

Laser Acupuncture for Neonatal Abstinence Syndrome: A Randomized Controlled Trial

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abstract

BACKGROUND: Neonatal abstinence syndrome (NAS) is usually treated with opiate derivatives and supported with nonpharmacological treatment.

METHODS: This prospective, randomized, controlled, blinded, single-center study was carried out between March 2009 and November 2014. Newborn infants diagnosed with NAS after maternal opioid substitution therapy were eligible for inclusion. Infants were randomly allocated to the acupuncture group (combining laser acupuncture and pharmacological therapy of morphine and phenobarbital) or control group (pharmacological therapy alone). Laser acupuncture was performed with a LABpen MED 10 (675 nm/10 mW) at 5 ear and 4 body acupuncture points, bilaterally, and sessions were repeated every day. The primary outcome measure was duration of oral morphine therapy for NAS. Secondary outcomes included highest single Finnegan score, time to highest single Finnegan score, maximum amount of oral morphine solution (in milliliters per kilogram and milligrams per kilogram), time to maximum amount of oral morphine solution, and length of hospital stay.

RESULTS: Twenty-eight newborns (14 in each group) were eligible for analysis. Duration of oral morphine therapy was significantly reduced in the acupuncture group compared with the control group (28 vs 39 days, respectively, $P = .019$). In addition, we observed a significantly reduced length of hospital stay in the acupuncture group compared with the control group (35 days [interquartile range 25 to 47] vs 50 days [36 to 66], $P = .048$).

CONCLUSIONS: Adjunctive laser acupuncture significantly reduced the duration of morphine therapy in newborns with NAS.

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Dr Raith conceptualized and designed the study, provided oversight for the research procedures and data acquisition, contributed to the interpretation of the data, wrote the first draft of the article, and revised the final manuscript; Dr Schmölzer made substantial contributions to the conceptualization of the study and performed data acquisition and interpretation of data; Drs Schmölzer, Resch, Reiterer, and Avian made substantial contributions to the design of the study; Drs Raith, Resch, Reiterer, Avian, Köstenberger, and Urlesberger reviewed the manuscript and made revisions; Drs Resch and Reiterer made substantial contributions to the randomization procedures and maintained and ensured the masking of personnel; Dr Avian performed statistical analysis and interpretation of data; Dr Köstenberger was involved in the acquisition and analysis of data and contributed to the interpretation of the results; Dr Urlesberger was responsible for trial design and data analysis; and all authors approved the final version of the manuscript for submission and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

WHAT'S KNOWN ON THIS SUBJECT: The impact of neonatal abstinence syndrome is of concern because the number of newborns showing symptoms of withdrawal after intrauterine drug exposure is increasing worldwide. Newborns developing neonatal abstinence syndrome require prolonged medical treatment and longer hospital admission after birth.

WHAT THIS STUDY ADDS: This first randomized controlled trial presents data on newborns with neonatal abstinence syndrome treated with laser acupuncture. The findings suggest that adjuvant laser acupuncture has the potential to reduce duration of morphine therapy and length of hospital stay.

The incidence of the neonatal abstinence syndrome (NAS), a drug-withdrawal syndrome that most commonly occurs after in utero exposure to opioids, is known to have increased.¹ This puts a heavy burden on health resources, since newborns developing NAS require prolonged medical treatment and longer hospital stays after birth.^{2,3} In the first few days of life, newborns will develop withdrawal, which is diagnosed using the Finnegan score.⁴ Once the Finnegan score exceeds a certain threshold (eg, >8), newborns are treated with orally administered morphine solution.⁵ However, the optimal oral substitution therapy and treatment duration in newborns suffering from NAS remains controversial.^{1,5} Alternatively, nonpharmacological adjunct therapies are used to treat newborns with NAS.¹ Recently, Sublett reported that tight swaddling and nonnutritive sucking might reduce infant stress as well as decrease erratic, hypertonic, and uncoordinated movements.⁶

