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Review

A Review on Acupuncture as a Non-Pharmacological Treatment for Neonatal Abstinence Syndrome (NAS)

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Abstract

***Background*:** The incidence of Neonatal Abstinence Syndrome (NAS) has been on the rise over the past decade. There are many factors that have possibly contributed to this increase such as more mothers using illicit drugs and the overuse of opioid medication. This results in an increase in costs and resources for the healthcare system. Newborns with NAS might experience withdrawal symptoms that can cause pain, distress, and may potentially increase the risk of future health complications. It is therefore important to find effective treatments that can alleviate NAS. Various non-pharmacological treatments are used in conjunction with pharmacological treatments to reduce the length of hospital stay and duration of drug treatment. The objective of our review is to assess the safety and efficacy of acupuncture.

***Methods*:** PubMed, Google Scholar, EMBASE and Clinicaltrials.gov were searched using the terms: 'acupuncture', 'acupressure', 'auricular therapy', 'infant', 'neonatal abstinence syndrome', 'complementary medicine', 'opioids' and 'neonatal withdrawal'.

***Results*:** We included eight studies examining safety and efficacy of acupuncture for NAS. Results showed that acupuncture is safe and feasible. However, the results on acupuncture's efficacy as a treatment for NAS were inconclusive.

***Conclusions*:** Acupuncture is safe and feasible. However, studies on its efficacy are limited and have demonstrated contradictory results. More studies on acupuncture and NAS are recommended to better assess the potential of acupuncture as an adjunctive treatment for NAS.

Keywords

Infants; newborn; neonatal abstinence syndrome; acupucnture

1. Introduction

Canada is among the highest ranked country globally with opioid consumption for pain relief [1]. Furthermore, over the past decade, there has been a significant increase in opioid use during pregnancy [2]. This opioid crisis does not only affect the mother, but also the fetus and the newborn. Infants, who are exposed to opioids in utero have a high chance of developing Neonatal Abstinence Syndrome (NAS) [2]. NAS is a disorder characterized by symptoms including tremors, agitation, disrupted sleep, feeding difficulty, vomiting, and diarrhea [3]. Between 2000 and 2009, a substantial increase in NAS incidence and maternal opiate use in the United States was observed [2]. This puts a large burden on health care resources due to the prolonged treatments required for neonates diagnosed with NAS [4].

All infants with in-utero opioid exposure or a high pre-test probability of exposure should be monitored with a standard assessment tool such as the Finnegan Score to determine the severity of NAS and the decision of pharmacological therapy (Table 1) [5]. The Finnegan score classifies symptoms of NAS as autonomic, respiratory, and gastrointestinal, with a Finnegan score of >9 indicating that treatment is required (Table 2) [6]. Non-pharmacological methods are often the first-line treatment for infants developing NAS, alternatively opioid therapy is used as standard care[5]. Non-pharmacological methods including swaddling, positioning, breastfeeding, rooming in, and skin to skin contact have been shown to be safe and effective in reducing the duration of opioid treatment and length of hospital stay (LOS) in NAS infants [5].

The most common pharmacological treatments include morphine, methadone and buprenorphine [5, 7]. However, there are some negative effects associated with the use of pharmacological treatments for a long duration. They are often associated with longer LOS and disruption of the mother-child dyad, which can have detrimental effects on the child's development [8]. Also, low dose morphine during the neonatal stage has been associated with a decreased head circumference and body weight, an increase in response times for short-term memory tasks, and an increase in social problems later in childhood [9]. Therefore, we should be cautious in using pharmacological treatments for a long duration and identify alternatives to decrease opioid exposure in newborns.

Table 1 Representative modified finnegan score.

