

## ASSESSMENT OF SAFETY AND EFFICACY OF TRAMADOL IN MANAGEMENT OF PAIN IN POSTOPERATIVE CANCER PATIENTS

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### ABSTRACT

**Background:** Cancer is the second common cause of death worldwide.

One of the well-known treatment options in early stages of cancer is tumor excision through surgery. The management of pain postoperatively is one of the main aim of clinicians to enhance post-operative health quality as well as patients satisfaction towards the therapy. **Objectives:** This study was conducted to assess the safety and efficacy of tramadol in the management of pain in postoperative cancer patients as well as to assess improvements in quality of life of patients after surgery. **Materials & Methods:** A prospective, cross-sectional, observational study was conducted among the postoperative cancer patients who were treated with 100mg of tramadol intravenously twice

a day to manage the pain. The pain intensity was measured on post-operative day (POD) 1, 3 & 5 using VAS scale to find the efficacy of tramadol. Patients were also observed for occurrence of ADRs. Further patients were assessed for quality of life (QoL) at baseline and after a month of surgery using SF-36 questionnaire. **Results:** The mean VAS score on POD 1, 3 and 5 were 6.18, 3.69 and 1.37 ( $P < 0.0001$ ) respectively. Constipation was the most commonly experienced ADR (55.4%). The QoL assessment with SF-36 questionnaire revealed that there was improvement in Physical functioning, energy, social functioning, emotional well-being, and general health and decrease in bodily pain after a month ( $p < 0.00001$ ) among all the subjects. But all the subjects showed increase in role limitations due to physical health and emotional problems. **Conclusion:** By this study it was confirmed

that tramadol was found to be effective in managing post-operative moderate to severe pain. Improvement in QoL of cancer patients was observed. The ADRs occurred were mild which could be managed without any intervention. Hence tramadol is found effective and safe in management of post-operative pain.

**KEYWORDS:** Cancer, Surgery, Tramadol, VAS, SF-36, QoL.

## INTRODUCTION

Worldwide cancer turned as second common cause of death.<sup>[1]</sup> Every year, around 6 million fatalities i.e., about 12% and merely 10 million new cases were reported due to incidence of cancer. According to the estimations globally more than 22 million people would be living with cancer, at any given point of time.<sup>[2]</sup> In India, the cancer cases each year is more than one million and is expected to double during the next two decades.<sup>[3]</sup> In Karnataka, the prevalence of 1.5 lakh cancer cases can be seen and about 35,000 new cancer cases gets added to this pool every year.<sup>[2]</sup> Surgical management is considered as one of the essential component in the treatment of cancer<sup>[4]</sup> as it is the mainstay in the cure and control of most of the malignant tumors, that can save or improve the lifespan of people suffering from cancer.<sup>[5]</sup>

The experience of postoperative acute pain is observed in many patients after both major and minor surgery<sup>[6]</sup> since pain is a natural protective mechanism and unavoidable.<sup>[7]</sup> In general pain is described as the uncomfortable sensations in the body.<sup>[8]</sup> According to the International Association for Study of Pain (IASP), it is defined as an “unpleasant emotional and sensory experience due to actual or potential tissue damage or described in terms of such damage”.<sup>[7,9]</sup> The maximum intensity of pain is experienced in the early post-operative hours.<sup>[10]</sup> The main cause of all pain is inflammation and inflammatory response.<sup>[8]</sup> Thus, it acts as a response to an acute inflammatory process that starts with surgical trauma and ends with tissue healing.<sup>[7]</sup> In the past 3 to 4 decades it has been confirmed by studies that 20 to 80% of patients who undergo surgery suffer from inadequately treated pain. Thus both in the developed and in developing countries, pain is said to be a serious complication.<sup>[11]</sup>

The major goals of postoperative management are to ensure effective pain relief for the patients who underwent surgery. It is desirable to have medicines that provide effective pain relief with minimal side effects.<sup>[12]</sup> The preferable analgesics like non-steroidal anti-inflammatory drugs (NSAID) and opioids are on trend currently for the management of

pain.<sup>[8]</sup> Opioid analgesics are the traditional choice for the management of postoperative moderate-to-severe type of pain.<sup>[12]</sup> Tramadol is a centrally acting analgesic by activating the  $\mu$ -opioid receptor and another by inhibiting the neurotransmitter reuptake of norepinephrine and serotonin.<sup>[12,13,16]</sup> and it is used to treat moderate to severe cancer and non-cancerous pain from many decades. It is considered to be the Step 2 analgesic in WHO pain ladder<sup>[14]</sup> and has different pharmacodynamic characteristics compared to other more classic opioids, thus it is considered to be the first member of atypical opioids group.<sup>[15]</sup> Tramadol has rapid onset of action with no ceiling dose therefore, pain management can be individually tailored to patient/pain response.<sup>[17]</sup>