In the early 1970s, Wen et al reported that acupuncture can alleviate symptoms of addiction in adults.⁷ The National Acupuncture Detoxification Association (NADA) developed a protocol to treat withdrawal symptoms with ear acupuncture.^{8,9} A recent review of 48 clinical trials on acupuncture treatment of alcohol, cocaine, nicotine, and opioid dependence demonstrated positive results for the reduction of craving and withdrawal symptoms.¹⁰ Several randomized controlled clinical trials reported that acupuncture combined with an opioid agonist significantly decreased the dosage of methadone needed to allay withdrawal symptoms,¹¹ alleviated side effects of the opioid agonist,^{11,12} and has the potential to significantly modulate several measures of mood and anxiety.^{10,13}

Our current understanding of the mechanisms of acupuncture suggests

a relevant role in the neurophysiology of dependence: acupuncture increases the levels of endomorphin 1, β -endorphin, enkephalin, and serotonin in plasma and brain tissue and causes analgesia and sedation.¹⁴ Illicit drugs stimulate dopamine release, and withdrawal leads to low levels of dopamine,¹⁵ inducing cravings and withdrawal symptoms. Animal studies suggest that auricular acupuncture activates γ -aminobutyric acid receptors, which reduces symptoms of morphine withdrawal,¹⁶ and there is support for the hypothesis that opioid release stimulated by acupuncture helps to restore the release of dopamine.¹⁷ In particular, auricular acupuncture potentially modifies autonomic dysfunction by increasing parasympathetic activity¹⁸ and reduces sympathetic hyperactivity,¹⁹ and stimulation of the liver 3 acupuncture point (LR 3; *Tai Chong*) activates several cortical and subcortical regions responsible for acute and chronic pain.²⁰ Recently, acupuncture treatment has been described as effective and safe in children²¹ and newborns.²² The development of laser acupuncture allows a noninvasive therapeutic approach, minimizing pain and eliminating the risk of infection.²³ Based on recently published scientific studies dealing with peripheral^{24,25} and central changes,²⁶ laser acupuncture appears to be safe.

The aim of this study was to assess whether a combination of laser acupuncture and pharmacological therapy reduces the duration of therapy in newborns diagnosed with NAS compared with pharmacological therapy alone.

METHODS

Participants and Setting

All newborns were born at and admitted to the Division of Neonatology, University Hospital of Graz, a tertiary NICU. The trial was conducted between March 2009 and

November 2014. Newborns admitted to the NICU who were born to mothers undergoing opioid substitution treatment were eligible for inclusion. Newborns were excluded if there was excessive maternal alcohol consumption during pregnancy (determined by self-report), maternal polysubstance abuse, or abnormalities that might adversely affect neurologic status. The trial was approved by the Ethics Committee of the Medical University of Graz. Research personnel obtained informed consent from parents when the clinical decision was made to start pharmacologic treatment, based on assessments made with the Finnegan scoring system.

Randomization

Newborns were randomly allocated to laser acupuncture combined with pharmacological therapy (acupuncture group [AG]) or pharmacological therapy alone (control group [CG]) in a 1:1 ratio using a permuted-block randomization with block sizes of 6. A member of the research team opened a sequentially numbered, sealed, opaque envelope containing the allocation before the first treatment session.

Blinding

Acupuncture was performed in a dedicated treatment room. Infants in both groups were transported into the treatment room; AG infants received treatment and CG infants lay in a bed. To allow treatment concealment for the clinical staff, newborns in both groups spent the same amount of time in the treatment room without support from nursing or medical staff. Laser acupuncture does not leave any skin irritations, and therefore unmasking of any study participant in the acupuncture group by the nursing and/or medical staff was impossible.²⁶ The physician who performed the acupuncture treatment was not involved in the clinical treatment or daily Finnegan score assessments.

Intervention

Study Protocol

Newborns were all admitted to the NICU. The bedside nurse and the responsible physician assessed the Finnegan score 3 times daily. All members of the NICU involved in the study were trained to recognize signs of NAS and were familiar with the Finnegan scoring system and the standardized therapy protocol.

