Effects of intra-operative infusion of lidocaine on postoperative pain and quality of recovery in patients undergoing gynecological laparoscopic surgery: A randomized controlled trial

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Introduction

Postoperative recovery encompasses a variety of outcomes, such as pain, recovery of physiological parameters, incidence of adverse events, and changes in psychological status. In this era of ambulatory surgery, an early resumption of routine activities is a very important determinant of the success of a daycare procedure and can be defined in the terms of “Quality of Recovery”.[1] It depends on several factors, like nausea and vomiting, duration of ileus, attainment of physical independence and comfort, early ambulation, etc.

Abstract

Background and Aims: Early recovery is desirable after day care surgery. Intravenous lidocaine has anti-inflammatory, anti-hyperalgesic, and analgesic effects and by reducing postoperative pain, nausea, vomiting, and duration of postoperative ileus and hospital stay, might be a useful adjuvant to improve recovery after gynecological laparoscopic surgery.

Material and Methods: Fifty female patients, aged 18–55 years, undergoing gynecological laparoscopic surgery were randomly allocated to two groups. In Group L, patients received intravenous lidocaine 1.5 mg/kg at induction of anesthesia followed by infusion of 2 mg/kg/hour until the completion of surgery and in Group NS, patients received normal saline infusion. The Global QoR-40 score at 24 hours, pain score in PACU and at 24 hours, nausea/vomiting, PADSS score in PACU and analgesic consumption over 24 hours were assessed and data were analyzed using SPSS version 17 software.

Results: Demographic data were comparable in both groups. The mean Global QoR-40 score in Group L was 197.30 ± 2.3 versus 178.74 ± 6.02 in Group NS (P < 0.001). The mean time to attain PADSS ≥9 was 50 min shorter in Group L than in Group NS (P < 0.001). Nausea, vomiting, and anti-emetic requirement were also significantly reduced in Group L as compared to Group NS (P = 0.005) as was the mean pain score over 24 h (P < 0.001) and the total analgesic consumption over the first 24 h after surgery (P < 0.005).

Conclusion: Intraoperative intravenous lidocaine infusion resulted in an improved overall Quality of Recovery in patients undergoing ambulatory gynecological surgery.

Keywords: Ambulatory surgery, gynecological surgery, laparoscopic surgery, lidocaine, outpatient surgery, postoperative pain, quality of recovery
It has been seen that intraoperatively administered systemic lidocaine improves the quality of recovery by reducing postoperative pain, nausea/vomiting, postoperative ileus, and the duration of hospital stay.[2,7] It’s exact mechanism of action remains elusive, although the main therapeutic effect is attributed to central anti-hyperalgesic effect. It is known that mechnano-insensitive nociceptors are tonically activated by chemicals released during surgery leading to the induction of central sensitization to pain and hyperalgesia. These nociceptors are particularly sensitive to intravenous lidocaine[9] administered perioperatively which prevents the induction of central hyperalgesia, leading to enhanced postoperative pain relief, and an improvement in the quality of postoperative recovery.[9] It has also been suggested in various studies that this improved recovery may be due to reduced opioid consumption in the postoperative period.

Several studies done in the past have established that use of intraoperative systemic lignocaine is associated with lesser side-effects and earlier discharge of the patients. But none of them shows its benefits in gynecological laparoscopic surgeries, which are very common day care procedures. Improving quality of recovery in such patients is of utmost importance as these patients are required to resume their routine household activities very soon, which was the rationale behind conducting this study. The Global QoR-40 questionnaire has been used to evaluate the quality of recovery and a multitude of studies show that intravenous lidocaine enhances the quality of recovery after laparoscopic surgical procedures [Annexure 1].[10]

We hypothesized that intravenous lignocaine has no effects on postoperative quality of recovery in patients undergoing gynecological laparoscopic surgery. The aim of our study was to evaluate the effects of systemic lidocaine on postoperative analgesia and quality of recovery using the Global Quality of Recovery-40 (QoR-40) score at 24 h in these patients. The primary objective of the study was to assess Global QoR-40 scores at 24 h postoperatively in the study and control groups. Secondary outcomes included pain score, analgesic consumption within 24 h postoperatively, presence of nausea/vomiting, and PADSS score.

