Research Summary

1. **Protocol Title:**
   Effects of Lavender Oil on Postoperative Pain, Sleep Quality and Mood.

2. **Purpose of the Study:**
   The purpose of this study is to evaluate the integration of lavender essential oil in surgical patients during the perioperative and postoperative phase of care. The study will assess patients' pain, sleep quality, and mood. The goal is to support that lavender oil will decrease pain scores and narcotic use, increase sleep quality, and decrease anxiety by improving overall patient satisfaction and supporting their natural sense of well-being. This research project will help support the use of complementary medicine in a hospital setting. The increased awareness and use of complementary medicine in a hospital setting will strengthen the patient centered care model that all hospitals strive to achieve.

3. **Background & Significance:**
   Essential oils have been formally documented in use since the time of the Egyptians. The Ebers Papyrus document notes Egyptians using frankincense for different physical ailments [1]. In Greece Hippocrates used essential oils to fumigate the city of Athens to fight off the plague [1]. In medieval periods lavender essential oil was used for its antidepressive, anxiolytic, sedative, and analgesic properties. Medieval Persian physicians made records of their treatment plans which included lavender for depression and pain for headaches [2,3]. With the invention of steam distillation to separate the essential oil from the plant Europe began to use oils in perfumes and for medicinal benefits in the 1500's. Two physicians named Hieronymus and Brunschwig wrote one of the earliest printed books on the distillation and use of essential oils for medical benefits [4]. By the 19th century a French chemist Rene- Maurice Gattefosse was known for studying essential oils and their therapeutic benefits. His work and documentation led the way for the support of essential oil in medical ailments. Robert Tisserand in the early 1990s reviewed the French chemists work and added to his research to help make essential oils more known to the public in present day [1].

   In recent years lavender has been studied on human subjects to tests its known reputation for sedative, anxiolytic, and analgesic properties. In one clinical trial oral administration of lavender was compared to Ativan 0.5mg for generalized anxiety disorder. The study supported that the oral lavender oil called Silexan was as effective as 0.5mg of Ativan in adults with generalized anxiety disorder [5]. A second clinical trial analyzing sleep quality found that ischemic heart patients in the intensive care unit received better sleep with 100% lavender oil undiluted placed on a cotton ball within 20cm from the patient from the hours of 9pm-6am [6]. Two studies have used lavender oil through inhalation in the recovery room with an oxygen mask after surgery for pain control. The first study was patients after breast biopsy, the second was patients who just had laparoscopic adjustable gastric banding [7,8]. The study with the breast biopsy patients showed a higher satisfaction rate with pain. The patients undergoing laparoscopic banding also showed a higher rate of satisfaction with pain as well as decreased opioid use in the recovery room. Furthermore one study used 100% lavender oil undiluted on the skin of pediatric patients undergoing tonsillectomy as a topical application and asked the patients to inhale. The study showed a decrease use in Tylenol usage postoperatively [9].

4. Design & Procedures:

Design

Randomized study with control group and test group. Using a 1:1 treatment allocation ratio, the total of 60 patients (30 per arm) will be randomly assigned to control or treatment arm. The Statistical Investigator will generate the randomization scheme and monitor the randomization process over the course of the trial. The study will use randomization with random permuted blocks. The test group will receive 50% lavender oil diluted in fractionated coconut oil and the control group will have the current standard of care with no essential oil intervention (coconut oil only) will be applied. Fractionated coconut oil is being used because it is colorless, odorless, does not stain clothing, and has a long shelf life. It also serves as a carrier oil for the essential oil to absorb into the skin instead of evaporating off the skin due to essential oils volatile nature.

Study Procedure

The lavender essential oil used will be from the company doTERRA. This essential oil company was chosen because this company has a medical and science governing board made up of physicians, surgeons, chemists and pharmacists. The oil is also third party tested by Dr. Robert Pappas a trusted chemist in the essential oil community for purity and quality. Gas chromatography and mass spectrometry are used to ensure purity and no unwanted substances are in the essential oil. doTERRA's essential oils have also already been used in a hospital setting at Vanderbilt University hospital in Tennessee. doTERRA's essential oils were diffused in the Vanderbilt ER at the nursing stations. After 3 months of diffusing staff felt less work related stress, less time feeling overwhelmed, and had more energy at work [13].