In both groups, once the Finnegan score totaled >24 on 3 consecutive assessments or there was a single Finnegan score >12, treatment was started. Infants in both groups received oral morphine therapy (diluted tincture of opium, 0.4 mg/mL morphine) according to our standardized treatment protocol. The starting dose of oral morphine in both groups was 0.02 mg/kg (~0.05 mL/kg) 6 times a day. Oral morphine dose was adjusted according to changes in the Finnegan score: increased by 0.04 mg/kg (~0.1 mL/kg) if Finnegan score totaled >24 over 3 consecutive assessments; reduced by 0.02 mg/kg (0.05 mL/kg) if total Finnegan score remained <24 over 3 consecutive assessments; and further decreased every 72 hours if total Finnegan score remained <24 over 3 consecutive assessments.

Phenobarbital (Luminal Desitin Arzneimittel, Hamburg, Germany) was administered with the first NAS symptoms (single Finnegan score >8) with a loading dose of 10 mg/kg (two 5-mg/kg doses 12 hours apart), followed by maintenance therapy (5 mg/kg daily, split into 2 doses 12 hours apart) starting 12 hours after the last loading dose to achieve therapeutic blood levels of 20 to 30 mg/dL.²⁷ Phenobarbital serum levels were measured on day 4 of treatment and the dose was adjusted if necessary. According to our protocol, phenobarbital was administered for a fixed period of 10 days, reduced after 7 days by decreasing the half doses daily, and discontinued after the 10th day for all newborns.



FIGURE 1

Laser acupuncture on LR 3 (Tai Chong) using the LABpen MED 10: wavelength 675 nm, power 10 mW.

Our neonatal unit is part of a breastfeeding-friendly initiative for all babies; during oral morphine therapy infants were only formula fed. If no contraindications existed, expressed breast milk during oral morphine therapy was collected and stored. After discontinuation of NAS treatment, newborns were either breastfed or bottle fed with mother's milk.²⁸

Laser Acupuncture

The principle investigator (Dr Raith) is board certified in acupuncture and has >10 years' experience in NADA acupuncture and laser acupuncture. Laser acupuncture was performed every day in a special treatment room until morphine was discontinued. Each laser acupuncture session was carried out according to a standardized protocol, always commencing at the ear (right ear first), followed by body acupuncture, also starting on the right side of the body from head to toe. This procedure was then repeated on the left side. Each laser acupuncture session was performed when the newborn was in a relaxed state (~1 hour after feeding and administration of morphine solution). Laser acupuncture was carried out using a LABpen MED 10 (Behounek, Graz, Austria), a continuous wave semiconductor GaAs laser with wavelength of 675 nm and output power of 10 mW, diameter 1.5 mm.²⁹ Ear acupuncture was performed according to the NADA protocol. Ear acupuncture points used were (1)

sympathetic point (point 51), (2) Shen Men (point 55), (3) kidney point 95, (4) liver point 97, and (5) lung point 101. In addition, 4 further acupuncture points were used: (1) LR 3 (Fig 1), (2) large intestine 4 (LI 4; He Gu), (3) kidney 3 (Tai Xi), and (4) heart 7 (Shen Men).

Acupuncture points are described following the international nomenclature³⁰. Acupuncture treatment is described according to the current Standards for Reporting Interventions in Clinical Trials of Acupuncture guidelines.³¹

Each ear acupuncture point was treated for 30 seconds (0.3 J/point), and body acupuncture points were treated for 60 seconds (0.6 J/point), resulting in an energy dosage of 17 and 34 J/cm², respectively.

Safety Precautions During Laser Acupuncture

According to the European Norm (EN 60825-1), low-level lasers are classified as 3R, equivalent to the old classification 3b, meaning that radiation can be a risk of serious damage to the eye.²⁹ The acupuncturist wore specific protective glasses to avoid retinal damage. Newborns receiving laser acupuncture had their eyes covered using an eye protector (Natus Biliband Eye Protector, Natus Medical, San Carlos, CA) to avoid any injury to their eyes (Fig 2).^{25,26} The same eye protector is routinely used in infants receiving phototherapy for neonatal jaundice. The effectiveness of this protection method and application of the low-level laser were tested and approved by the Department of Technical and Organizational Safety of the Medical University of Graz. Due to the short duration of wearing the eye protector during the laser acupuncture time, noticeable pressure lines on the babies' heads could not be identified by any of the assessing nurses, which would have the potential to unblind the study allocation.