Signs and Symptoms	*Severity*	*Score*
Crying	Excessive high pitched Continuous high pitched	2 3
Sleeps	< 1 hours after feeding < 2 hours after feeding < 3 hours after feeding	3 2 1
Moro Reflex	Hyperactive Markedly Hyperactive	1 2
Tremors: Disturbed	Hands or feet only, up to 3 seconds Arms or legs, over 3 seconds	1 2
Tremors: Undisturbed	Hands or feet only, up to 3 seconds Arms or legs, over 3 seconds	1 2
Increased Muscle Tone	Difficult but possible to straighten arm and head lag present	1
	Unable to straighten arm and head lag absent	2
Excoriation	Skin is red but intact or healing	1
	Skin not intact	2
Generalized Seizure		8
Fever > 37.3 C (99.2 F)		1
Frequent Yawning	>4 or more successive times	1
Sweating		1
Nasal Stuffiness		1
Sneezing (4 or more successive times)	>4 or more successive times	1
Tachypnea	Respiratory Rate >60/mm	2
Poor feeding		2
Vomiting (or regurgitation)		2
Loose Stools	Diaper is > half liquid/half solid	2
Failure to thrive	Current weight > 10% below birth weight	2
Excessive Irritability	Consoling calms infant in <5 min	1
	Consoling calms infant in 6-15 min	2
	Inconsolable	3
	Summed Score	
Recorded, unscored elements		
Convulsions Fever > 38.4 C (101.2 F) Mottling Excessive sucking Watery Stools Projectile vomiting Retractions Nasal flaring Myoclonic jerks		

Table 2 Identified studies that examined acupuncture in newborns with NAS.

Source (1st author, year)	Study Design	Sample (age range, number)	Method	Results	Conclusion
Weathers, 2015	Pilot study	>37 wks old; 20 infants with NAS	Needle acupuncture on ear	• 2% of needles dislodged but replaced in 3 days • no skin breakdowns or cellulitis	Needle acupuncture is safe and feasible for newborns with NAS.
Raith, 2010	Case study	39 wks old; one infant with NAS	PS 3 detection pen	• detected psychovegetative rim, R point and frustration point	Acupuncture points were present in this newborn with NAS.
Kurath-Koller, 2016	Pilot study	> 35 wks old; 30 infants with NAS	PS 3 detection pen	• all neonates had psychovegatative rim • R point in 27 infants, frustration point in 23 infants and PT 1 point in 10 infants	Acupuncture points were present in newborns with NAS and there is specificity in their activity.
Filippelli, 2012	Chart Review	33.2 to 42.1 wks old; 54 infants with NAS	NIA on head and limbs	• better sleep and higher caloric intake	There is potential for NIA as an adjunctive treatment for NAS.
Golianu, 2014	Pilot study	5 wks old- 7 months; 10 infants with acute withdrawal	Needle acupuncture+ pressure on ear and body	• After 24 hrs, amount of opioids reduced in all patients • after 48 hrs, 89% reduction in number of opioid doses	Acupuncture can relieve withdrawal symptoms in infants.
Raith, 2014	Case study	39.3 wks gestational age; 1 infant with NAS	Laser acupuncture on ear and body (NADA protocol)	• higher caloric intake, better sleep and decreased Finnegan score	There is potential for for the use of laser acupuncture as adjunctive treatment for NAS.
Raith, 2015	Prospective blinded RCT	28 infants with NAS: control (n=14); acupuncture (n=14)	Laser acupuncture on ear and body (NADA protocol)	• reduced length of hospital stay vs. control (35 days [IQR 25- 47] vs 50 days [36-66], p =0.048)	Acupuncture is safe and feasible and reduces LOS and duration of morphine treatment
Schwartz, 2011	randomized prospective unblinded study	> 37 wks old; 76 infants with NAS: control (n=37); acupuncture (n=39)	ear acupressure (NADA protocol)	• No significant differences in LOS, length of pharmacologic treatment, or average NAS scores	Acupuncture is safe and feasible but its effectiveness should be studied further.

NAS=Neonatal Abstinence Syndrome, NIA=Non-insertive acupuncture, NADA =National Acupuncture Detoxification Association, IQR=interquartile range.