According to WHO report, adverse reactions of tramadol in the therapeutic dose include nausea and dizziness (> 10%), dry mouth, drowsiness, fatigue, constipation headache, increased sweating, vomiting (1-10%), cardiovascular dysregulation and diarrhea (0.1-1%). Respiratory depression, epileptiform convulsions, tremor, bradycardia, hallucinations, and anxiety are rare (0.01-0.1%).<sup>[18]</sup> For the patients undergoing surgery, the sedative effect of tramadol could be beneficial, but other effects are undesirable during postoperative period.<sup>[12]</sup> Tramadol in short term use for postoperative pain management has no significant risk of addiction<sup>[17]</sup> and has lesser risk of inducing respiratory depression than other opioids due to its nonopioid action.<sup>[12]</sup> The tolerability profile of tramadol is favourable when compared to other strong classical opioids, so it is usually preferred initially in the management moderate to severe cancer and noncancerous-related pain.<sup>[14]</sup> The present study was planned to assess the effectiveness of tramadol in regulating the post -surgical pain management in cancer patients.

## MATERIALS AND METHODS

A prospective cross-sectional observational study was conducted in Department of Surgery, S S Institute of Medical Science and Research Centre - A Tertiary Teaching Hospital, Davangere, Karnataka, India for a period of three months. The ethical clearance for the study was obtained from "The Bapuji Pharmacy College Institutional Ethics Committee" Davangere, Karnataka, India. The study was conducted according to principles of declaration of Helmsinki. From reference to literature<sup>[3]</sup>, a prevalence of 50.7% was assumed and sample size was calculated and was anticipated to be 384 patients. The patients were selected based on the inclusion and exclusion criteria. The inclusion criteria were age greater than 18 years, either gender, patients with any type of cancer, who had undergone tumor excision, with no

history of drug abuse, who were communicative & cooperative and exclusion criteria were patients who were on treatment with other analgesics, naloxone therapy, previously treated with other strong opioids, those with the symptoms of respiratory insufficiency, disorders of consciousness, central nervous system primary neoplasm or brain metastases, impaired sensory or cognitive function, clinically significant liver dysfunction and or renal dysfunction, pregnant and lactating women.

Post-operatively patients were administered with tramadol at 100mg twice a day. Visual analogue scale (VAS) was employed for measurement of pain intensity on post-operative days (POD) as on POD1, POD3 and POD5 to find the effect of tramadol. The ADRs due to administration of tramadol were also recorded. The causality and severity assessment of ADRs was done using Naranjo scale<sup>[25]</sup> and Hartwig scale<sup>[26]</sup> respectively. In addition, the quality of life (QoL) of cancer patients was assessed during the hospital stay (baseline) and after a month using short form -36 (SF-36).

## RESULTS

Among 165 cancer patients, a total of 152 subjects were included in the current study. Notably, there were no subjects from the age group of 18-30. 31-45 years age group had 33(21.71%) participants, age group of 46-60 years had 78(51.32%) subjects and participants who aged between 61-75 years were 41(26.97%). The mean age group of the subjects was 53.96 years. The mean age group of the subjects was 53.96 years, in total 103(67.76%) subjects were females and 49(32.24%) were males.

**Table 1: Demographic data of the subjects.**

| Demographic variables | Groups     | n(%)        |
|-----------------------|------------|-------------|
| Age (years)           | 31-45      | 33 (21.71)  |
|                       | 46-60      | 78(51.32)   |
|                       | 61-75      | 41(26.97)   |
| Gender                | Female     | 103 (67.76) |
|                       | Male       | 49(32.24)   |
| <b>Total</b>          | <b>152</b> |             |

As represented in table 2, the majority of subjects had reported with various cancer type such as breast cancer 71(46.71%), lung Cancer 16(10.53%), cervical cancer 13(8.55%), colorectal cancer 11(7.24%), ovarian cancer 10(6.58%), cheek cancer 8(5.26%), prostatic cancer 7(4.6%), thyroid cancer 5(3.29%), throat cancer 4(2.63%), tongue cancer 4(2.63%) and least number of the subjects were suffered from liver cancer 3(1.97%).

As the proportion of females with breast cancer were more in the present study, the most commonly performed surgical procedure was modified radical mastectomy 47(30.92%) simple mastectomy 14(9.21%), breast lumpectomy 3(1.97%), central quadrantectomy 3(1.97%), palliative mastectomy 2(1.32%), toilet mastectomy 1(0.66%), breast conservative surgery 1(0.66%), partial lobectomy 16(10.53%). Other surgical procedures that were performed are hysterectomy 6(3.95%), radical hysterectomy 6(3.95%), pelvic lymphadenectomy 1(0.66%), laparoscopic colectomy 10(6.58%), open colectomy 1(0.66%), oophorectomy 10(6.58%), reconstructive surgery 6(3.95%), radical neck dissection 2(1.32%), radical prostatectomy 7(4.6%), thyroidectomy 3(1.97%), thyroid lobectomy 2(1.32%), partial laryngectomy 4(2.63%), partial glossectomy 4(2.63%) and partial hepatectomy 3(1.97%) as shown in table 2.