FIGURE 2

To protect infants' eyes during laser acupuncture, the eyes were covered by Biliband eye protectors.

Finnegan Score

The Finnegan score consists of 20 different clinical parameters to assess newborns with NAS. The Finnegan score includes assessment of (1) central nervous system (eg, irritability, high-pitched crying); (2) autonomic nervous system (eg, sniffing, yawning); (3) gastrointestinal system (eg, reflux, diarrhea); and (4) respiratory system (eg, tachypnea, apnea), with a maximum score of 45.^{1,32}

Main Outcome Measures

Our primary outcome measure was duration of oral morphine therapy for NAS. Secondary outcomes included highest single Finnegan score, time to highest single Finnegan score, maximum amount of oral morphine solution (milliliters per kilogram and milligrams per kilogram) administered, time to maximum amount of oral morphine solution, length of hospital stay (LOS), and active ear acupuncture points.

Data Collection and Analysis

At the start of the study, we did not have information about the effect size and therefore could not perform sample size estimation and power calculation a priori. Therefore this study was a pilot study. We planned enrollment of 12 subjects per group, as proposed by Julious³³ and Billingham et al.³⁴ An additional 20% (total of 15) was included for each treatment arm, anticipating subject

withdrawal or other unforeseen postenrollment exclusions from the study. Demographic and clinical characteristics of study infants were recorded. All infants were analyzed according to their group at randomization, ie, analysis was by intent to treat. Data are shown as median and interquartile range (IQR). To compare groups at baseline for continuous variables, Mann-Whitney *U* test or *t* test for categorical variables (Fisher exact test) was used. To compare primary and secondary outcomes between groups at birth, weight-adjusted analysis of covariance was used. Non-normally distributed variables were rank transformed for analysis of covariance. Adjustment for birth weight was made because the groups differed significantly regarding birth weight.³⁵ Furthermore, per-protocol analysis and analysis without weight adjustment as sensitivity analysis were performed. For data analysis, SPSS 20 (IBM SPSS Statistics, Chicago, IL) was used. A *P* value of <0.05 was considered statistically significant.

RESULTS

Forty newborns with a diagnosis of NAS were admitted to the NICU during the study period (Fig 3). Ten newborns were not enrolled due to maternal polysubstance misuse (*n* = 4), refused consent (*n* = 4), unclear maternal self-weaning of the substitution therapy during pregnancy (*n* = 1), and mother in trusteeship and therefore unable to give consent for the study within the time frame (*n* = 1) (Fig 3).

Thirty newborns were randomized; however, 2 more newborns had to be excluded. In the AG, 1 mother was diagnosed with illicit polysubstance use (maternal urine samples), and in the CG, 1 mother reported alcohol consumption and the newborn showed signs of fetal alcohol syndrome.

Therefore 28 newborns were included in intent-to-treat analysis. For per-protocol analysis, 2 newborns (1 in each group) were excluded because of nosocomial adenovirus- or norovirus-positive gastroenteritis;³⁶