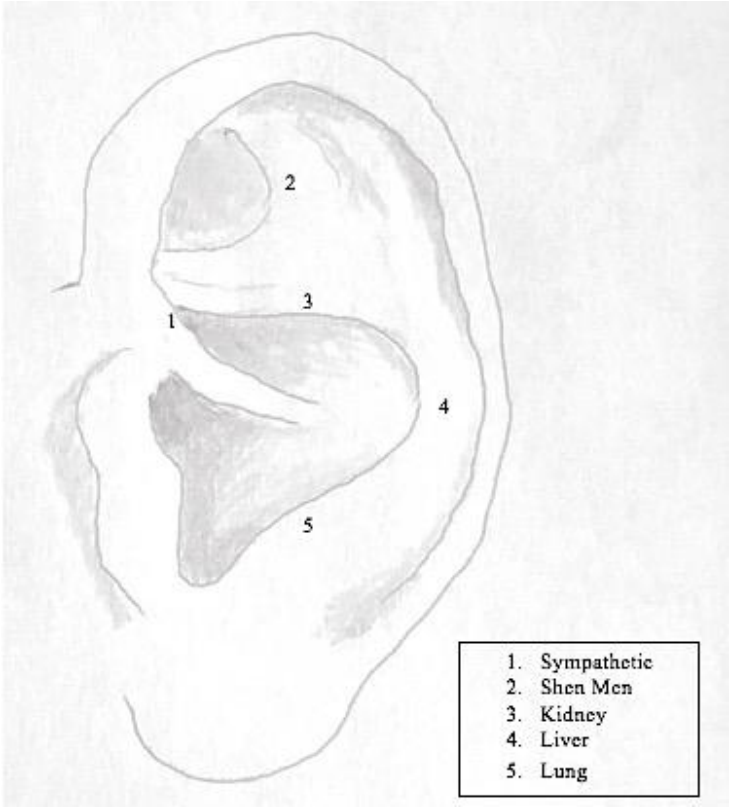

Figure 1 National Acupuncture Detoxification Association (NADA) protocol of acupuncture used on the ear. This protocol is used in adults for the treatment of withdrawal but is more recently being implemented for NAS.

A newer approach to non-pharmacological treatment is acupuncture. Acupuncture is the activation of specific points on the body through various methods such as needles, laser, magnets, and pressure. Non-invasive forms of acupuncture such as laser and magnets are more appropriate for use on premature infants since they prevent creating an entry for infections via the skin [10]. Previous studies have shown the therapeutic benefit of acupuncture in adult populations that are suffering from withdrawal symptoms [11, 12]. The National Acupuncture Detoxification Association (NADA) has formulated a standardized ear acupuncture protocol for substance abuse treatment in adults (Figure 1) [13]. The NADA protocol has been shown to be effective in adults and is increasingly being used in newborns [13]. The benefits of acupuncture have also been demonstrated in the pediatric population with its analgesic effects and its ability to reduce infant colic [14-16]. However, there are limited studies to show its effectiveness in treating NAS. This review will investigate if acupuncture is a safe, feasible and effective non-pharmacological treatment that can be used in conjunction with pharmacological treatments for NAS.

2. Materials and Methods

2.1 Inclusion and Exclusion Criteria

All studies published on indexed journals or databases reporting on acupuncture for infants with NAS were considered for inclusion. All study designs evaluating acupuncture as a treatment

for NAS infants were included. No language, setting, or publication period restrictions were applied. All studies conducted on adult populations were excluded. Studies which utilized acupuncture for a purpose other than NAS treatment (e.g., pain, infant colic) were excluded.

2.2 Search Strategy and Study Selection

We searched PubMed, Google Scholar, EMBASE, and Clinicaltrials.gov databases to identify completed and ongoing studies examining acupuncture for infants with NAS. The search term combinations, wildcards, and synonyms used for the search are included in Appendix A. Additionally, the citation lists of retrieved articles were manually screened to identify other studies of interest.