**Table 2: Distribution of subjects based on type of cancer and type of surgical procedure performed among the subjects.**

| Type of cancer    | n(%)       | Type of surgical procedure  | n(%)       |
|-------------------|------------|-----------------------------|------------|
| Breast Cancer     | 71 (46.71) | Modified Radical Mastectomy | 47 (30.92) |
| Lung Cancer       | 16 (10.53) | Simple Mastectomy           | 14 (9.21)  |
| Cervical Cancer   | 13 (8.55)  | Breast Lumpectomy           | 03 (1.97)  |
| Colorectal Cancer | 11 (7.24)  | Central Quadrantectomy      | 03 (1.97)  |
| Ovarian Cancer    | 10 (6.58)  | Palliative Mastectomy       | 02 (1.32)  |
| Cheek Cancer      | 08 (5.26)  | Toilet Mastectomy           | 01 (0.66)  |
| Prostatic Cancer  | 07 (4.6)   | Breast Conservative Surgery | 01 (0.66)  |
| Thyroid Cancer    | 05 (3.29)  | Partial Lobectomy           | 16 (10.53) |
| Throat Cancer     | 04 (2.63)  | Hysterectomy                | 06 (3.95)  |
| Tongue Cancer     | 04 (2.63)  | Radical Hysterectomy        | 06 (3.95)  |
| Liver Cancer      | 03 (1.97)  | Pelvic Lymphadenectomy      | 01 (0.66)  |
|                   |            | Laparoscopic Colectomy      | 10 (6.58)  |
|                   |            | Open Colectomy              | 01 (0.66)  |
|                   |            | Oophorectomy                | 10 (6.58)  |
|                   |            | Reconstructive Surgery      | 06 (3.95)  |
|                   |            | Radical Neck Dissection     | 02 (1.32)  |
|                   |            | Radical Prostatectomy       | 07 (4.6)   |
|                   |            | Thyroidectomy               | 03 (1.97)  |
|                   |            | Thyroid Lobectomy           | 02 (1.32)  |
|                   |            | Partial Laryngectomy        | 04 (2.63)  |
|                   |            | Partial Glossectomy         | 04 (2.63)  |
|                   |            | Partial Hepatectomy         | 03 (1.97)  |
| <b>Total</b>      | <b>152</b> | <b>Total</b>                | <b>152</b> |

#### Assessment of efficacy of tramadol in cancer related post-operative pain

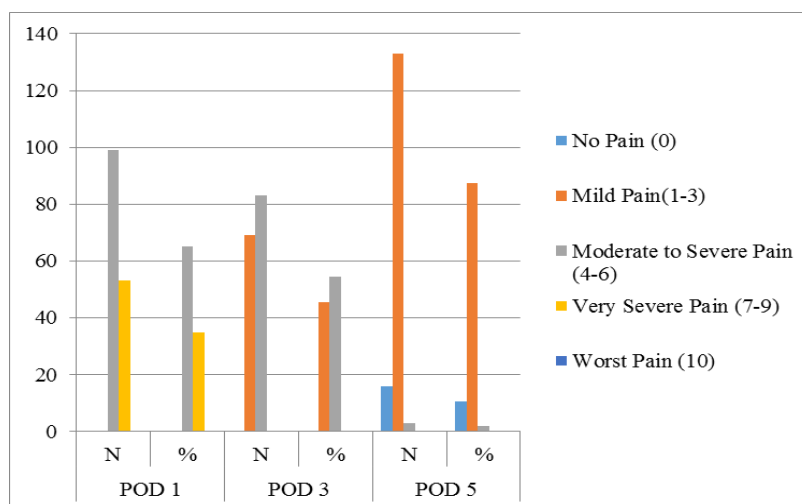
After the initiation of tramadol administration, 99 (65.13%) of them had moderate to severe pain, 53(34.87%) had very severe pain on POD 1. 83 patients had moderate to severe pain, 69 patients had mild pain on POD 3 and 133 patients had mild pain, 16 patients had no pain and

3 patients had moderate to severe pain on POD 5 as show in in table 3. On POD 5, we witnessed drop in the number of patients with moderate to severe pain, as well as very severe pain, and number of patients noticed with mild pain or no pain.

After receiving 100 mg tramadol (i.v.) twice daily, the individuals' pain intensity was measured on POD1, POD 3 and POD5 and the mean VAS score was 6.18,3.69 and 1.37 respectively ( $p<0.0001$ ). It was observed that individuals saw a significant reduction in pain and is represented in table 4. Thus, tramadol can be used to relieve pain ranging from moderate to severe.