**Material and Methods**

The study was approved by the Hospital Ethical Committee and is registered with CTRI. This randomized, double-blind controlled trial was conducted from November 2012 to February 2014 in the Department of Anaesthesiology of our institution on 50 ASA physical status I female patients aged 18–55 years, undergoing gynecological laparoscopic surgery. Patients with history of allergy to local anesthetics, chronic use of opioid analgesics or corticosteroids, and drug or alcohol abuse were excluded from the study as were pregnant patients. On the basis of results of a previous investigation by GS De Oliveira et al.,[6] to achieve a power of study equal to 80% and a P value of 0.05 and to obtain a difference in mean QoR scores of 5 between the two study groups and a standard deviation equal to 2.5, total sample size was calculated to be 25. We recruited 50 patients in our study who were randomly allocated to 2 study groups, Group L (n = 23) and Group NS (n = 27) [Annexure 2]. Using computer generated random number tables, sequentially numbered opaque envelopes were prepared beforehand by an independent observer. A detailed pre-anesthetic evaluation was done and written informed consent obtained. During the pre-operative visit, patients were familiarized with 0-10 pain Numeric Rating Scale (NRS) where 0-No pain; 1-3: Mild pain; 4-6: Moderate pain and 7-10: Severe pain[11] and the QoR questionnaire[10] [Annexure 1].

Patients were allocated to Group L (Lidocaine) or Group NS (normal saline) by the primary anesthesia provider by opening the envelopes immediately before surgery. The investigator and patients were blinded to the group allocation. On arrival in OT, intravenous access and standard non-invasive monitoring was instituted. Vital signs were recorded, and all patients were given 1 mg intravenous midazolam. Five minutes later, patients in both groups received the study drug. Patients in Group L received intravenous lidocaine 1.5 mg/kg followed by an infusion at 2 mg/kg/h. Patients in Group NS were given an equivalent volume of normal saline followed by an infusion of saline in a similar manner. All the study medications were prepared by the primary anesthesia provider and all observations were made by principal investigator.

General anesthesia was induced with fentanyl 2 μg/kg followed by propofol 1-2 mg/kg. Rocuronium 0.6 mg/kg was administered for neuromuscular blockade and airway secured by an appropriate size cuffed endotracheal tube or ProSeal laryngeal mask airway. Maintenance of anesthesia in both groups was with 50% N₂O in O₂, isoflurane, and intermittent rocuronium as required. Fentanyl 0.5 μg/kg was repeated every hour after the first hour. Fifteen minutes prior to the end of surgery, all patients received intravenous ketorolac 30 mg and ondansetron 4 mg. After skin closure and dressing was done, the infusions of the study drugs were discontinued. Neuromuscular blockade was reversed with neostigmine and glycopyrrolate and patients were shifted to the Post Anesthesia Care Unit (PACU). If there was conversion from a laparoscopic to an open approach after the study drug was administered, that case was to be excluded from statistical analysis.
On arrival in the PACU, patients were asked to rate their pain on the NRS. If the patient complained of pain, morphine 1.5 mg intravenously was administered every 5 min to achieve an NRS pain score <4/10. On arrival in the PACU, the Ramsay Sedation Score (RSS) was also recorded as (i) Patient anxious and agitated or restless, or both (ii) Patient co-operative, oriented, and tranquil (iii) Patient responds to commands only (iv) Patient exhibits brisk response to light glabellar tap or loud auditory stimulus (v) Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus (vi) Patient exhibits no response.[12] Any incidence of post-operative nausea and/or vomiting was recorded and treated with 10 mg intravenous metoclopramide, followed by ondansetron 4 mg, if necessary. The anti-emetic requirement was noted. Discharge readiness was assessed using the Modified Post Anesthesia Discharge Scoring System (PADSS) score every 15 min until the patients met discharge criteria. PADSS assesses 5 criteria: vital signs, ambulation, pain, nausea and/or vomiting, and surgical bleed. Each criterion was scored on 0-2 scale and a score ≥9 was considered as readiness for shifting from PACU to ward.[13]