Appendix A: Search strategy example for one database. All databases including PubMed, Google Scholar, EMBASE and ClinicalTrials.gov followed the same search strategy and the PubMed database is presented. All databases were last searched on July 23rd, 2019, following PRISMA guidelines.

#1 Neonat* OR Newborn* OR Infant* OR Baby OR Babies n= 1,481,881
#2 “Neonatal Abstinence Syndrome” OR “Neonatal Withdrawal” n= 1617
#3 Acupuncture OR Acupressure n= 31,063
#4 Opioid* OR Opiat* n= 124,200
#5 Auricular therapy n= 5437
#6 “Complementary Medicine” n= 257,513
#7 Treatment* n= 4,755,523
Search Strategy: #1 AND #2 AND (#3 OR #4 OR#5 OR #6 OR #7) [n=15, 823, 1, 18, 1222].

3. Results

This review included eight studies in total that describe the potential of acupuncture as a treatment for NAS or acute withdrawal symptoms. We included two studies that evaluated the presence of acupuncture points. One study assessed the safety and feasibility of acupuncture in the NAS population. And five studies reported the efficacy of acupuncture as a treatment for NAS. Two of the five efficacy studies also reported on safety and feasibility so they were discussed in both sections. The study types that were included ranged from RCTs, case studies, pilot studies to chart reviews. The acupuncture types in this review include non-insertive acupuncture (n=2), needle acupuncture (n=2), and laser acupuncture (n=2).

3.1 Detection of Acupuncture Points in Neonates with NAS

Two studies that observed the presence of acupuncture points in neonates with NAS were identified. Previously, the presence of acupuncture points has been shown in the neonatal population [17, 18]. The aim of these included studies was to confirm the presence of acupuncture points in neonates with NAS. Both studies used the PS-3 pen method to detect acupuncture points on the ear and the body [19, 20]. A flash of light and a noise from the PS-3 pen indicate locations where skin conductivity differs which corresponds to the location of an acupuncture point [19].

A case report by Raith et al on a term female newborn assessed the presence of auricular acupuncture points [19]. The infant was afflicted with NAS and was experiencing acute distress

with periods of crying and agitation. The Finnegan score was in the high range (>9) which indicates the need for treatment. The points that were detected include the following: psychovegetative rim, R point, and frustration point on the left and right ear; the mouth, the esophagus, and the lung point on the right ear. This study, however, is a case report with only one infant. Thus, the evidence presented in this study cannot be generalized to all infants with NAS.

Kurath-Koller et al used the same PS-3 pen method on 30 neonates with NAS to determine the presence of active somatic and psychic ear acupuncture points [20]. Active somatic points are locations on the outer ear that represent all body organs [21]. And active psychic points on the ear are able to influence the entire body once they are stimulated [21]. In this study, the psychovegatative rim was the most frequently detected active somatic ear acupuncture point and was found in all neonates. Psychic ear acupuncture ear points were also found in all neonates but in differing degrees: R point (27/30), frustration point (23/30) and PT 1 (10/30). This study concludes that there are active somatic and ear acupuncture points in infants with NAS. In comparison to the case study by Raith et al, this study included infants and both active somatic and psychic ear points were included.

3.2 Safety, and Feasibility of Acupuncture in Neonates with NAS

One study assessed the safety and feasibility of needle acupuncture in neonates with NAS [22]. This pilot study by Weathers et al was conducted on 20 infants with NAS. They received needle acupuncture at 3 or 4 points on the ear. Needles were kept in one ear for 3 ± 1 days before removal and placement in the opposite ear. Treatments continued until methadone treatment was discontinued or a discharge dose was established. Safety was assessed by the incidence of skin breakdown and cellulitis, and feasibility by the rate of needle displacements, number and type of adverse events, and study retention rate. Overall, none of the infants developed skin breakdown or cellulitis, suggesting that needle acupuncture is safe. Furthermore, only 2% of the needles became dislodged, which indicates feasibility. No adverse events were reported.