**Table 3: Distribution of study subjects based on severity of pain.**

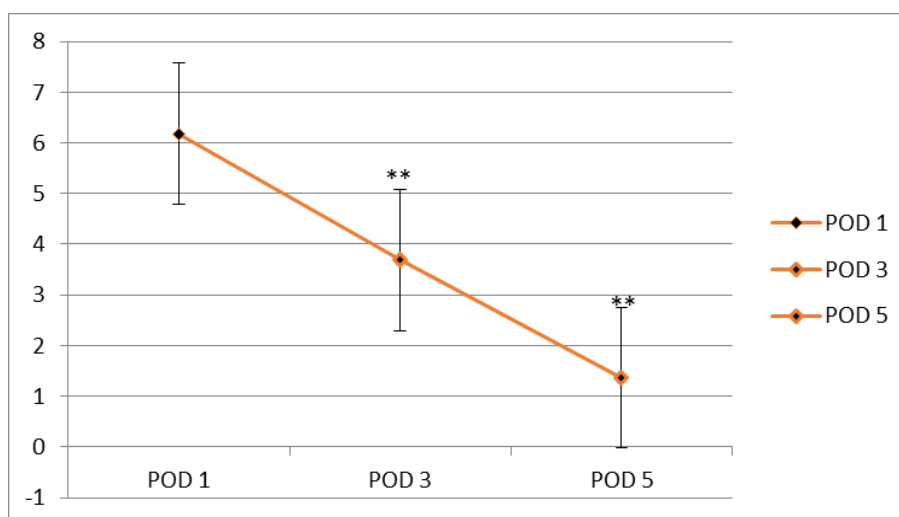
| Pain assessment with VAS score | Number of patients(n=152) |                |                |
|--------------------------------|---------------------------|----------------|----------------|
|                                | POD 1<br>N (%)            | POD 3<br>N (%) | POD 5<br>N (%) |
| No Pain (0)                    | 0 (0)                     | 0 (0)          | 16 (10.53)     |
| Mild Pain(1-3)                 | 0 (0)                     | 69 (45.40)     | 133 (87.50)    |
| Moderate to Severe Pain (4-6)  | 99 (65.13)                | 83 (54.60)     | 3 (1.97)       |
| Very Severe Pain (7-9)         | 53 (34.87)                | 0 (0)          | 0              |
| Worst Pain (10)                | 0(0)                      | 0(0)           | 0              |



**Figure 1: Distribution of study participants based on severity of pain on POD1, POD3 and POD5.**

**Table 4: Post-operative pain control on POD 1, POD 3 and POD 5 using tramadol.**

|       | VAS score (mean $\pm$ SD) | p-value    |
|-------|---------------------------|------------|
| POD 1 | 6.18 $\pm$ 0.76           | -          |
| POD 2 | 3.69 $\pm$ 0.85           | < 0.0001** |
| POD 5 | 1.37 $\pm$ 0.81           | < 0.0001** |



**Figure 2: Representation of pain intensity using mean VAS score on POD1, POD3 and POD5.**

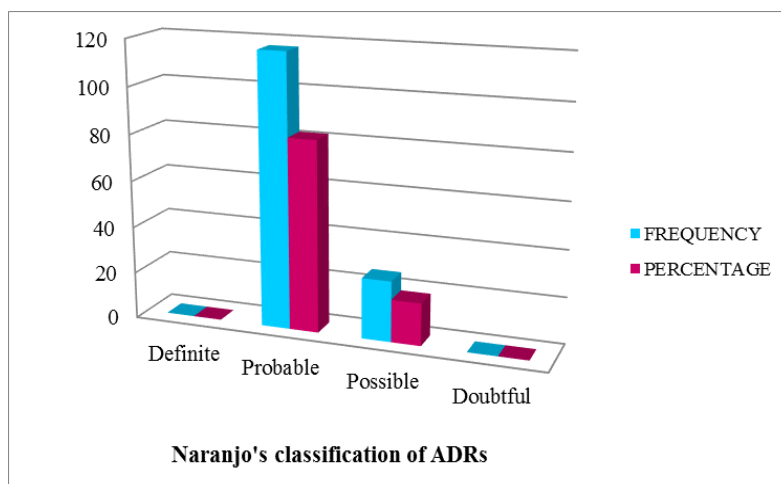
#### **Assessment of ADRs experienced by the subjects and causality assessment of ADRs using Naranjo's scale**

Upon administration of tramadol (i.v), a total of 107(70.40%) subjects experienced ADRs. Constipation was the most commonly experienced ADR among the subjects 59(55.14%) followed by dry mouth 47(43.92%), fatigue 25(23.36%), nausea 8(7.48%), dizziness 3(2.80%) and sedation 1(0.94%) was least experienced ADR as represented in table 5. The ADRs experienced by the participants were assessed for their causality by Naranjo's scale. The total number of ADRs experienced by the subjects were 143, out of which 117(81.82%) ADRs were categorized as probable and 26(18.18%) as possible, and there were no ADRs in the definite and doubtful categories as shown in Table 5.

**Table 5: Details of the subjects who experienced ADRs and causality assessment of ADRs using Naranjo's scale.**

| ADRs         | n(%)       | Causality assessment by Naranjo's scale                                  | n(%)        |
|--------------|------------|--|-------------|
| Constipation | 59 (55.14) | <b>Definite</b><br><b>Probable</b><br><b>Possible</b><br><b>Doubtful</b> | 0 (0)       |
| Dry Mouth    | 47 (43.92) |  | 117 (81.82) |
| Fatigue      | 25(23.36)  |  | 26 (18.18)  |
| Nausea       | 8 (7.48)   |  | 0 (0)       |
| Dizziness    | 3 (2.80)   |  |             |
| Sedation     | 1 (0.94%)  |  |             |
| Others       | 0 (0)      |  |             |
| <b>Total</b> | <b>107</b> | <b>Total</b>   | <b>143</b>  |





**Figure 3:** Graphical representation of causality assessment of ADRs using Naranjo's scale.

### Severity assessment of ADR using Hartwig's scale

The safety assessment of tramadol use was made by applying Hartwig's severity assessment scale and we found that all the ADRs experienced by the subjects were under mild category 143(100%) and is represented in table 6. Therefore, tramadol is considered as a safe analgesic to be used in the age group of 31- 75 years at a dose of 100 mg twice daily.