Once in the ward, the patients were instructed to take ibuprofen 400 mg orally every 6 h. For further rescue analgesia, patients were advised injection diclofenac 1.5 mg/kg intramuscularly. The post-operative analgesic consumption over 24 h was recorded. After 24 h, all patients were contacted by an investigator unaware of group allocation and the QoR-40 questionnaire [Annexure 1] was administered. The questionnaire consists of 40 questions that examine 5 domains of patient recovery using a 5-point Likert scale. The 5 domains include physical comfort, pain, physical independence, psychological support, and emotional state.[10]

The data were collected and analyzed using SPSS version 17 statistical software. The primary outcome variable was the Global QoR-40 score. The scores range from 40 to 200 representing, respectively, very poor to outstanding quality of recovery. Secondary outcomes included NRS, analgesic consumption within 24 h postoperatively, presence of nausea/vomiting and PADSS score. Normally distributed interval data was recorded as mean ± SD and was evaluated with student “t”-test, with unequal variance assumed. Non-normally distributed interval and ordinal data was reported as median (interquartile range [IQR]) and was compared among groups using the Mann Whitney test. Categorical data were compared using the Chi-square test (for normal distribution) and the Fisher exact test (for non-normal distribution). A P value of <0.05 was considered significant.

**Results**

The demographic profile of patients in both the groups was comparable and all patients underwent gynecological laparoscopic procedures, either diagnostic or operative. The number of patients undergoing diagnostic or operative procedures was similar in both the groups as was the mean duration of surgery [Table 1]. The mean NRS pain score of patients on arrival in the PACU was significantly lower in Group L as compared in Group NS. On arrival in PACU, patients in Group L showed a mean Ramsay sedation score of 2.22 ± 0.85, while the score was 1.63 ± 0.63 in Group NS (P = 0.004), suggesting that patients who received lidocaine infusion were more sedated than those patients who did not [Table 2].

The morphine requirement in the PACU was significantly lower in patients who had received lignocaine infusion intraoperatively [Table 2]. Twenty-two patients (96%) in Group L and only 6 patients (22%) in Group NS did not require any morphine (P = 0.000). One patient in Group L and 15 patients (56%) in Group NS required a single dose (P = 0.000). No patient in Group L and 5 patients (19%) in Group NS required 2 doses (P = 0.015) and no patient in Group L and 1 patient in Group NS required 3 doses of morphine in the PACU (P = 0.176). In Group L, 2 patients (9%) experienced nausea and vomiting and required antiemetics, as opposed to 11 patients (41%) in Group NS (P = 0.005). A PADSS score ≥9 was achieved in Group L significantly faster than in Group NS [Table 2].

The requirement of rescue analgesia over 24 h was also significantly lower in Group L. In Group L,

| Table 1: Demographic data |
|---------------------------|
| **Demographic Data**      | **Group L** | **Group NS** | **P**  |
| Age (years) (Mean±SD)     | 28.22±4.59  | 29.59±4.49   | 0.145  |
| Weight (kg) (Mean±SD)     | 54.70±12.32 | 55.22±8.14   | 0.429  |
| Height (cm) (Mean±SD)     | 155.22±8.52 | 156.07±7.58  | 0.354  |
| BMI (kg/m²) (Mean±SD)     | 22.45±3.32  | 22.71±3.38   | 0.393  |
| Duration of Surgery (min) (Mean±SD) | 68.70±35.55 | 56.30±21.51  | 0.068  |
| Diagnostic/surgical laparoscopy (number of patients) | 12/11     | 15/12        | 0.406  |
22 patients (96%) did not require any rescue analgesia, as against 6 patients (22%) in Group NS ($P < 0.005$). In Group L, one patient required a single rescue dose of inj. Diclofenac 1.5 mg/kg intramuscular during the first 24 hours as opposed to 9 patients in Group NS ($P < 0.005$). No patient in Group L required 2 rescue doses, as opposed to 12 patients in Group NS ($P < 0.005$). The mean pain score at 24 h in Group L was significantly less than in Group NS [Table 2]. The mean QoR-40 scores at 24 h and the values of all the subcomponents of the QoR-40 score showed a better score in the patients who received lidocaine than the patients in saline group. The difference in the two groups was statistically significant for all the sub-components after surgery suggested that the overall quality of recovery was superior in patients receiving lidocaine infusion intraoperatively. [Table 2, Figure 1]

