AWAKE P6 STIMULATION FOR POST-OPERATIVE NAUSEA AND VOMITING USING JAPANESE ACUPUNCTURE NEEDLE AMONG CHILDREN 5-18 YEARS OLD AT PHILIPPINE CHILDREN'S MEDICAL CENTER

MARY ESTHER R. MAALA, JANETTE T. FUSILERO-PASCUAL

ABSTRACT

OBJECTIVE: To compare the effectiveness of preoperative Japanese acupuncture for prevention of post-operative nausea and vomiting (PONV) in non-sedated children for surgery under general anesthesia**.**

METHODS: This is an RCT studying the effectiveness of press-tack Japanese needles in P6 prior to any sedatives in children age 5-18 years old for surgery under general anesthesia (n=66). Patients were randomized to receive either press-tack needle (n=33) or an identical press-tack without the metal component (n=33). Incidence of PONV was reported using BARF scale. Children, parents, anesthesiologists, and nurses were blinded to group assignment.

RESULTS: Eight of 33 (22%) in the intervention group while 17 of 33 (51.52%) in the placebo group experienced PONV (RR = 0.47, 95% CI [0.24-0.94], p-value 0.0224). One case reported an adverse event of worsening of nausea and vomiting.

CONCLUSIONS: Japanese acupuncture at P6 prior to sedation using press-tack needle significantly reduced the incidence of PONV in children after general anesthesia.

KEYWORDS: PONV, POV, P6, PC6, Japanese acupuncture, Acupuncture, RCT

INTRODUCTION

Over the past decades, acupuncture has gained acceptance as a complementary treatment in the practice of western medicine. But research in this area is limited with use of sham-needling as control. Recent reports criticize sham-needling in providing a reliable control setting. There is even greater paucity of data regarding use of acupuncture in pediatrics.

Among perioperative uses of acupuncture, treatment for post-operative nausea and vomiting (PONV) had been the most studied in the adult population. In children, only postoperative vomiting (POV) is usually described due to difficulty in assessing occurrence of nausea. Nausea is believed to be underreported. Current evidence supports the multimodal approach to lessen PONV in children, but most pediatric anesthesiologists are equipped with only pharmacologic options.

Currently, acupuncture is not being utilized in our institution as a complementary option to care for children. The perioperative applicability of acupuncture remains elusive in anesthetic

management even for the general population. More challenging would be the implementation of this alternative treatment in children undergoing surgical procedures. Significant amount of research for incorporation of pediatric acupuncture in perioperative period is lacking. No study on acupuncture had been done in children prior to induction of anesthesia mainly due to the fear of needles. [1] Previous studies in which acupuncture was started after the induction of anesthesia, revealed reduced efficacy, or a lack of efficacy, although the mechanism underlying this phenomenon is not known.[2]

The most studied use of perioperative acupuncture is prevention and treatment of PONV. In children, incidence of post-operative vomiting is twice as frequent as compared to adults. [3] Severe POV can result in wound dehiscence, dehydration, electrolyte imbalance and pulmonary aspiration. It is one of the leading causes of parental dissatisfaction after surgery and is the leading cause of unanticipated hospital admission following ambulatory surgery. Research in occurrence of perioperative nausea is also lacking since vomiting and retching are only the usual endpoints used. Occurrence of nausea and its impact in children recovering from surgery is thus underreported.

Japanese acupuncturists developed press-tack needles that are easy to use even by non-acupuncturist and is virtually painless upon application with its filiform tip (Figure 1).[4] These features might provide applicability among children in the perioperative period, especially prior to any drug administration, a period where acupuncture treatment had been shown to be more effective. [2]

Acupuncture has greater safety profile as compared to pharmacologic interventions for PONV. This study aims to address the feasibility of preventing post-operative nausea and vomiting in the pediatric population with preoperative use of innovative press-tack needles. With ease of applicability even for non-acupuncturist, this may provide a safer option in the practice of pediatric anesthesiology.

Consequently, by lessening the incidence of PONV, this may also be economically beneficial for shorter PACU stay and may provide evidence of use for ERAS program in pediatric surgery. Other subspecialties may benefit as well since this study may establish applicability of needling in unanesthetized pediatric patients with the use of finer Japanese acupuncture needles.

