Comparative evaluation of different volumes of 70% alcohol in celiac plexus block for upper abdominal malignancies

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Abstract

Context: Celiac plexus block (CPB) is an effective way to reduce cancer-associated pain in upper abdominal malignancies. Aims: To evaluate the efficacy and safety of different volumes of 70% alcohol in CPB. Settings and Design: Prospective, randomized, controlled clinical study. Subjects and Methods: Thirty patients of carcinoma gall bladder were randomly divided into three groups (n = 10) to receive 20, 30, and 40 ml of 70% alcohol in CPB. Statistical Analysis Used: All the continuous data were assessed analysis of variance followed by post-hoc tests (Tukey’s Honestly Significant Difference test). Ordinal data were compared using Kruskal-Wallis H-test followed by Mann-Whitney U-test. Categorical comparisons were performed using Chi-square test. Results: A significant difference in visual analog scale (VAS) score of Group I, Group I and Group III was observed from week 6 onward until the end of the study. At all these time intervals, VAS scores in Group I was higher than both Group II and III during this time interval. VAS scores in Group III were significantly lower as compared to Group II from week 10 onward until the end of the study. As compared to baseline, at all the follow-up intervals, mean morphine requirement was significantly lower in Group II and Group III. A quality of life (QOL) score of Group III were higher as compared to Group I. Between Group II and Group III, significant difference was observed at week 16 only when Group III had a higher score as compared to Group II. Conclusions: VAS score, QOL, and reduction in morphine consumption were increased on increasing the volume of alcohol in CPB, 40 ml being most effective.

Key words: Alcohol, celiac plexus, lignocaine, malignancy, neurolysis, pain, transdiscal

Introduction

Abdominal pain is a common debilitating problem in patients with abdominal malignancy and often dramatically affects the quality of life (QOL) and survival.[1-3] Management of cancer-related abdominal pain is a complex and challenging issue.[4-6] An effective means of alleviating the intractable pain associated with abdominal malignancy is imaging-guided celiac plexus block (CPB) and neurolysis.[7] A cocktail of absolute ethanol (95-100%), bupivacaine, and contrast material, with a ratio of 6:3:1 is the most frequently used neurolytic blocking mixture.[8,9] This prospective, randomized, controlled clinical study was conducted to compare the degree of pain relief in patients of upper abdominal malignancies using 20, 30, and 40 ml of 70% alcohol in CPB.

Subjects and Methods

After getting approval from Institutional Ethics Committee, this prospective, randomized study was conducted on 30 patients of upper abdominal malignancies, of either sex having age between 25 and 70 years and in who pain was not relieved by nonsteroidal anti-inflammatory drug (NSAID) or strong opioids like morphine (according to WHO ladder III). Patient on anticoagulants, nonsteroidal anti-inflammatory drug (NSAID), or strong opioids like morphine were excluded from the study. An informed consent was taken from all the patients. The CPB was performed in patient and subjective evaluation of degree of pain relief was done. Patients were randomly divided into three groups of 10 patients each using a computer generated the table.

Sample size estimation

We are comparing the degree of pain relief in patients of upper abdominal malignancies using different volume 20, 30, and 40 ml of 70% alcohol. We are targeting a mean difference in visual analog scale (VAS) score to the tune of 2 with a pooled variability of 1 to be detrimental in the selection of the regimen. For this purpose, the sample size was calculated using the formula: 

\[ n = \left( \frac{16 \times \sigma^2}{d^2} + 1 \right) \]

For the purpose of the present study, \( d = 2 \) and \( \sigma = 1 \). Now putting these values in the above equation we get: 

\[ n = \left( \frac{16 \times 1^2}{2^2} + 1 \right) = 16/4 + 1 = 5. \]

Thus, the calculated sample size was 5 for each group. However, we targeted a sample size of 10 in each group.

Results:

Thirty patients of carcinoma gall bladder were randomly divided into three groups (n = 10) to receive 20, 30, and 40 ml of 70% alcohol in CPB. A significant difference in visual analog scale (VAS) score of Group I, Group I and Group III was observed from week 6 onward until the end of the study. At all these time intervals, VAS scores in Group I was higher than both Group II and III during this time interval. VAS scores in Group III were significantly lower as compared to Group II from week 10 onward until the end of the study. As compared to baseline, at all the follow-up intervals, mean morphine requirement was significantly lower in Group II and Group III. A quality of life (QOL) score of Group III were higher as compared to Group I. Between Group II and Group III, significant difference was observed at week 16 only when Group III had a higher score as compared to Group II. Conclusions: VAS score, QOL, and reduction in morphine consumption were increased on increasing the volume of alcohol in CPB, 40 ml being most effective.