Additionally, the two included RCTs made conclusions about safety and feasibility. The study by Raith et al deemed laser acupuncture to be safe due to no visible skin changes, distress or discomfort during laser acupuncture [23]. They also concluded laser acupuncture to be feasible as there was a cost reduction of 26.4% in the acupuncture group. Schwartz et al utilized acupressure and concluded the method to be safe and feasible due to no adverse events during acupressure and a high patient recruitment rate [24].

3.3 Efficacy of Acupuncture as a Treatment for NAS

We identified five studies describing acupuncture as a treatment for NAS or acute withdrawal symptoms. Various methods of acupuncture were used including non-insertive acupuncture (n=2), needle acupuncture (n=1), and laser acupuncture (n=2).

Filippelli et al conducted a chart review on 54 newborns with NAS that received non-insertive acupuncture (NIA) on the head and the limbs [25]. Overall, 28/54 infants fell asleep during or immediately after NIA. Relaxing effects were also found in babies that were previously agitated. Further, in eight infants, feedings and caloric intake improved after NIA-treatment.

A case series (n=10) by Golianu et al examined needle acupuncture and its effects on acute withdrawal symptoms in neonates that were exposed to opioids and benzodiazepines [26]. These

infants were not diagnosed with NAS but this study is still important to include since these withdrawal symptoms that they experienced are similar to NAS symptoms. Treatment with acupuncture reduced withdrawal symptoms and amount of opioids needed, and within 48 hours, opioid doses were reduced by 89%.

Raith et al used laser acupuncture on one infant with a high initial Finnegan score of 16 [27]. Laser acupuncture was administered using the NADA protocol (Figure 1) one hour after morphine treatment. Additional body acupuncture points included Tai Chong (LR3), He Gu (LI4), Tai Xi (KI3) and Shenmen (HT7). After laser acupuncture, the baby was reported to have a higher caloric intake and a decrease in the Finnegan score. Nurses also reported that the baby was more relaxed and fell asleep quicker after laser acupuncture.

Raith et al randomized 28 newborn infants with NAS to laser acupuncture + morphine + phenobarbital (n=14) compared to morphine + phenobarbital alone (n =14) to assess duration of oral morphine therapy [23]. The median (interquartile range) duration of oral morphine was significantly reduced in the acupuncture group compared to the control (28 (22-33) vs. 39(32-48) days, p=0.019). The LOS was significantly reduced in the acupuncture group compared to the control group (35 (25-47) vs. 50 (36-66) days, p=0.048). While this is promising, infants in the control group had a significantly lower birth weight (mean difference -573g), which might have contributed to these results.

A prospective study randomized 76 neonates with NAS to either standard treatment + NADA protocol acupuncture (n=39) compared to standard treatment alone (n=37) to assess LOS [24]. Their method of acupuncture involved the taping herbal seeds to points on the ear. Overall, there were no differences in LOS, length of pharmacologic treatment, or average NAS scores between infant groups. However, there was a tendency that the acupressure treated infants required less pharmacologic support compared the control group.

3.4 Ongoing Studies

Currently, there are three ongoing studies examining acupuncture as a treatment for NAS [28-30]. Brown et al aims to recruit 15 term infants with NAS for auricular acupuncture to assess the number of participants recruited compared to number actually enrolled [28]. Another similar study is plans to recruit 12 term infants with NAS for auricular acupuncture to primarily assess the percentage of eligible patients enrolled [29]. Balakrishnan et al are planning to randomize 48 infants with NAS to either standard treatment+auricular acupuncture or standard treatment alone to assess the number of infants requiring methadone [30]. The results of all these studies are pending.