5. Selection of Subjects:

Potential subjects will be selected from the clinic of Dr. Scott Hollenbeck. Subjects will be consented by investigators or study key personnel.

Inclusion Criteria:

Women undergoing any form of breast reconstruction therapy
Ages 18-85
At least a one night stay in hospital after surgery

Exclusion Criteria:

Sensitivity or allergy to coconut
Use of sleeping aide drugs
Use of benzodiazepines
History of any of the following: asthma, eczema, allergy to flowers, smell disorders
Sensitivity to lavender oil or any of its ingredients
Pregnant women will be excluded from the study. During routine preoperative testing the patient's menstrual history or urine pregnancy test will be performed to identify any patient who is pregnant.

6. Subject Recruitment & Compensation:

Enrollment goal will be 60 subjects. We anticipate enrolling 60 subjects over 6 months and anticipate the trial to be complete within 1 year. The subjects will not be compensated for the study.

7. **Consent Process** – see Section 14 of the e-IRB submission form and complete the questions in that section.

8. **Subject's Capacity to Give Legally Effective Consent:**

9. **Study Interventions:**

After informed consent is obtained, exactly 4 drops of 50% lavender solution will be placed on the wrist over the radial artery. The patient will rub her wrists and hands together and then inhale and exhale slowly for one minute. This will occur thirty minutes before being taken to the operating room. The dilution of 50% was chosen after reviewing Robert Tisserand's book on essential oil safety, consulting a local certified aromatherapist, Cynthia Loving, and consulting Dr. David Hill, executive vice president and chief medical officer of doTERRA essential oils [10]. This percent dilution is recommended on skin and is not likely to cause irritation to the skin. Repeated insult patch skin testing from doTERRA has supported this dilution rate to be safe to the skin. Furthermore a previous study used 100 % lavender oil on children age 5-12 undergoing tonsillectomy with no adverse reactions [9]. The first dose will be given thirty minutes prior to the operating room because it takes 20 minutes for lavender to be absorbed thought the skin and reach peak plasma levels [11,12].

During surgery the patient will receive 4 drops of 50% solution lavender oil on the temple region over the temporal artery every 2 hours until completion of surgery. This will be applied by the anesthesia team. If the temporal region is not accessible the shoulders or feet will be alternate locations of application. When the patient arrives to the recovery room she will receive lavender oil through an oxygen mask. A 50 % solution will be used by placing 4 drops of the lavender solution on the mask and wiping it around the mask with a cotton ball. This delivery method will be used because this was used in a study from New York University Medical Center studying postoperative pain and no adverse events occurred [7]. When the patient is on the post-operative floor she will receive 50 % lavender oil on the wrist every 4 hours in the same manner as preoperatively from the hours of 6am to 9pm. Nightly (9pm-6am), 8 drops of 50% lavender oil will be placed on the cotton ball situated within 20cm of the patient. This method and concentration was chosen after reviewing a study in ischemic heart patients in the intensive care unit. The patients received lavender at bedside on a cotton ball and had statistically significant better sleep quality [6]. The control group will have coconut oil applied without any lavender oil applied in the same sequence as listed above. This will ensure the same procedures are carried out under both arms.

Blood pressure, pulse, respiratory rate, and oxygen saturation will be monitored in the preoperative area before lavender is given and 30 minutes after it is given. The level of pain will also be asked prior to application and at the second set of vitals. The control group will get two sets of vital measurements and pain scale measurements without any intervention. The same vitals will be recorded while the patient is under anesthesia every 30 minutes. There will be a notation in the chart when lavender is given to correlate time from application to time of vitals recorded. A review of the electronic medical record will be done to record amount of narcotic needed interop in both groups.

In the recovery room after the patient is given lavender through the oxygen mask the same vital signs and pain score measurement will be taken 15, 30, and 60 minutes from lavender application. In the control group on arrival to the recovery room the same data points will be

measured with the same time intervals with coconut oil only. The amount of narcotic needed in the recovery room will be taken from the electronic medical record for each group.
Postoperatively on the floor vital signs as noted above will be recorded every 4 hours. At each 4 hour interval after the vital signs are taken lavender will be applied to the experimental group and no intervention in the control group. One more set of vitals signs will be recorded 45min after application of lavender each time lavender is applied. There will be a review of narcotic use from the electronic medical record from both groups. There will be a notation when lavender was given to correlate lavender application and narcotic use.
The anxiety questionnaire will be given preop before the application of lavender and then daily for every post-op day they stay. The questionnaire is called the hospital anxiety and depression scale.