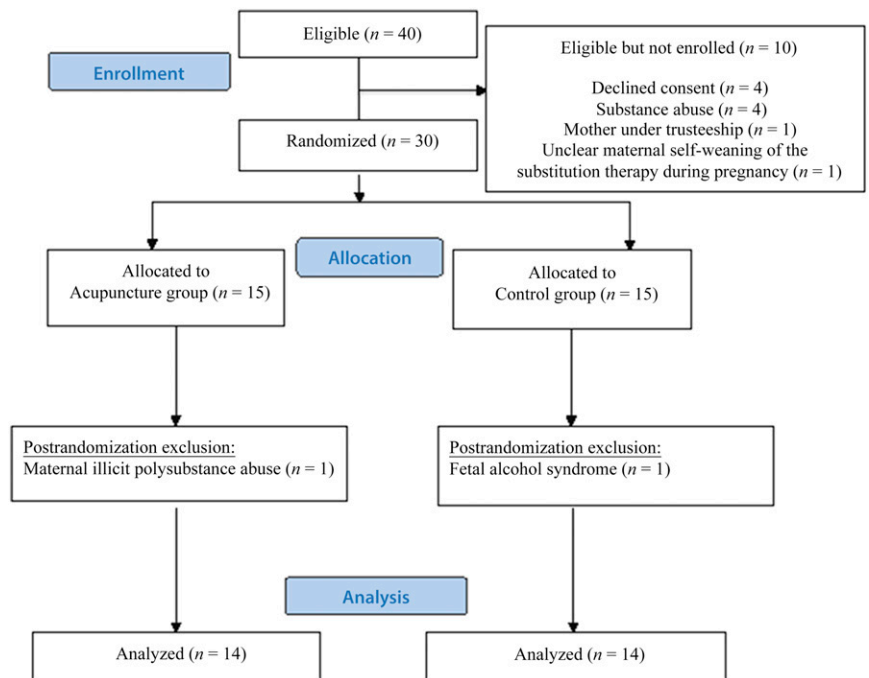


FIGURE 3

Study flow chart.

symptoms of gastroenteritis have a wide variety (including neurologic symptoms) and the potential to confound the diagnosis of NAS during the weaning period.³⁷

Baseline demographics of all 28 newborns are presented in Table 1. Baseline characteristics were similar between the groups, except birth weight, which was significantly higher in the acupuncture group (median birth weight 3190 vs 2617 g, $P = .029$). The serum levels of phenobarbital were within our treatment ranges measured on day 4 (CG, 36.7 mg/dL [31.5 to 41.4] vs AG, 36.5 mg/dL [31.2 to 40.9]).

Duration of Morphine Treatment (Primary Outcome)

AG newborns had significantly shorter median (IQR) drug treatment duration compared with CG newborns: 28 days (22 to 33) vs 39 days (32 to 48), respectively, $P = .019$ (Table 2). Per-protocol analysis showed comparable results ($P = .013$). Sensitivity analysis showed an even more pronounced effect (intention to treat, $P = .006$; per-protocol, $P = .002$). Maternal substitution treatment is presented in Table 3.

Secondary Outcomes

Overall, the highest single Finnegan score, peak time to highest single Finnegan score, maximum amount of oral morphine solution (single dose in milliliters per kilogram and milligrams per kilogram), and peak

time to maximum amount of oral morphine solution were similar between groups (Table 2).

We observed a significantly reduced length of hospital stay in AG compared with CG: 35 days (25 to 47) vs 50 days (36 to 56), respectively, $P = .048$ (Table 2). Per-protocol analysis for LOS showed a trend toward a reduced stay in the acupuncture group ($P = .058$). Sensitivity analysis again showed significant differences between groups for intent-to-treat and per-protocol comparisons.

We observed comparable pharmacological support (milligrams per kilogram per day of inpatient care) regarding morphine (CG, 0.60 [0.36 to 0.89]; AG, 0.40 [0.25 to 0.63], $P = .496$) and phenobarbital (CG, 4.9 [4.1 to 5.1]; AG, 4.0 [3.6 to 4.8], $P = .184$). Per-protocol analysis for pharmacological support also showed comparable pharmacological support (morphine, $P = .49$; phenobarbital, $P = .24$). Sensitivity analysis again showed no significant differences between groups for intent-to-treat and per-protocol comparisons. Average Finnegan scores per day were comparable between groups (CG, 7.2 [6.2 to 8.0]; AG, 7.1 [5.6 to 8.0]; intent-to-treat analysis, $P = .99$; per-protocol analysis, $P = .91$).

Safety

All newborn infants tolerated the acupuncture well, and none developed any clinically visible skin changes. We

did not observe any patient distress or discomfort during laser acupuncture, and we observed that newborns fell asleep during and after the laser acupuncture treatment. We did not receive any negative feedback from hospital staff or family members.