METHODOLOGY

This is a double-blinded, randomized controlled trial (RCT) among children 5-18 years old who underwent surgery using general inhalational anesthesia. Stimulation at P6 using Japanese press-tack acupuncture needles (*Pyonex*) prior to administration of any anesthetics. P6 was stimulated by tapping at least 10 times.

After Ethics Committee – Institutional Review Board (IRB) approval, recruitment of potential subjects was done during preoperative evaluation of patients at OPD every afternoon during weekdays. Upon

admission and after screening, informed consent from the parent/guardian was obtained; assent was secured for patients ages 7-17. Seventy (70) patients who underwent elective surgery under general inhalational anesthesia were included in this double-blinded randomized controlled trial.

The intervention, as well as the possible adverse events that may arise from the study, were explained to the parent/s or guardian. Actual acupuncture press-tack needle was shown to parents and guardian. They were oriented to use of BARF scale as well. All the questions or clarifications passed by the primary caregiver were addressed by the investigator. After the steps, only then was consent and assent obtained.

Patients were randomized using computer-generated random numbers. Randomization schedule was placed in sealed opaque envelopes which were opened only before the intervention. The patient, primary caregiver, anesthesia provider and PACU nurse were blinded to the type of intervention that the patient will receive. Only the investigator who performed the acupuncture was aware of the group assignment.

Vital signs at the ward were recorded immediately prior to transport to the OR complex. Patients were wheeled in to the OR complex 30 minutes prior to the contemplated procedure. Based on the randomization schedule, the intervention was performed by the investigator at the OR complex waiting area. Group A received acupuncture as follows: Left P6 point identified by the investigator, press-tack needle placed and then covered by a medical bandage.

Group B received placebo as follows: Left P6 identified by the investigator, identical press-tack without the needle tip placed and covered by an identical medical bandage.

Anesthesia provider is a PCMC pediatric anesthesiologist consultant/fellow-in-training other than the primary investigator or supervising investigator. After placing the intervention, anesthesia provider stimulated P6 acupressure point by gently tapping at least ten times.

Standard anesthetic induction proceeded in this order: (1) Fentanyl 1-2 ug/kg (2) Midazolam 0.2mg/kg (3) Atropine 0.02mg/kg (4) Propofol 2-3mg/kg. Airway was secured with either (1) endotracheal tube (2) laryngeal mask airway or (3) face mask with muscle relaxant of standard dose as necessary. Standard regional anesthesia was given as necessary.

After the surgical procedure, total anesthetic time was recorded. Total dose of opioid use was computed as well. Intervention was stimulated by the anesthesiologist-in-charge after inhalational gas has been turned off and prior to transfer to PACU. Initial BARF scale was recorded by the PACU nurse upon arrival at the recovery room; this was time 0.

Pain regimen was also administered during end of surgery using Paracetamol IV

15mg/kg and Ketorolac at an initial dose of 0.6mg/kg. Adjunct pain regimen was a standard rescue opioid dose as necessary for severe pain using age appropriate pain scale (FLACC age >5 to 7 years old, FACES scale 8-12 years old, NRS >12 years old).

For every 15 minutes for the first 3 hours, BARF scale was taken by the PACU nurse who was blinded from the type of intervention. For episodes of nausea, retching or vomiting (BARF ≥4/10) intervention was stimulated again by the anesthesiologist-in-charge. After five minutes without relief, a rescue dose of Ondansetron 0.1mg/kg IV (not exceeding 8mg/day) was given and recorded.

Intervention was removed by the investigator prior to discharge from PACU with Pediatric Post-Anesthesia Discharge Scoring System (Ped-PADSS) > 9/10 (*see Appendix*). Immediate adverse events were recorded.

Parent/s or guardian reoriented to the BARF scale were given monitoring sheet for scoring hourly during waking hours, from the 4^{th} to 24^{th} hour after withdrawal from anesthetic. Adverse events were also documented. Satisfaction rating using bipolar Likert scale of 1-5 was taken from the primary caregiver at the end of study period.

The investigator recorded the following data:

1. Demographics
2. PONV risk factors
3. BARF scale for the first 24 hours
4. Rescue acupuncture
5. Rescue anti-emetic
6. Adverse events
7. Satisfaction rating

The research team declares no conflict of interest. The study did not receive any support or funding from any company or institution. The clinical study underwent approval from the IRB of PCMC. A written consent and assent, if necessary, were obtained. Participation in the study was purely voluntary and without financial compensation.