**Table 6:** Classification of ADRs based on severity.

| Severity of ADRs | N (%)     | Examples   |
|------------------|-----------|--|
| Mild-Level 1     | 143(100%) | Constipation, dry mouth, fatigue, nausea, dizziness, sedation. |
| Mild-Level 2     | 0         | -  |
| Moderate-Level 3 | 0         | -  |
| Moderate-Level 4 | 0         | -  |
| Severe-Level 5   | 0         | -  |
| Severe-Level 6   | 0         | -  |
| Severe-Level 7   | 0         | -  |

### Assessment of QoL using SF-36 questionnaire in cancer patients

Patients were also assessed for the quality of life (QoL) using SF-36 during the hospital stay (baseline) and after a month, the mean total score of the SF-36 was  $60.37 \pm 25.11$  and  $61.32 \pm 23.49$ . Table no 7 shows the mean and standard deviation for the SF-36 subscales. With a  $p < 0.0001$  there was improvement in Physical functioning, energy, social functioning, emotional well-being and general health. Subjects showed decrease in bodily pain. But all the subjects showed more role limitations due to physical health and emotional problems.



Table 7: Quality of life assessment using SF-36.

| Domains                                    | Mean $\pm$ SD     |                   | p value    |
|--|-------------------|-------------------|------------|
|  | Baseline          | After a month     |            |
| Physical functioning                       | 34.18 $\pm$ 11.59 | 74.24 $\pm$ 9.29  | <0.00001** |
| Role limitations due to physical health    | 75.33 $\pm$ 30.99 | 39.47 $\pm$ 27.53 | <0.00001** |
| Role limitations due to emotional problems | 74.17 $\pm$ 30.88 | 41.22 $\pm$ 27.34 | <0.00001** |
| Energy or Fatigue                          | 49.80 $\pm$ 10.58 | 65.13 $\pm$ 13.15 | <0.00001** |
| Emotional well being                       | 58.00 $\pm$ 8.16  | 65.90 $\pm$ 12.70 | <0.00001** |
| Social functioning                         | 83.55 $\pm$ 15.32 | 69.08 $\pm$ 13.57 | <0.00001** |
| Pain                                       | 83.16 $\pm$ 17.05 | 76.41 $\pm$ 10.63 | <0.00001** |
| General Health                             | 39.28 $\pm$ 10.03 | 44.67 $\pm$ 8.55  | <0.00001** |

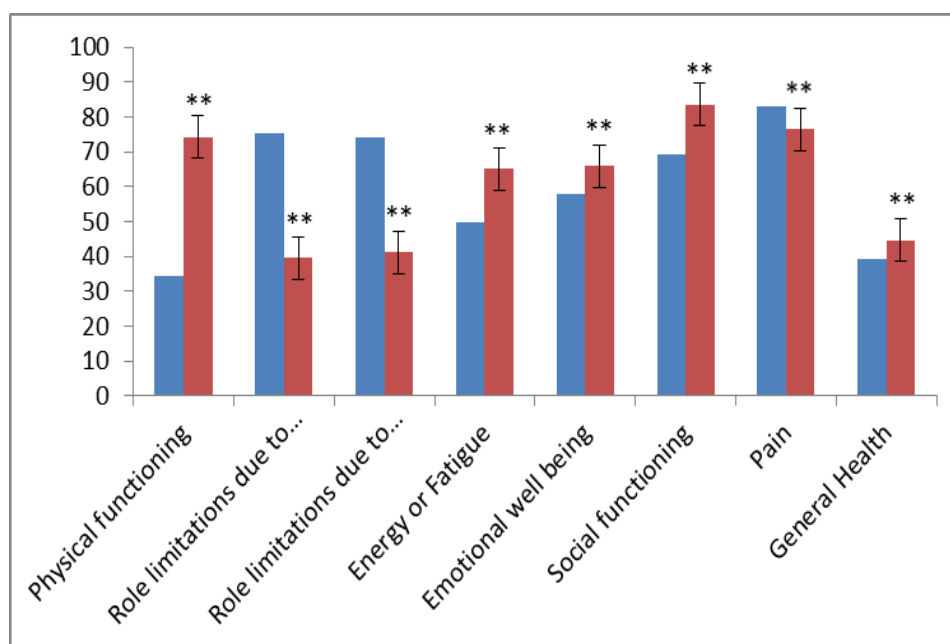


Figure 4: Representation of quality of life (QoL) of cancer patients using SF-36 at baseline and after a month.