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urine, or cerebrospinal fluid was made before careful aspiration. 2ml contrast (urografin) was injected in order to check the position of needle in the disc. The needle position was confirmed in lateral images by seeing the hugging of dye anterior to the intervertebral disc and in antero-posterior images dye was midline in a position anterior to the intervertebral disc. After this depth is ascertained, the right sided needle was inserted in a similar fashion to a depth of 1.0–1.5 cm farther. After checking the position of the needle, a 3 ml of local anesthetic was given before injection of study solution to prevent the irritation of alcohol. 10, 15, and 20 ml of study solution were used in each needle, in 10 patients of each group, respectively. Before removal of the needle, 2 ml normal saline was injected into each needle to prevent alcohol from tracking back along the needle path.

The effect on pain relief, requirement of oral analgesics and QOL were compared. The patients were divided into one of the following groups using a computer generated random number list:

- **Group I**: Patient on oral morphine (60–90 mg/day) and to block celiac plexus 20 ml of study solution was used
- **Group II**: Patient on oral morphine (60–90 mg/day) and to block celiac plexus 30 ml of study solution was used
- **Group III**: Patient on oral morphine (60–90 mg/day) and to block celiac plexus 40 ml of study solution was used.

The following parameters were recorded:

- **Hemodynamic parameters** - heart rate (HR), systolic, diastolic and mean arterial BP and SpO₂, hypotension was defined as a decrease in systolic arterial pressure ≥20% from baseline and was treated with fluid boluses and intermittent IV mephentermine (0.1 mg/kg). Bradycardia was defined as decrease in HR <60 beats/min and was treated with IV atropine (0.01 mg/kg)
- **Degree of pain relief** - was assessed by using VAS score (0–10) at weekly interval up to 16 weeks. Based on 10 cm line, the left extremity represented no pain at all (score 0) and right extremity represented unbearable pain (score 10). The procedure was considered successful if there was satisfactory pain relief VAS score ≤3 with or without morphine or reduction in the dose of morphine
- **Requirement of oral analgesics** - were also assessed at baseline and weekly interval up to 16 weeks. All the patients before CPB were consuming 60–90 mg morphine per day and they were advised to consume same amount of morphine for 1 week after CPB and after that their dosing were changed according to VAS score
- **QOL of the patients** - was assessed using 100 point scale. The patients were asked to define deterioration in QOL assuming QOL before the disease as 100 on the scale
- **Incidence of side effects/complications i.e.,** pain at injection site, back pain, hypotension, bradycardia, diarrhea, respiratory depression, arrhythmias, paraplegia, visceral puncture, pneumothorax, retroperitoneal fibrosis, impotence were recorded, and treated accordingly.

Data were analyzed using Statistical Package for Social Sciences, version 15.0 (IBM). As sample size was small, hence normality check was performed. As the distributions were normal, hence all the continuous data were assessed using analysis of variance followed by post-hoc tests (Tukey’s Honestly Significant Difference test). Ordinal data were compared using Kruskal–Wallis H-test followed by Mann–Whitney U-test for between group comparisons. Categorical comparisons were performed using Chi-square test. The confidence level of this study was kept at 95%, hence a P < 0.05 indicated a statistically significant difference.

**Results**

Demographic variables of patients are shown in Table 1. As systolic BP, diastolic BP, mean arterial pressure, and HR were continuous variables, but the sample size was small (<30 for each group); hence, normality of the distributions was checked to determine the plan of analysis. Normality of distribution was assessed only at baselines. All the distributions were normal; hence, a parametric evaluation plan was adopted for evaluation of these parameters in different groups. No clinically significant changes were noted in hemodynamic parameters.

VAS scores are shown in Table 2 and Figure 1. Statistically, significant intergroup differences were observed from week 6 to the end of study ($P < 0.001$). A significant difference in VAS score of Group I, Group II and Group III was observed from week 6 onward to the end of study. At all these time intervals, VAS scores in Group I was higher than both Groups II and III during this time interval. VAS scores in Group III were significantly lower as compared to Group II from week 10 onward to the end of study. At baseline, all the patients had same requirement of Morphine. After CPB the morphine requirement was reduced as shown in Tables 3 and 4.

At baseline, QOL scores did not show a significant intergroup difference ($P = 0.165$). An intergroup difference in QOL scores was observed at week 3 onward until the end of study as shown in Table 5 and Figure 2.

Except for pain at injection site, mild back pain or diarrhea in few patients, no significant side effects were observed in any of the groups. Statistically too, the differences in these features among different groups were not significant ($P > 0.05$) [Table 6 and Figure 3].

**Discussion**

Upper Abdominal cancer patients may experience severe pain that is, resistant to oral opioids. In addition, excessive sedation or other side effects may limit the acceptability and usefulness of oral opioids therapy. Neurolysis of celiac plexus (NCPB) appeared boon to cancer pain. It appears to be a safe, cost-effective approach to treating visceral pain associated with cancer. The benefits include improved analgesia, reduced opioid consumption, favorable economic implications, and superior clinical effects due to the avoidance of deleterious properties of high-dose chronic opioid therapy.

**Degree of pain relief**

There was significant pain relieved in patients of all the three groups after CPB. This was demonstrated by decrease in VAS score. In the present study, VAS score ≤3 with or without opioid medication was taken as a successful CPB.