**Discussion**

In the present study, a better postoperative quality of recovery was noted in patients who received perioperative systemic lidocaine compared with the control group who received perioperative saline infusion. Besides an improvement in the overall Global QoR-40 score ($P < 0.001$), subjects reported better scores in the physical independence, comfort, and pain subcomponents of the Global QoR-40 questionnaire. Quality of recovery is particularly important in the ambulatory procedures as these patients are often sent home and do not have the structured support of hospital staff and a faster functional recovery is thus desirable.

Patients in the lidocaine group had substantially better postoperative recovery as observed by superior mean QoR scores compared to the saline group ($P < 0.001$). A recent study done using systemic lidocaine in similar doses in patients undergoing laparoscopic bariatric surgery also found that the global QoR-40 scores at 24 h were greater in the lidocaine group, median (IQR) of 165 (151–170) compared to the saline group, median (IQR) of 146 (130–169) [p =0.01].[14] Two more recent studies also demonstrated this improvement in Global QoR score in patients undergoing thyroid surgery and breast cancer surgery who received lidocaine infusion intra-operatively.[15,16] However, systemic lidocaine was not found to improve quality of recovery in patients undergoing robotic thyroidectomy, though it decreased the incidence of chronic post-surgical pain at 3 months.[17] This could be due to use of a higher dose of intravenous lidocaine as compared to other studies, which could have resulted in prolonged sedation of the patients, hence, affecting the overall quality of recovery. This higher dose might also explain the decreased chronic post-surgical pain in study group by a more complete and effective preemptive blocking of nociceptors.

All the 5 sub-components of the QoR-40 score were also found to be superior in the lidocaine group in our study. Similar results were also reported by a recent study reporting the

**Table 2: Results**

| Parameter                                      | Group L          | Group NS          | $P$   |
|------------------------------------------------|------------------|-------------------|-------|
| NRS pain score on arrival in PACU [Median (IQR)] | 0 (0-2)          | 4 (4-5)           | <0.001|
| Ramsay Sedation Score on arrival in PACU [mean±SD] | 2.22±0.85        | 1.63±0.63         | 0.004 |
| No requirement of morphine in PACU (number of patients) | 22 (96%)         | 6 (22%)           | <0.005|
| Nausea & vomiting requiring antiemetics (number of patients) | 2 (9%)           | 11 (41%)          | 0.005 |
| Time to achieve PADSS score ≥9 (mins) [mean±SD] | 30.65±12.37      | 80.00±20.38       | <0.001|
| NRS pain score at 24 h [Median (IQR)] | 1 (0-1)          | 3 (2-3)           | <0.001|
| No requirement of rescue analgesia over 24 h (number of patients) | 22 (96%)         | 6 (22%)           | <0.005|
| Quality of Recovery [Median (IQR)] | 197 (196-199)    | 178 (175-181)     | <0.001|
| Emotional State [Median (IQR)] | 45 (44-45)       | 41 (40-42.5)      | <0.001|
| Physical Comfort [Median (IQR)] | 59 (58-60)       | 52 (49-53.5)      | <0.001|
| Psychological Support [Median (IQR)] | 35 (35-35)       | 33 (32-33)        | <0.001|
| Psychological Independence [Median (IQR)] | 25 (25-25)       | 23 (21.5-23)      | <0.001|
| Pain [Median (IQR)] | 35 (34-35)       | 31 (30-32)        | <0.001|