Adverse reactions that developed were reported accordingly. Patients were given appropriate treatment without delay. They were reminded that they can withdraw from the study at any time. The investigator shouldered the cost of medications given for an adverse event that occurred during the study.

All data were encoded using Microsoft Excel and checked for duplicates. Data was be analyzed using Stata14MP. Patient information was kept with anonymity by utilizing code numbers. Data was encoded by the supervising investigator. Only the primary and supervising investigators had access to the password protected file.

To describe the homogeneity of the population, categorical variables such as gender and history of PONV were summarized using actual counts and frequencies. Continuous variables (i.e. age,

weight, or height) were described in terms of mean and standard deviation. Comparison of numerical variables between the study groups was done using t-test. For categorical data, Chi square test or Fisher exact test was performed. Level of significance was set at 0.05.

Data were processed using a per protocol analysis. For the primary outcome (occurrence of PONV), Chi-square test was used to compare the difference in the two groups. Risk ratio was also computed. For secondary outcomes such as rescue antiemetic and adverse events, Chi-square test or Fisher exact test was used. The cut-off for statistical significance was also set at $P<0.05$ for all tests.

RESULTS

Seventy (70) patients were eligible in the study (Figure 2). Four patients were excluded from the study, two from each study group. For the acupuncture group, two had a change in anesthetic management. For the control group, one withdrew from the study before the intervention was given and the second was excluded due to breach in protocol (unable to give acupuncture stimulation at the conclusion of surgery).

As can be seen from Table 1, the two groups were comparable. There were no statistically significant differences in the history of motion sickness, previous PONV, time of exposure to anesthetic gas, nor to opioid use perioperatively.

The incidence of nausea and vomiting was lower in the acupuncture group immediately after surgery (Figure 3). Same result was obtained with the analysis of BARF scales collected from the ward (Figure4).

There was a significant difference between groups for the primary endpoint: experiencing post-operative nausea and vomiting over the 24-hour observation period. The incidence and severity of PONV was reduced in the P6 acupuncture group (11 of 33; P = 0.02; Table 2) as compared with controls (17 of 33). The risk of PONV was computed to be 53% less in the treatment group versus the control group. Among the study subjects, only one guardian, from the acupuncture group, reported an adverse event of worsening nausea and vomiting. This was treated with IV antiemetic as per protocol.

There was no significant difference in the number of patients needing rescue acupuncture between the two groups. Thirteen (13 of 33) in the acupuncture group while 8 of 33 in the control group required rescue acupuncture at the PACU. However, in the treatment group, out of the 13 patients who received rescue acupuncture, 10 had relief from PONV and did not require further pharmacologic rescue medication. Similarly, the use of rescue antiemetic was significantly higher in the placebo group. (10 of 33; P = 0.03) compared to the acupuncture group (3 of 33; p-value 0.030).

Using the bipolar Likert scale, the acceptability of Japanese acupuncture to unanesthetized children was computed to be 74%. (49 of 66 parent/guardian were

satisfied with the non-pharmacologic intervention).

DISCUSSION

The results of this study provide significant evidence that press tack Japanese acupuncture needle prior to anesthesia reduces incidence of PONV in pediatric patients. This contrasts with studies in acupuncture in children for PONV concluding this modality initially as ineffective.[5-8]

Majority of previous trials in adjunct acupuncture have focused on Chinese method of needling. Control groups in these studies either used "contact needling" or "shallow needling". However, these methods are actual treatment modalities in Japanese acupuncture.[9] This study therefore questions reliability of previous conclusions and provides a new option of setting a randomized controlled trial.[4] Through perspective of biophysics and neuroscience, Quiroz-Gonzales, et al. provided a mechanism why "sham needling" in the control group may provide the same effect as the standard TCM needling in the treatment group. They studied the relationship between acupuncture points and receptive fields. The sensory signals from the receptive fields near the standard acupuncture points can still activate the same central nervous pathways for the intended standard acupuncture points.[10] This phenomenon has led to confusing results with both the two arms of intervention having the same results.[11] To date, experimental and clinical studies have shown that minimal or "sham acupuncture", used as placebo, is not necessarily inert from a physiological perspective.[12]