#### Comparison of demographic, cancer – related and treatment related variables with sub-domains of SF-36

The determinants impacting quality of life (QoL) in cancer patients were assessed by comparing after a month SF-36 subscale mean scores with specific demographic and disease-related characteristics. Table 8 shows that there were no significant differences in the QoL among different age groups and gender.

**Table 8: Comparison of demographic variables with sub domains of SF-36.**

| Variables      | PF     | RP     | RE     | E/F     | EWB    | SF     | BP     | GH     |
|----------------|--------|--------|--------|---------|--------|--------|--------|--------|
| <b>Age</b>     |        |        |        |         |        |        |        |        |
| 31-45          | 75.45  | 76.52  | 77.98  | 65.76   | 67.15  | 84.85  | 86.14  | 43.48  |
| 46-60          | 74.87  | 75.96  | 72.65  | 66.67   | 68.00  | 85.74  | 83.81  | 45.26  |
| 61-75          | 72.07  | 73.17  | 73.99  | 61.71   | 60.88  | 78.35  | 79.51  | 44.51  |
| <b>P value</b> | 0.2075 | 0.8709 | 0.7099 | 0.1409  | 0.1102 | 0.1105 | 0.1110 | 0.6049 |
| <b>Gender</b>  |        |        |        |         |        |        |        |        |
| Male           | 76.63  | 68.37  | 78.37  | 62.35   | 63.84  | 80.61  | 81.63  | 45.41  |
| Female         | 73.11  | 78.64  | 72.17  | 66.46   | 66.87  | 84.95  | 83.88  | 44.32  |
| <b>P value</b> | 0.2829 | 0.5579 | 0.248  | 0.71549 | 0.1689 | 0.1028 | 0.4487 | 0.4652 |

**PF-** Physical functioning; **RP-**Role limitations due to physical health; **RE-** Role limitations due to emotional problems; **E/F-** Energy or Fatigue; **EWB-**Emotional Well-being; **SF-** Social functioning; **BP-** Bodily pain; **GH-**General health.

The comparison of cancer related variables with sub-domains of SF-36 revealed that, patients with various forms of cancer ( $p=0.00057$ ) and those who underwent surgery ( $p=0.00004$ ) had low physical functional mean scores. Patients with various forms of cancer ( $p=0.0001$ ) and patients who underwent surgery ( $p=0.00004$ ) had considerably increased role limitations owing to physical health. Cancer patients who underwent surgery had significantly lower mean ratings for role limitation due to emotional issues ( $p=0.0387$ ). Subjects with various cancer types ( $p=0.017$ ) showed significant reduction in energy. Subjects with various forms of cancer ( $p=0.019$ ) and patients who underwent surgical procedures ( $p=0.013$ ) had significantly lower emotional well-being scores which is represented in table 9. Table 9 also shows that patients who underwent surgery had a lower mean score for general health ( $p=0.0351$ ).

**Table 9: Comparison of cancer related variables with sub domains of SF-36.**

| Variables             | PF       | RP       | RE     | E/F    | EWB    | SF    | BP    | GH    |
|-----------------------|----------|----------|--------|--------|--------|-------|-------|-------|
| <b>Type of cancer</b> |          |          |        |        |        |       |       |       |
| Breast cancer         | 74.08    | 75.00    | 72.30  | 66.27  | 67.32  | 85.21 | 85.04 | 44.37 |
| Lung cancer           | 74.67    | 65.00    | 73.36  | 53.33  | 57.07  | 72.50 | 83.83 | 46.00 |
| Cervical cancer       | 66.15    | 84.62    | 71.79  | 65.38  | 72.31  | 84.62 | 84.81 | 40.77 |
| Colorectal cancer     | 67.27    | 93.18    | 90.92  | 68.64  | 59.64  | 87.50 | 85.91 | 46.82 |
| Ovarian cancer        | 77.50    | 95.00    | 53.35  | 71.00  | 65.60  | 85.00 | 77.25 | 46.50 |
| Cervical cancer       | 80.62    | 90.62    | 48.12  | 66.88  | 64.00  | 81.25 | 74.69 | 44.38 |
| Prostate cancer       | 80.71    | 32.14    | 100.00 | 70.00  | 65.71  | 87.50 | 74.29 | 49.29 |
| Thyroid cancer        | 79.00    | 70.00    | 66.66  | 62.00  | 59.20  | 85.00 | 83.00 | 43.00 |
| Throat cancer         | 80.00    | 31.25    | 66.65  | 60.00  | 76.00  | 84.38 | 83.75 | 42.50 |
| Tongue cancer         | 80.00    | 100.00   | 100.00 | 73.75  | 75.00  | 93.75 | 95.00 | 46.25 |
| Liver cancer          | 75.00    | 83.33    | 77.77  | 56.67  | 69.33  | 70.83 | 74.17 | 45.00 |
| <b>P value</b>        | 0.00057* | <0.0001* | 0.063  | 0.017* | 0.019* | 0.133 | 0.519 | 0.740 |