NRS - Numeric Rating Scale; PACU - Post anesthesia care unit; PADSS - Post anesthesia discharge scoring system; QoR - Quality of recovery
difference in scores in 2 groups with Confidence Interval (CI) for the 5 subcomponents as: physical comfort [6 (0–10)] (P = 0.003); physical independence [4.5 (1–6)] (P = 0.008); emotional state [3.5 (1–6)] (P = 0.02); psychological support [1.5 (1–3)] (P = 0.07); and pain [3 (0–5)] (P = 0.001). Thus, all the subcomponents of the QoR score were better in the group of patients who received lidocaine infusion. [6]

Another important finding is the better postoperative analgesia and reduced requirement of postoperative analgesics and of rescue analgesia in patients who received lidocaine infusion. These findings have been observed by various other investigators. [16,14,18–22] It has been found that patients who consume less opioids report a better postoperative quality of recovery and are discharged earlier than patients who receive a higher dose of opioids. In this study, 96% of patients in the lidocaine group required no opioid supplementation in the PACU versus 22% patients in the saline group (P = 0.000). This difference in opioid consumption may have contributed to a delay in time to discharge in the saline group. A mean reduction of 49.35 min in time to meet hospital discharge criteria was seen in lidocaine group compared with saline (P < 0.001). This time difference may have important ramifications with regards to cost of health care. The finding that systemic lidocaine reduced length of hospital stay after surgery has been seen in previous studies. [18–20] McKay A and colleagues reported no reduction in discharge time after ambulatory surgery in patients who received lidocaine. [22] This may be due to use of different doses of lidocaine and the difference in the timing of administration. Also, different types of surgeries may lead to different modes and patterns of peripheral and central sensitization. In a study done in patients undergoing abdominal hysterectomy also, the intra-operative administration of intravenous lidocaine did not result in reduction of hospital stay. [23] Although 23 additional patients reached discharge fitness on the morning of postoperative day-2, they remained in hospital. The main reason for obtaining such results was found to be discrepancies between discharge fitness and actual discharge. This gap between discharge readiness and discharge from hospital occurred despite prompts from study personnel indicating that patients had met discharge criteria. Such discrepancies are most commonly due to social reasons. [13]

Other common reasons for delay among discharge-ready patients were expected to stay longer, waited for staple removal, no one at home etc., In a meta-analysis done recently on efficacy of intravenous lidocaine on postoperative analgesia following laparoscopic surgery, it was observed that IV lidocaine was associated with decreased pain scores at 24 h, lower opiate requirements, reduced nausea and vomiting and a shorter time until resumption of diet. But again, the duration of hospital stay did not vary between the two study groups. [24]

The Ramsay sedation score on arrival in PACU was higher in patients who received lidocaine (mean RSS = 2.22) as compared to the control group (mean RSS = 1.63) (P = 0.004). Despite this difference, patients who had received lidocaine still attained discharge criteria earlier than control group patients suggesting that the sedation caused by systemic lidocaine is short acting and may not have much clinical significance. Another study done in patients undergoing ambulatory laparoscopic surgery did not find clinically significant differences in sedation scores [difference = 0 (99% CI = (−1)−1)] (P = 0.76) between two study groups at arrival in the PACU. [6] The reason behind these findings could be that the sedation caused by lidocaine in study group was equivalent to sedation caused by hydromorphone bolus doses in the control group, thus showing no clinically significant difference between groups.