Alizadeh et al. concluded that two acupuncture points versus a single acupuncture point is more effective in preventing PONV.[13] Interestingly, our single point modality offered clinical significance post-operatively. Congruent to the Japanese acupuncture theme of lesser point stimulation is the lesser intensity in stimulation.[14]The tapping technique used in this research is a gentler technique compared to standard stimulation in TCM acupuncture.[15] This deemphasizes the core concept of Chinese acupuncture which is to seek De-Qi sensation before achieving a therapeutic effect.[16]

In this trial, only one case reported an adverse event (worsening of symptoms). Current data on safety of acupuncture mainly rely on TCM method of stimulation. Identified common adverse events include pain, bruising, bleeding and worsening of symptoms. Computed incidence of these mild adverse events was 11.8% with the use of Chinese acupuncture needles. Serious adverse events such as site infection or joint fibrosis in TCM acupuncture were related to substandard practice and inadequate training.[17]

Another result was the decrease in use of ondansetron, a serotonin antagonist, in the treatment group after the rescue acupuncture was provided. This supports the study done by Somri et al. where acupuncture was a valid non-pharmacologic alternative

treatment for vomiting.[7] Different subtypes of serotonin (5-HT) receptors are believed to be involved in the antiemetic and prokinetic effects of acupuncture. The antiemetic effect involved 5-HT3 mechanism while the prokinetic effect was observed to downregulate 5-HT4 receptors.[18]

Acupuncture for children has gained wide acceptance in Western medicine. However, the limited evidence is based mainly on TCM approach. Ethical considerations exist in its use in children since this Chinese approach is inherently painful for adults. [19]There are no studies in children due to fear of pain both by the children and parents.[1]This study will be the first to provide data through its painless approach with the use of innovative filiform needles in sticker form.

RECOMMENDATIONS

Collaboration with Japanese acupuncturists will be beneficial to expanding knowledge in this treatment strategy.[15] In Japanese acupuncture, duration and intensity of stimulation will further vary per age group.[20] With the wide age range of this study, utilizing a narrower age group might reveal a more precise treatment method.Ease in application and non-specialized skill in stimulation may also empower non-acupuncturists in hospitals. However, point localization by these non-acupuncturists should also be explored to established actual applicability in clinical setting. Point localization can vary greatly even among acupuncturists.[22]

With high acceptability in non-sedated children, other possible uses for anxiety and pain in the perioperative period should be explored. As this is an introductory pediatric research to use of Japanese acupuncture in the Philippine setting, a separate study exhausting possible adverse events from press tack needles will be contributory to holistic approach to children.

CONCLUSION

This study provided a statistically significant data in using single point acupuncture to decrease the incidence of PONV. By preventing use of anti-emetic post-operatively, effectivity of P6 point stimulation to symptomatic patients was also concluded. This study also established Japanese acupuncture using press-tack needles as an acceptable treatment approach to children and their parents in a hospital setting. Thus, Japanese acupuncture for PONV may provide an alternative to the popular alternative TCM.

ACKNOWLEDGEMENT

I would like to thank my sensei, Toru Nakamura, for his continued support and expert advice that led to the successful completion of this clinical trial using Japanese Acupuncture in the pediatric population. He is a keystone to understanding the centuries-old Eastern art of healing and applying it to modern practice of Western medicine.

REFERENCES

(1) Chernyak GV, Sessler DI. Perioperative Acupuncture and Related Techniques. Anesthesiology. 2005 May; 102(5):1031-1078

(2) Lee A, Done MI. The use of nonpharmacologic techniques to prevent postoperative nausea and vomiting: a meta-analysis. Anesth Analg. 1999: 88: 1362-1369 [PubMed: 10357346]

(3) Martin S, Baines D, Holtby H, Carr AS. APA Guidelines on the Prevention of Post-operative Vomiting in Children. APA Guidelines. Autumn 2016

(4) Miyazaki S, Hagihara A, Kanda R, Mukaino Y, Nobutomo K. Applicability of Press Needles to a double-blind Trial. Clin J Pain. 2009; 25: 438-444

(5) Rusy LM, Hoffman GM, Weisman SJ. Electroacupuncture prophylaxis of postoperative nausea and vomiting following pediatric tonsillectomy with or without adenoidectomy. Anesthesiology2002; 96: 300-305 [PubMed: 11818760]