4. Discussion

The main finding of this review can be summarized as follows: acupuncture is safe and feasible with contradicting results for efficacy in neonates with NAS. Noteworthy, there were no adverse or severe adverse events reported using any acupuncture method. Unfortunately, none of the studies included a long-term neurodevelopmental follow-up. Two studies were able to detect acupuncture points in neonates with NAS which suggests that newborns can be treated with acupuncture [19, 20]. There is some evidence that acupuncture decreases LOS, duration of pharmacological treatment, and the Finnegan score [23, 26, 27]. These all can translate into a

longer time spent with the mother that can be beneficial for the child's neurodevelopment [8]. Acupuncture was also shown to decrease agitation and help increase sleep, caloric intake and weight gain [25, 27]. However, only two RCT studies were found for acupuncture and NAS and one of the two studies showed results that were not significant between the acupressure and control groups [24]. These results show that it is difficult to establish a positive relationship between acupuncture and a reduced LOS, reduced need for pharmacological treatment or reduced Finnegan score since there are not many controlled studies and the many variations that exist between the studies.

4.1 Limitations of Acupuncture Studies for NAS

Studies on NAS are difficult to conduct due to a multitude of reasons. For example, there can be a large variation on the types and amounts of drugs that infants are exposed to in utero. Also, it can be difficult to assess the severity of the symptoms using the Finnegan scoring due to the extensive training required for its use and the difficulties in judging some items correctly (e.g. the difference between "mild" and "marked" tremors) [31]. Most studies in the current review used the Finnegan score or a modified version of it to assess the need to treat NAS and the efficacy of acupuncture to alleviate NAS symptoms [23, 24, 27]. However, two studies used other measurements including subjective assessment from nurses or the amount and number of opioid dosages given throughout the study period [25, 26]. This makes it difficult to combine these studies to determine acupuncture's efficacy. Additionally, the included studies used different types of acupuncture (e.g. needles or laser) and different acupuncture points (e.g., NIA in the head and limbs or NADA protocol), which further increases the difficulty to compare them.

4.2 Gaps in the Literature

Our search only identified two RCTs that evaluated acupuncture for newborns with NAS. The other study types included case studies (n=2), a chart review (n=1), and pilot studies (n=3). The quality of the evidence from these study types is low due to small sample size or subjective measurements. This makes it difficult to draw conclusions from the included studies in this review. We recommend that additional RCTs be conducted to investigate acupuncture's efficacy as a treatment for NAS.

4.3 Future Studies

Due to the limited number of studies on acupuncture and NAS, we propose some future studies. A comparison of the different types of acupuncture techniques would be beneficial at determining the best type of intervention for neonates with NAS. Also, another auricular acupuncture protocol known as battlefield acupuncture has shown significant pain relieving effects in adults and it may have the potential to show similar effects in the pediatric population [32, 33]. Battlefield acupuncture involves the use of gold semi-permanent needles that are placed at up to five specific sites in one or both ears for about three days [34]. An ongoing clinical trial on this protocol is randomizing 90 preterm infants to either magnetic acupuncture or a placebo control group to assess the reduction of pain [35]. Due to promising results in adults, the therapeutic value of battlefield acupuncture in newborns with NAS should be investigated. Long term follow up should

also be investigated in all infants who have undergone acupuncture to observe if there are any long-term effects.

5. Conclusions

Acupuncture is a safe and feasible non-pharmacological intervention than can be used in neonates with NAS. However, when looking at the efficacy of acupuncture as a treatment for NAS, the results are inconclusive. There can be many limitations when conducting acupuncture studies on NAS infants such as the incorrect usage of the Finnegan scoring tool or variations of in utero drug exposure. Additionally, our review demonstrated the gaps in the literature and the low quality of available studies due to low sample size or subjective measurements. Thus, more RCTs should be conducted to gather stronger evidence for acupuncture's potential of treatment of NAS.

Abbreviations

-NAS: Neonatal Abstinence Syndrome; -NADA: National Acupuncture Detoxification Association; -NIA: Non-insertive Acupuncture; -RCT: Randomized Control Trial; -LOS: Length of hospital stay; -IQR: Interquartile Range.

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Author Contributions

Avneet K. Mangat and Georg M. Schmölzer did all the works, which include conception, data acquisition, data analysis, interpreting of results, drafting of the manuscript, critical revision of the manuscript, and final approval of the manuscript.

Competing Interests

The authors have declared that no competing interests exist.

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