Intravenous lidocaine may cause adverse effects on the central nervous and cardiovascular systems. Venthram et al. [24] conducted a meta-analysis on the efficacy of intravenous lidocaine for postoperative analgesia after laparoscopic surgery. The IV lidocaine dose range used in the included studies was a bolus of 1–2 mg/kg (median 1.5 mg/kg) followed by an intraoperative infusion of 1–3 mg/kg/h (median 2 mg/kg/h). Most studies based their doses of IV lidocaine on previously published regimens. The bolus IV dose for treatment of ventricular arrhythmias is 1.5 mg/kg. [25] Evidence of lidocaine toxicity commences at plasma levels >5 μg/ml, convulsive seizures generally require concentrations of 10–15 μg/ml, followed subsequently by cardiovascular depression and collapse. [26] Kaba et al. [4] reported that measured plasma levels of lidocaine were all lower than 5 μg/ml (mean of 2.4 μg/ml (SD 0.6, max 4.0 μg/ml)) at termination of surgery and 2.7 μg/ml (SD 1.1, max 4.6 μg/ml) at the end of a 24 h infusion. It has been demonstrated by various other studies by measuring blood lidocaine levels, that small-dose lidocaine infusion is safe in clinical practice. [3,9,27,28] In our study, we used intravenous lidocaine 1.5 mg/kg loading dose before induction followed by an infusion at 2 mg/kg/h till the end of surgery as these doses have been proven safe in above mentioned studies. [3,9,27,28] No cardiovascular side-effects were observed with the use of intravenously administered lidocaine in our study. It was not possible to comment on early signs of CNS toxicity as all patients received general anesthesia with muscle paralysis.

There was a markedly reduced incidence of nausea and vomiting and thus, anti-emetic requirement in the postoperative period in the patients who had received lidocaine infusion (P = 0.005). In a meta-analysis on effects of intravenous lidocaine on postoperative recovery
after abdominal surgeries, nausea, and vomiting as a single entity was reported in five trials (170 patients). Its incidence was found to be 32% in the lidocaine group and 52% in the control group [odds ratio 0.39 (95% CI 0.20 to 0.76); \( P = 0.006 \). The mechanism behind this effect could again be the opioid-sparing effect of intravenous lidocaine, thus contributing to decreased incidence of postoperative nausea and vomiting.

In a recent systematic review, 45 trials were included to evaluate the efficacy and safety of systemic lidocaine for postoperative analgesia and recovery after surgery. It was observed that intravenous lidocaine reduced postoperative pain at 1–4 h and there was limited evidence to suggest a positive effect of lidocaine on postoperative gastrointestinal recovery, opioid requirements, postoperative nausea and vomiting and length of hospital stay. This systematic review concluded that intravenous lidocaine might be a useful adjuvant in general anesthesia because of its beneficial impact on several outcomes after surgery. The results of our study support these observations. The intraoperative administration of lignocaine markedly improved the overall quality of recovery in patients undergoing gynecological laparoscopic surgery. There were some limitations in our study. Plasma lidocaine levels were not measured as previous investigators have found that plasma levels do not attain toxic levels when administered in the doses used. Also, we studied only one subgroup of patients undergoing gynecological laparoscopic surgery and further studies are required in patients undergoing different types of surgical procedures.

**Conclusion**

Intraoperative systemic lidocaine administration was found to improve postoperative quality of recovery after ambulatory laparoscopic gynecological surgery. The lidocaine infusion is safe, cheap, and easy to administer with no requirement of any complex equipment and may prove to be a highly effective strategy to improve analgesia and quality of recovery after ambulatory surgery.

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**Conflicts of interest**

There are no conflicts of interest.