(6) Wang SM, Kain ZN. P6 acupoint injections are as effective as droperidol in controlling early postoperative nausea and vomiting in children. Anesthesiology2002; 97: 359-366 [PubMed: 12151925]

(7) Somri M, Vaida SJ, Sabo E, Yassain G, Gankin I, Gaitini LA. Acupuncture versus ondansetron in the prevention of postoperative vomiting. A study of children undergoing dental surgery. Anaesthesia 2001; 56: 927-932. [PubMed 11576093]

(8) Lee A, Done MI. The use of nonpharmacologic techniques to prevent postoperative nausea and vomiting: a meta-analysis. Anesth Analg. 1999: 88: 1362-1369 [PubMed: 10357346]

(9) Vlessides, M. (2016).Pediatric Post-Op Nausea Identified with BARF scale. Retrieved from www.anesthesiologynews.com/Article/PrintArticle?articleID=38416

(10) Quiroz-Gonzalez S, Torres-Castillo S, Lopez-Gomez R, Estrada I. Acupuncture Points and their relationship with Multireceptive Fields of Neurons. Journal of Acupunctureand Meridian Studies. 2017; 10(2):81-89

(11) Ernst E. Acupuncture--a critical analysis. J Intern Med.2006 Feb; 259(2):125-37

(12) Lund I, Naslund J, Lundeberg T. Minimal acupuncture is not a valid placebo control in randomised controlled trials of acupuncture: a physiologist's perspective. Chin Med.2009; 30, 4-1

(13) Alizadeh R, Sara E, Saeed S, Bagheri-Hariri B, Shoar N. Acupuncture in Preventing Post-operative nausea and vomiting: efficacy of two points versus single one. Journal of Acupuncture and Meridian Studies.2014;7(2):71-75

(14) Chant B, Madison J, Coop P, Dieberg G. Contact Tools in Japanese Acupuncture:

An Ethnography of Acupuncture Practitioners in Japan. J Acupunct Meridian Stud.2017;10(5):331-9

(15) Kivity O. Japanese acupuncture and moxibustion: What's so unique? European Journal of Oriental Medicine.2018

(16) Chant B, Madison J, Coop P, Dieberg G. Beliefs and values in Japanese Acupuncture: An Ethnography of Acupuncture Practitioners in Japan. Integrative Medicine Research.2017;6(3):260-8

(17) Adams D, Cheng F, Jou H, Aung S, Yasui Y, Vohra S. The safety of pediatric acupuncture: a systematic review. Pediatrics. 2011 dec; 128(6):e1575-87

(18) Zhang X, et al. Effects and mechanisms of transcutaneous electoacupuncture on chemotherapy-induced nausea nd vomiting. Evid Based Complement Alternat Med.2014:860631

(19) Skjeie H, Brekke M. Big needles, small bodies--the absence of acupuncture treatment for infants in contemporary Shanghai: a qualitative study. BMJ. 2015 Volume 5, Issue 11

(20) Birch S. Shonishin: Japanese Pediatric Acupuncture. Thieme.2016

(21) McCoy CE. Understanding the Intention-to-Treat principle in Randomized Controlled Trials. West J Emerg Med. 2017 Oct; 18(6):1075-1078

(22) Godson DR, Wardle JL. Accuracy and precision in acupuncture point location: A critical systematic review. J Acupunct Meridian Stud. 2019 Apr; 12(2):52-66