![Figure 1: Intergroup comparison of visual analogue scale scores at different time intervals](image-url)
Mecradante[10] found that CPB made pain control possible with a reduction in opioid consumption for a mean survival period of about 51 days. Furthermore, Eisenberg et al.[4] suggested that NCPB has long-lasting benefit for 70–90% of patients with pancreatic and other intra-abdominal cancers, regardless of the technique used. Bridenbaugh et al.[11] concluded that this simple procedure proved effective in controlling the pain without any serious complications. Kawamata et al.[12] found that VAS scores significantly improved for 4 weeks after CPB and concluded that the VAS scores were lower in CPB group than MOR group. Amr and Makharita[13] found that the analgesia induced by the celiac block after medically controlling pain was
better and more sustained when compared with the outcome on performing a celiac block at a high VAS score >7.

In the present study, a fall in VAS scores was observed 15 min after intervention in all the three groups, which was due to the effect of local anesthetic agent lidocaine. The lowest VAS score in all the three groups was observed at the end of 2nd week. This finding of our study is supported by Eisenberg et al.\textsuperscript{[4]} In their study, good to excellent pain relief was reported in 89% of patients during the first 2 weeks after NCPB. Furthermore,

Soweid and Azar\textsuperscript{[41]} found that 78% of patients reported a drop in pain score 2 weeks after the procedure. In 2013, Seicean\textsuperscript{[45]} also found that average pain and worst pain had decreased significantly by 2 weeks after the procedure, but complete relief using pain killers was not significantly different, although some patients gave up their morphine-based medication.

In the present study, VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically. In Group I, the VAS scores in Group I were lower as compared to baseline at all follow-up intervals except from 12 weeks onward to the end of study where the difference from baseline was not significant statistically.
The values were significantly higher (improved QOL) at all the follow-up intervals in the Group II and Group III. At all these intervals, the values were significantly higher (improved QOL) as compared to Group I. Between Group I and Group III, significant differences were observed from week 2 onward until the end of the study. QOL score of Group III were higher (improved QOL) as compared to Group I. Between Group II and Group III, significant difference was observed at week 16 only when Group III had higher score (improved QOL) as compared to Group II.

This result of our study is supported by Amr and Makharita. They found that QLQ-C30 assessment revealed a significant improvement in daily life activity and QOL after injection in both groups but with more significant improvement in the group in which the celiac block was performed after medical therapy. Similarly, Rykowski and Hilgier concluded that patients who had good pain relief after neurolysis had improved alertness and QOL. Matamala et al. concluded that decreased opioid consumption may improve the QOL by decreasing sedative effect of opioids and enhance the immune system as it was shown that opioids had a negative effect on immunity at cellular level. However, Kawamata et al. found that sufficient pain management with the least side effects does not remarkably improve QOL in patients with pancreatic cancer pain, but it can prevent deterioration in QOL. To improve the QOL significantly, socio-environmental supports including home care are necessary, as well as pain management and palliative care, and concluded that CPB does not directly improve QOL in patients with pancreatic cancer pain, but it may prevent deterioration in QOL by the long-lasting analgesic effect, limitation of side effects, and the reduction of morphine consumption, compared to treatment only with NSAID-morphine. Similarly, Wong et al. concluded that NCPB improves pain relief as compared to systemic analgesic intervention alone but it does not influences QOL or survival. From the observations of our study, we cannot comment on the improvement survival of the patients received CPB because first; we had excluded those patients, who did not complete the 16 weeks follow-up period for any reason, second, due to the short follow-up period, and finally, it was not included in the objective of our study.

### Complications

In the present study except for pain at injection site, mild back pain, and diarrhea were noticed in few patients, and they were transient in nature, no other side effects were observed in any of the groups. Eisenberg et al. concluded that common adverse effects were transient, including local pain (96%), diarrhea (44%), and hypotension (38%). In the present study, none of the patient experienced bradycardia or hypotension. The may be due to preloading with Ringer’s lactate by increasing amount of 70% alcohol up to 40 ml the incidence of side effects were not increased in the present study.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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However, there is insufficient data for the possible consequences of tamoxifen. Therefore, there should be proper discussion and counseling regarding the possible teratogenic and fetal adverse effects of tamoxifen.

Tamoxifen treatment may cause genital defects in humans, potentially leading to developmental defects. It is important to note that it may take 4–5 months for the cycle to become regular. Animal studies have shown that tamoxifen can causeamenorrhea in premenopausal breast cancer patients. Due to its high incidence in young women, with 10% of cases diagnosed before the age of 40, breast cancer is the most common malignancy affecting young women.

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Dear Editor,

We recently reported a case of pregnancy on tamoxifen as a treatment for advanced breast cancer, using tamoxifen. In the initial phase of tamoxifen treatment, it may stimulate ovulation and thus make the woman more fertile. In premenopausal breast cancer patients, Tamoxifen is the mainstay of adjuvant hormonal treatment in young women, offering a 20–30% reduction in breast-cancer recurrence compared with chemotherapy.

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