Maternal anxiety and depression: 29/73 (40%) versus 26/75 (35%), aRR 1.12 (95% CI 0.65 to 1.93)

Maternal health-related quality of life: mean [standard deviation (SD)]: 0.85 (0.18) versus 0.87 (0.12), adjusted mean difference 0.00 (95% CI −0.07 to 0.07)

Maternal and infant NHS health-care resource use: mean (SD) £497 (£854) versus £483 (£529), mean cost difference £21 (95% CI −£221 to £263)

Any breastmilk feeding at 6 months: 55/66 (83%) versus 60/71 (85%), aRR 0.98 (95% CI 0.84 to 1.14)

Adverse events occurred in three infants (one infant had bleeding, one infant had salivary duct damage, and the third infant had an accidental cut to the tongue and salivary duct damage). There were no other serious adverse events causally related to the intervention.

Pre-specified subgroup analyses

There were no notable differences between both the arms for any of the selected subgroups except that the rate of breastmilk feeding at 3 months appeared higher in the frenotomy with breastfeeding support arm compared to the breastfeeding support arm (92% vs. 83%) before the trial paused due to the COVID-19 pandemic. After the trial restarted the rate appeared higher in the breastfeeding support arm compared to the frenotomy with breastfeeding support arm (91% vs. 81%).

Economic evaluation

There were no statistically significant differences in health-care resource use, costs and benefits between the two groups. Given the current sample size to conduct the cost-effectiveness analysis and the number of infants in the breastfeeding support group receiving frenotomy, there is substantial uncertainty about whether frenotomy represents good value for money of NHS resources when compared to breastfeeding support only.

Site monitoring: barriers and facilitators to recruitment

The main challenge to the trial concerned equipoise, which was a barrier to recruitment both due to staff attitudes and parents' expectations. More than half of women recruited to the trial believed that frenotomy would help their baby and fewer than half were truly in equipoise.

In several areas the onset of the COVID-19 pandemic saw the withdrawal of breastfeeding support services, either in person or at all. In areas where all support was withdrawn, as Trusts did not consider breastfeeding support to be an essential service, the trial had to stop. Similarly in some areas frenotomy lists ceased.

Conclusions

The statistical power of the analysis was extremely limited due to not achieving the target sample size because of the early cessation of the trial and the high proportion of infants in the breastfeeding support arm who underwent frenotomy. There was no evidence of differences between trial arms in any outcomes. Rates of continued breastmilk feeding were high at 3 months in both the frenotomy with breastfeeding support and breastfeeding support groups. Complications of the procedure were not uncommon, occurring in around 1 in 50 infants.

Most infants in the control groups of the five previous trials identified in a previous Cochrane review also underwent frenotomy (77–100%). On this basis all five trials were considered of low quality and at high risk of bias. The 73% frenotomy rate in the breastfeeding support arm that we observed in FROSTTIE is comparable, but on this basis it must also be regarded as at high risk of bias.

This trial does not therefore provide sufficient information to assess whether frenotomy in addition to breastfeeding support improves breastfeeding rates in infants diagnosed with tongue-tie. The effectiveness and cost-effectiveness of the procedure still need to be established. Other study designs will need to be considered to address this objective.

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Trial registration

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