(23) Ford I, Norrie J. Pragmatic Trials. N Engl J Med. 2016; 375:454-463

Table 1. Patient Demographics

	Acupuncture n=33	Sham n=33	p-value
Age (years)	9.63 ± 4.02	9.88 ± 4.29	0.8136
Weight (kg)	32.76 ± 15.51	32.30 ± 2.69	0.9053
Height (cm)	126.94 ± 20.86	126.06 ± 19.17	0.8591
BMI (kg/m^2)	19.30 ± 4.88	19.39 ± 5.00	0.9407
Gender Male Female	 20 (60.61%) 13 (39.39%)	 22 (66.67%) 11 (33.33%)	0.609
ASA PS I II	 23 (69.70%) 10 (30.30%)	 20 (60.61%) 13 (38.24%)	0.438
PONV history No Yes	 22 (66.67%) 11 (33.33%)	 24 (72.73%) 9 (27.27%)	0.592
Motion sickness history No Yes	 25 (75.76%) 8 (24.24%)	 28 (84.85%) 5 (15.15%)	0.353
Menarche (females) No Yes	 1 (14.29%) 6 (85.71%)	 2 (22.22%) 7 (77.78%)	0.687
Surgical procedure Head and neck Intraperitoneal Extraperitoneal	 12 (36.36%) 10 (30.30%) 11 (33.33%)	 17 (51.52%) 12 (36.36%) 4 (12.12%)	0.116
Airway used Mask LMA ETT	 6 (18.18%) 3 (9.09%) 24 (72.73%)	 6 (18.18%) 1 (3.03%) 26 (78.79%)	0.583
Adjunct regional anesthesia No Yes	 20 (60.61%) 13 (39.39%)	 21 (63.64%) 12 (36.36%)	0.800
Anesthetic duration (min)	147.27 ± 103.67	171.45 ± 113.72	0.3701
Fentanyl use (mcg/kg/hr)	1.20 ± 0.77	1.09 ± 0.83	0.5697
Opioid use post-op No Yes	 10 (30.30%) 23 (69.70%)	 10 (30.30%) 23 (69.70%)	1.000
Opioid used Nalbuphine Tramadol Morphine	 16 (69.57%) 2 (8.70%) 5 (21.74%)	 18 (78.26%) 1 (4.35%) 4 (17.39%)	0.755

Table 2. BARF scale score ≥4 (per protocol analysis)

BARF >4	Acupuncture n=33	Placebo n=33	p-value
No	25 (75.76%)	16 (48.48%)	0.022
Yes	8 (24.24%)	17 (51.52%)	