DISCUSSION

In the current study, we combined laser acupuncture with pharmacological therapy (AG) and compared it to pharmacological therapy alone (CG). A significantly shortened duration of morphine treatment was detected in AG (Table 2). In addition, we observed a significant reduction of LOS in AG (Table 2). We believe this is of clinical significance, as less pharmacological treatment and reduced hospital stay have the potential to reduce side effects of oral morphine therapy and improve bonding with parents, and a reduction in LOS has the potential to reduce costs of hospital treatment.² The costs of hospitalization vary according to country, but we calculated the costs for our hospital, showing a cost reduction 26.4% for the acupuncture group.

The data about acupuncture treatment in infants with NAS are limited.^{38,39,40,41} Schwartz et al³⁸ found no difference in LOS in neonates with NAS treated with acupressure seeds in addition to standard care. However, they reported a trend toward less pharmacologic support in an acupressure-treated group. Filippelli et al,³⁹ in a retrospective chart review, reported that noninsertive acupuncture could calm restless infants and improve feeding. Raith et al^{40,41} described positive effects on better sleeping and higher calorie intake due to better relaxation in the first case of laser acupuncture treatment in a newborn with NAS.

Janssen et al⁴² randomly assigned pregnant women to either acupuncture or standard care and

TABLE 1 Baseline Demographics of Infants

Characteristic	AG	CG	<i>P</i>
<i>n</i>	14	14	
Birth weight (g)	3190 (2520–2880)	2617 (2670–3190)	.029 ^a
Gender (M/F)	3/11	8/6	.053
Small for gestational age	2 (14)	5 (36)	.385
Premature	2 (14)	4 (29)	.648
1-min Apgar score	9 (9–9)	9 (9–9)	.756
5-min Apgar score	10 (10–10)	10 (10–10)	.756
Microcephaly	1 (7)	3 (21)	.596
Maternal nicotine misuse	14 (100)	10 (71)	.098

Values are expressed as median (IQR) or *n* (%).

^a Significant difference.

TABLE 2 Newborns in the Acupuncture Group Had Significantly Shorter Drug Treatment Durations Than Those in the Control Group

Drug treatment	AG	CG	P
Duration of medical treatment, d	28 (22–33)	39 (32–48)	.019 ^a
Highest single Finnegan score	15 (13–18)	16 (14–19)	.747
Time to highest single Finnegan score, d	4 (2–5)	4 (2–5)	.351
Maximum amount of oral morphine solution			.615
mL/kg	0.7 (0.4–0.8)	0.6 (0.5–0.9)	
mg/kg	0.28 (0.16–0.32)	0.24 (0.2–0.36)	
Time to maximum amount of oral morphine solution, d	6 (4–8)	6 (4–8)	.505
LOS, d	35 (25–47)	50 (36–66)	.048 ^a

Values are expressed as median (IQR).

^a Significant difference.

found no difference in the average length of treatment with morphine in newborns with NAS. However, a post hoc analysis among newborns of women who were compliant with the acupuncture regimen (compared with the noncompliant and control groups) showed a potentially shorter duration of NAS. But these differences were not statistically significant.

Laser acupuncture has been used with the purpose of achieving pain relief in children and adults. Gottschling et al⁴³ investigated the efficacy of laser acupuncture in children with headache and documented significant decreases in headache frequency, monthly cumulative headache hours, and headache pain intensity. Other research has demonstrated that laser acupuncture is beneficial for addressing vomiting in children.⁴⁴ However, optimal points, output power, and duration of stimulation for the laser acupuncture method remain controversial. In particular, the dose ranges used for laser acupuncture stimulation differ in the literature.^{29,45,46} Because this was a feasibility study, a standard approach of once a day was chosen. Further

studies are needed to investigate whether a decrease in frequency would show similar results.