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Annexure – 1

Annexure 1: QoR-40 Questionnaire

| Question                                           | None of the time | Some of the time | Usually | Most of the time | All of the time |
|----------------------------------------------------|------------------|------------------|---------|------------------|-----------------|
| Able to breathe easy                               | 1                | 2                | 3       | 4                | 5               |
| Feeling comfortable                                 | 1                | 2                | 3       | 4                | 5               |
| Able to return to work, or usual daily activities  | 1                | 2                | 3       | 4                | 5               |
| Able to write                                       | 1                | 2                | 3       | 4                | 5               |
| Have a good sleep                                   | 1                | 2                | 3       | 4                | 5               |
| Have normal speech                                  | 1                | 2                | 3       | 4                | 5               |
| Able to wash, brush teeth or shave                  | 1                | 2                | 3       | 4                | 5               |
| Able to look after own appearance                   | 1                | 2                | 3       | 4                | 5               |
| Having a general feeling of well-being              | 1                | 2                | 3       | 4                | 5               |
| Feeling able to enjoy food                          | 1                | 2                | 3       | 4                | 5               |
| Feeling rested                                      | 1                | 2                | 3       | 4                | 5               |
| Feeling in control                                  | 1                | 2                | 3       | 4                | 5               |
| Able to communicate with hospital staff             | 1                | 2                | 3       | 4                | 5               |
| Able to communicate with family or friends         | 1                | 2                | 3       | 4                | 5               |
| Getting support from hospital doctors               | 1                | 2                | 3       | 4                | 5               |
| Getting support from hospital nurses                | 1                | 2                | 3       | 4                | 5               |
| Having support from family or friends               | 1                | 2                | 3       | 4                | 5               |
| Able to understand instructions or advice           | 1                | 2                | 3       | 4                | 5               |
| Nausea                                             | 5                | 4                | 3       | 2                | 1               |
| Vomiting                                            | 5                | 4                | 3       | 2                | 1               |
| Dry retching                                        | 5                | 4                | 3       | 2                | 1               |
| Moderate pain                                       | 5                | 4                | 3       | 2                | 1               |
| Severe pain                                         | 5                | 4                | 3       | 2                | 1               |
| Feeling restless                                    | 5                | 4                | 3       | 2                | 1               |
| Shaking or twitching                                | 5                | 4                | 3       | 2                | 1               |
| Shivering                                           | 5                | 4                | 3       | 2                | 1               |
| Feeling too cold                                    | 5                | 4                | 3       | 2                | 1               |
| Bad dreams                                          | 5                | 4                | 3       | 2                | 1               |
| Headache                                            | 5                | 4                | 3       | 2                | 1               |
| Muscle pains                                        | 5                | 4                | 3       | 2                | 1               |
| Backache                                            | 5                | 4                | 3       | 2                | 1               |
| Sore throat                                         | 5                | 4                | 3       | 2                | 1               |
| Sore mouth                                          | 5                | 4                | 3       | 2                | 1               |
| Feeling dizzy                                       | 5                | 4                | 3       | 2                | 1               |
| Feeling confused                                    | 5                | 4                | 3       | 2                | 1               |
| Feeling anxious                                     | 5                | 4                | 3       | 2                | 1               |
| Feeling angry                                       | 5                | 4                | 3       | 2                | 1               |
| Feeling depressed                                   | 5                | 4                | 3       | 2                | 1               |
| Feeling alone                                       | 5                | 4                | 3       | 2                | 1               |
| Difficulty falling asleep                           | 5                | 4                | 3       | 2                | 1               |

Total Score:
Annexure – 2

Enrollment

Assessed for eligibility \( (n = 67) \)

Excluded \( (n = 17) \)
  - Not meeting inclusion criteria \( (n = 13) \)
  - Declined to participate \( (n = 4) \)
  - Other reasons \( (n = 0) \)

Randomized \( (n = 50) \)

Allocation

Allocated to intervention (Group L, \( n = 23 \))
  - Received allocated intervention \( (n = 23) \)
  - Did not receive allocated intervention (give reasons) \( (n = 0) \)

Allocated to intervention (Group NS, \( n = 27 \))
  - Received allocated intervention \( (n = 27) \)
  - Did not receive allocated intervention (give reasons) \( (n = 0) \)

Follow-Up

Lost to follow-up (give reasons) \( (n = 0) \)

Discontinued intervention (give reasons) \( (n = 0) \)

Analysis

Analysed \( (n = 23) \)
  - Excluded from analysis (give reasons) \( (n = 0) \)

Analysed \( (n = 27) \)
  - Excluded from analysis (give reasons) \( (n = 0) \)