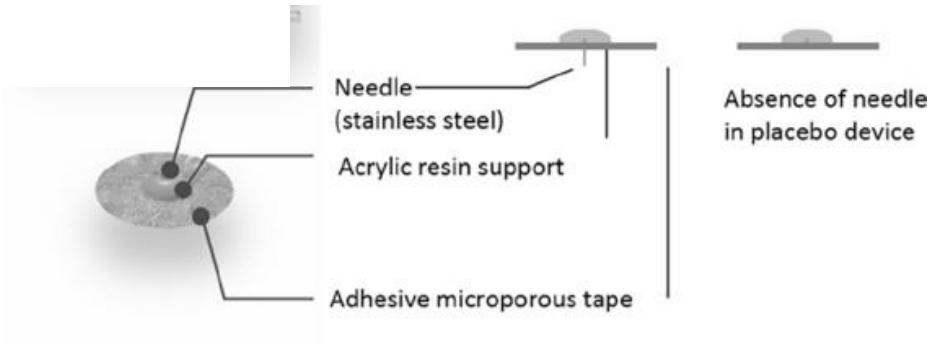

Figure 1. Press-tack needle and placebo device

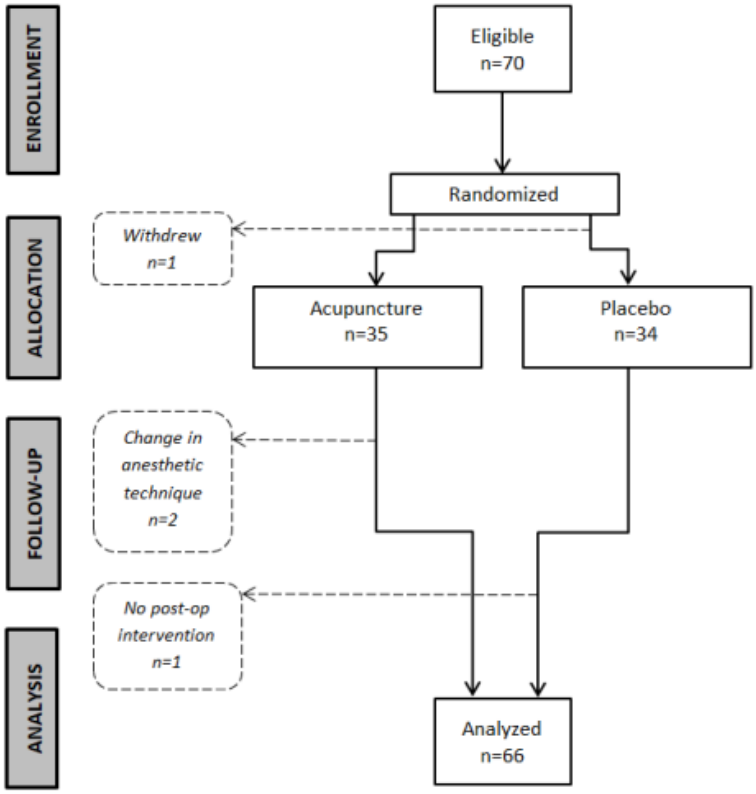

Figure 2. Flowchart for the clinical trial

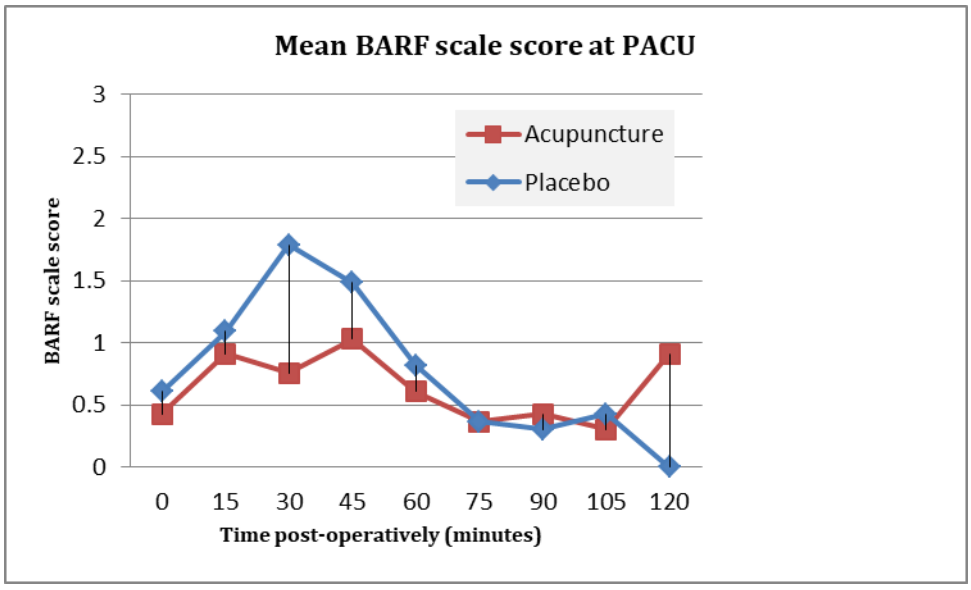

Figure 3. BARF scale score over time at the PACU

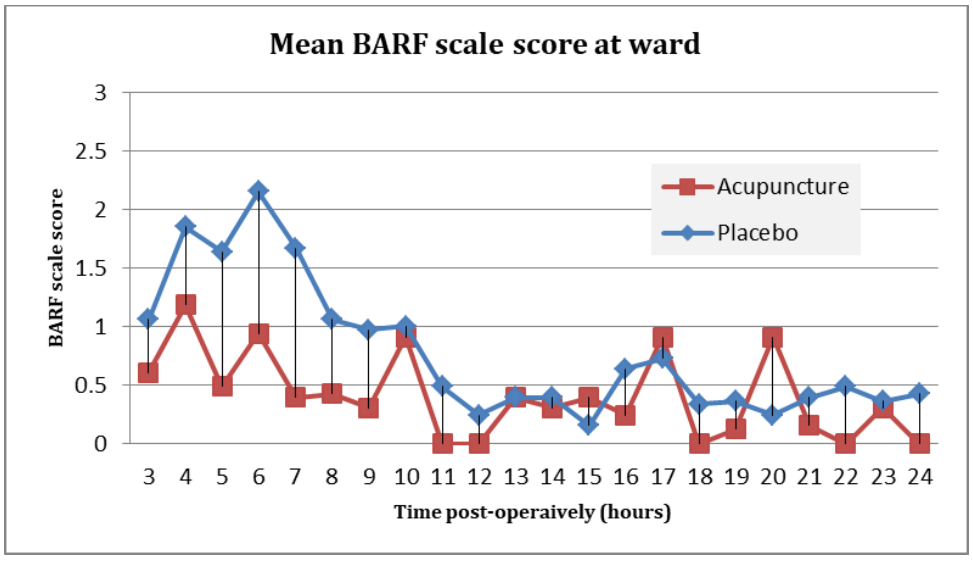

Figure 4. BARF scale score over time at the ward