In the current study, we combined auricular and body treatment points to reduce withdrawal symptoms. Acupuncture at LI 4 is well established as effective against pain in children,⁴⁷ and shorter periods of crying due to better relaxation are reported in newborns with colic receiving acupuncture at LI 4.^{43,48} Wen and Cheung⁷ originally discovered the effect of acupuncture using auricular and body acupuncture points¹⁰ in adults, and the best results of acupuncture treatment of opiate addiction are documented in randomized controlled clinical trials when acupuncture is combined with an opioid agonist that significantly decreases the dosage of methadone needed to allay withdrawal symptoms.^{10,11} This combination also alleviated side effects of opioid agonist.^{10,11,12}

Clinicians have treated NAS with a variety of opioid preparations.⁴⁹ In addition to opioid therapy, several other medications are in use as adjunctive therapy, such as clonidine

and phenobarbital.^{1,4,45} In a recent pilot study by Bada et al,⁴⁹ infants with NAS were treated with morphine (0.4 mg/kg per day) versus clonidine (5 mg/kg per day) divided into 8 doses. Treatment duration was significantly longer for the morphine group ($n = 15$; median 39 days) than for the clonidine group ($n = 16$; median 28 days) ($P = .02$), showing effects comparable to those of our pilot study (Table 2).

There are limitations to the current study. First of all, it was a pilot study with a small sample. Austria has a low incidence of NAS, and therefore only 40 infants were available throughout the study period.⁵⁰ The course of NAS is quite variable, and it is possible that with a larger number of subjects, the statistical difference for LOS ($P = .048$) might not be sustained.^{1,3} As in other countries,⁵¹ there is variability in the substitution therapy for pregnant mothers in Austria, resulting in differences regarding the prescribed maternal medication.⁵² Our study population was too small to perform a subgroup analysis of maternal substitution medications; however, NADA acupuncture has been reported to be effective independent of the type of addictive drug used.^{8,9,53}

Prior studies have shown increased vulnerability among males to more severe NAS outcomes during the postnatal period.⁵⁴ In our study, male gender did not differ significantly between groups ($P = .053$). Some evidence suggests a milder course of NAS in preterm neonates.⁵⁵ The rate of preterm infants did not differ between groups ($P = .648$).

Traditional strategies for NAS have focused on inpatient management, although several studies have examined the safety and efficacy of home treatment programs.⁴⁵ In this context, if acupuncture is available in an outpatient neonatal clinic, the newborns could be discharged earlier to home treatment combined with acupuncture.

TABLE 3 Maternal Substitution Treatment ($n = 28$)

Maternal Substitution	AG	CG	All	Dosage During Pregnancy, mg
Morphine sulfate pentahydrate	3	8	11 (39.2)	540 (240–600)
Morphine hydrochloride trihydrate	6	4	10 (35.7)	490 (400–800)
Methadone hydrochloride	3	2	5 (17.8)	55 (45–60)
Buprenorphine	2	0	2 (7.1)	50 (40–60)
Morphine sulfate pentahydrate and dihydrocodeine bitartrate	1	0	1 (3.5)	200 and 360

Values are expressed as n (%) or median (IQR).

Longitudinal studies¹ suggest that changes in behavioral outcomes occur after prenatal opiate exposure, and the effects of NAS or its treatment on later development remain unclear. Neurodevelopmental follow-up of our study patients is in progress.

CONCLUSIONS

The results of this pilot study with a limited sample size suggest that newborns with NAS treated with a combination of laser acupuncture and pharmacologic therapy required significantly shorter medical treatment compared with newborns treated with pharmacological therapy alone. Laser acupuncture appears to be safe, feasible, efficient, and well accepted by parents. The findings

suggest that laser acupuncture could be used as an adjunct in a multimodal therapy program to treat neonates with NAS.

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ABBREVIATIONS

AG: acupuncture group
CG: control group
LI 4: large intestine 4 acupuncture point (*He Gu*)
LOS: length of hospital stay
LR 3: liver 3 acupuncture point (*Tai Chong*)
NADA: National Acupuncture Detoxification Association
NAS: neonatal abstinence syndrome

This trial has been registered with the German Clinical Trial Registry (DRKS-ID: DRKS00004302); <http://www.drks.de/DRKS00004302>; <http://apps.who.int/trialsearch/Trial.aspx?TrialID=DRKS00004302>.

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