The sleep questionnaire will be given in preop before application of lavender and then daily for every post-op day they stay. The sleep questionnaire is called the Richard Campbell Sleep Questionnaire.

Daily starting on postop day 1 the patient will also record their level of satisfaction of pain control from a scale of 1-10 with 1 being not satisfied and 10 being satisfied. Patients typically stay in hospital 1-3 days post-op. A survey will be filled out daily.

10. Risk/Benefit Assessment:

The use of lavender essential oil could have potential benefits to the patient:

- Main benefits include decreased pain, better sleep, and better mood.
- Other benefits include relaxation, calming environment, pleasing aroma.

Risks are minimal, but there is potential for some adverse events:

- Possible side effects include skin irritation or coughing.
  - If skin irritation occurs, plain fractionated coconut oil will be applied to dilute the essential oil. Then a 4x4 cotton gauze will be used to wipe off the essential oil. The coconut oil will be applied a second time and then removed by a 4x4. Washing is not a recommend step because water will drive the essential oil into the skin further. If there is still a reaction and the patient is uncomfortable oral Benadryl will be given, 25mg PO Q6hrs prn itching or skin irritation. In the control arm, should the coconut oil irritate the skin it will be removed using a 4 x 4 cotton swab.
  - For coughing or any feeling of shortness of breath or chest discomfort, lavender oil therapy will be stopped. Any lavender applied to the skin will be diluted with fractionated coconut oil as mentioned above.
  - For any serious, unexpected event, which occurs to any subject during this study the appropriate DUHS IRB Adverse Event notification will be completed, e-signed by the PI and submitted to the DUHS IRB within 5 days of notification of the reported event.
  - Any patient who does not want to participate in the study can decline at any time.
  - The patient's demographics including name will remain confidential.

11. Costs to the Subject:

Study intervention and Lavender Oil will be provided to subjects at no additional cost. Subjects and/or their regular insurance provider will be responsible for all procedures and tests considered standard of care for their condition.

12. Data Analysis & Statistical Considerations:

Study Design/Endpoints: The primary outcome will be a difference in pain scores between the 2 groups and/or decrease in narcotic use and/or increased patient satisfaction of pain control. Secondary outcomes are better sleep and decreased anxiety.

Analytic Plan and Method: Differences in the change scores of pain in the two groups as well any other demographic and clinical continuous variables will be examined using t-test or Wilcoxon test, depending on whether the variables are normally or non-normally distributed respectively. The differences between the categorical variables will be examined using chi-squared or Fisher's exact test. Analysis will be conducted under the intention to treat (ITT). Missing data will be imputed under multiple imputation methods. Differences in the outcomes while controlling for potential covariates (age, etc) will be examined using linear regression. Significance of the tests will be assessed at alpha = 0.05. Analysis will be conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC.).

Power and Sample Size Calculations: A study called the effectiveness of lavender essence on sternotomy related pain intensity after coronary artery bypass grafting evaluated the effectiveness of lavender. The study observed pain scores of 6.45 (SD: 2.23) and 4.11 (2.13) in the control and treatment groups respectively [14]. For 80% power at alpha = 0.05, with the above observed means and standard deviations in the control and treatment groups, 15 subjects per group will be needed. Assuming about a 20% drop-out rate, the study would need 17 subjects per group.

13. Data & Safety Monitoring:

Data and safety monitoring will be reviewed by a team of experts (a least 2 physicians will be identified by the PI in this area of research and who are not associated with this study). Adverse events (AE) and serious adverse events (SAE) will be examined by the committee. We plan to have a review of the safety data in a meeting when half the study subjects are recruited into the study. The committee will decide on the continuity of the trial after reviewing the SAEs while ensuring the safety of the patients.

14. Privacy, Data Storage & Confidentiality – see Section 12 of the e-IRB submission form and complete the questions in that section.

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