| Type of surgery             |          |        |        |        |        |        |        |        |
|-----------------------------|----------|--------|--------|--------|--------|--------|--------|--------|
| Modified radical mastectomy | 73.72    | 71.28  | 71.63  | 64.79  | 65.28  | 83.78  | 84.42  | 43.83  |
| Simple mastectomy           | 75.00    | 91.07  | 69.04  | 70.00  | 69.14  | 89.29  | 86.43  | 47.50  |
| Breast lumpectomy           | 75.00    | 100.0  | 100.00 | 68.33  | 74.67  | 87.50  | 93.33  | 51.67  |
| Central quadrantectomy      | 80.00    | 83.33  | 77.77  | 71.67  | 78.67  | 87.50  | 93.33  | 40.00  |
| Palliative mastectomy       | 72.50    | 62.50  | 83.35  | 72.50  | 76.00  | 100.00 | 90.00  | 47.50  |
| Toilet mastectomy           | 75.00    | 25.00  | 33.33  | 55.00  | 76.00  | 75.00  | 67.50  | 30.00  |
| Breast conservative surgery | 60.00    | 00.00  | 66.70  | 60.00  | 56.00  | 62.50  | 52.50  | 25.00  |
| Partial lobectomy           | 73.75    | 60.94  | 68.78  | 52.50  | 56.50  | 70.31  | 82.03  | 45.31  |
| Hysterectomy                | 69.17    | 91.67  | 83.33  | 66.67  | 76.67  | 91.67  | 91.67  | 44.17  |
| Radical hysterectomy        | 62.50    | 79.17  | 61.10  | 63.33  | 66.67  | 77.08  | 79.17  | 38.33  |
| Pelvic lymphadenectomy      | 70.00    | 75.00  | 66.70  | 70.00  | 80.00  | 87.50  | 77.50  | 35.00  |
| Laparoscopic colectomy      | 69.50    | 92.50  | 90.01  | 69.50  | 59.60  | 87.50  | 86.75  | 47.50  |
| Open colectomy              | 45.00    | 100.00 | 100.00 | 60.00  | 60.00  | 87.50  | 77.50  | 40.00  |
| Oophorectomy                | 77.50    | 95.00  | 53.35  | 71.00  | 65.60  | 85.00  | 77.25  | 46.50  |
| Reconstructive surgery      | 80.00    | 95.83  | 73.33  | 65.83  | 60.67  | 81.25  | 73.33  | 46.67  |
| Radical neck dissection     | 82.50    | 75.00  | 100.00 | 70.00  | 74.00  | 81.25  | 78.75  | 37.50  |
| Radical prostatectomy       | 80.71    | 32.14  | 100.00 | 70.00  | 65.71  | 87.50  | 74.29  | 49.29  |
| Thyroidectomy               | 78.33    | 66.67  | 66.67  | 66.67  | 56.00  | 83.33  | 85.83  | 41.67  |
| Thyroid lobectomy           | 80.00    | 75.00  | 66.65  | 55.00  | 64.00  | 87.50  | 78.75  | 45.00  |
| Partial laryngectomy        | 80.00    | 31.25  | 66.65  | 60.00  | 76.00  | 84.38  | 83.75  | 42.50  |
| Partial glossectomy         | 80.00    | 100.00 | 100.00 | 73.75  | 75.00  | 93.75  | 95.00  | 46.25  |
| Partial hepatectomy         | 75.00    | 83.33  | 77.77  | 56.67  | 69.33  | 70.83  | 74.17  | 45.00  |
| <b>P value</b>              | 0.00004* | 0.00*  | 0.038* | 0.1801 | 0.011* | 0.0736 | 0.2373 | 0.035* |

Table 10 shows the effect of ADR on sub-domains of QoL. Patients who experienced ADR after tramadol treatment ( $p= 0.025$ ) had lower energy or weariness mean scores and significantly lower mean emotional well-being scores ( $p= 0.023$ ).

**Table 10: Comparison of treatment related variables with sub domains of SF-36.**

| Variables      | PF    | RP     | RE     | E/F    | EWB    | SF     | BP    | GH    |
|----------------|-------|--------|--------|--------|--------|--------|-------|-------|
| <b>ADRs</b>    |       |        |        |        |        |        |       |       |
| Constipation   | 73.48 | 72.88  | 71.19  | 61.44  | 65.70  | 83.26  | 81.70 | 44.07 |
| Dry mouth      | 75.96 | 76.06  | 71.78  | 68.08  | 69.70  | 85.37  | 87.07 | 46.70 |
| Fatigue        | 73.60 | 83.00  | 85.34  | 67.60  | 68.16  | 87.00  | 83.10 | 44.60 |
| Nausea         | 73.75 | 56.25  | 79.16  | 61.25  | 63.50  | 85.94  | 75.62 | 42.50 |
| Dizziness      | 75.00 | 100.00 | 100.00 | 68.33  | 74.67  | 87.50  | 93.33 | 51.67 |
| Sedation       | 80.00 | 75.00  | 100.00 | 80.00  | 64.00  | 100.00 | 80.00 | 45.00 |
| Others         | 00.00 | 00.00  | 00.00  | 00.00  | 00.00  | 00.00  | 00.00 | 00.00 |
| <b>P value</b> | 0.652 | 0.266  | 0.468  | 0.025* | 0.023* | 0.655  | 0.285 | 0.104 |

## DISCUSSION

In the present study, out of 152 subjects majority of the cancer patients belonged to the middle age group i.e, 46-60 years. According to the study conducted by Dharmappa B *et al.*<sup>[28]</sup> majority of cancer patients were also in the age group of 35-64 years. The subjects' average age was 53.96 years, and 103 (67.76 %) of them were females, which is similar to a study conducted by Abegaz TM *et al.*<sup>[29]</sup> in which the average age of the participants was 46.8 years, and more than half of the cancer patients were females 83 (52.9 %). As per the incidence of cancer given by cancerindia.org.in, breast cancer<sup>[30]</sup> is the most common type of cancer in females and lung cancer is the most common cancer in males, our study also reported more number of female patients with breast cancer 71(46.71%).

A study conducted by Nikola Besic *et al.*<sup>[19]</sup> found that on the 7th, 14th, 21st, and 28th days after surgery, there was a considerable reduction in pain, with mean VAS values for pain of 1.8, 1.6, 1.4, and 1.2. In our study, we found significant reduction in pain with mean VAS values of 6.18, 3.69, and 1.37 on the first, third, and fifth days after surgery, respectively.

The highest number of ADR reported in current study was constipation 55.14 % and it was also the most common ADR in a study conducted by Dhagudu NK *et al.*<sup>[31]</sup> which showed that constipation accounted for 20.4%. Majority of ADRs were probable 117(81.82%) and 26 (18.18%) were possible when the Naranjo scale was used to determine causality. The severity of ADRs was determined using Hartwig's scale, and all of the ADRs were classified as mild. The same results were found in a study conducted by Kamtane RA *et al.*<sup>[32]</sup> in which all of the adverse events encountered by the participants were classified as "Possible" as per Naranjo's scale and "mild" as per the severity assessed by Hartwig's.

We attempted to find variations in QoL of subjects at baseline and after a month, as cancer patients typically have the worse quality of life. A study conducted by Ramasubbu *et al.*<sup>[11]</sup> showed overall QoL mean score in cancer patients was 61.84 that is similar to our study where the overall mean score of QoL was found to be 61.23 which represents that there was no much improvement in QoL in cancer patients after surgery. A study conducted by Barbara Muzzatti *et al.*<sup>[33]</sup> found that among the eight QoL domains measured by the SF-36 at T0 and T1 where in comparison of T0 & T1, T1 participants had more limitations due to physical causes (p=0.028;CMD), less pain (p=0.008;CMD), better social functioning (p=0.001;CMD), and better mental health (p 0.001; CMD). Similar findings were drawn from our study, where physical functioning, energy, social functioning, emotional well-being, and general health all

improved. Subjects reported less discomfort in their bodies. However, all of the participants had significant role constraints due to their physical health and emotional problems. A study conducted by Hea- Jin Suh Oh *et al.*<sup>[34]</sup> assessed that patients who experienced ADR had lower physical and emotional well-being which in comparison to our study shows low emotional well-being and energy scores in patients who experienced ADRs.

Patients with metastasis had statistically significantly lower scores for two domains of the SF-36 (physical functioning,  $p = 0.009$ ; bodily pain,  $p = 0.016$ ) in a study by S Trippoli *et al.*<sup>[35]</sup> whereas our study shows significantly lower scores for three domains of the SF-36 (physical functioning,  $p=0.00057$ ; role limitation due to physical problem,  $p=0.0387$ ; and lower energy,  $p=0.025$ ). The limitations of our study was less sample size due to which the results obtained on QoL cannot be generalized to all cancer patients. The other barrier for the study was unavailability for procuring medical records that had information on stages of cancer. This research could be expanded upon by comparing other analgesics with tramadol in the treatment of cancer-related pain. International research might be conducted to reduce the negative influence of many factors on QoL in cancer patients.

## CONCLUSION

The present study concluded that majority of the subjects belonged to the middle age group with cancer and notably most of them are females participants commonly affected with breast cancer. After tramadol administration, we observed a drop in the number of patients with moderate to severe pain, as well as very severe pain, and a rise in the number of patients with mild pain or no pain when assessed with VAS scale. There was significant reduction in pain on POD 5. Constipation was the most common ADR, followed by dry mouth. The causality and severity assessment of ADRs showed that majority of the ADRs were probable and possible and belonged to mild category and required no special interventions.

The QoL assessment with SF-36 questionnaire revealed that there was improvement in physical functioning, energy, social functioning, emotional well-being and general health. Also the subjects showed decrease in bodily pain after a month. But all the subjects showed more role limitations due to physical health and emotional problems. The univariate comparison of some demographic variables, cancer related and treatment related variables. The demographic variables like age, gender showed no significant differences in subscale domains of QoL and subjects with cancer types and patients who experienced ADRs after tramadol treatment had lower energy or weariness mean scores, significantly lower mean

emotional well-being scores, the patients who underwent surgery had a lower mean score for general health.

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