

POSTOPERATIVE ANALGESIA WITH TRANSDERMAL DICLOFENAC VERSUS INTRAMUSCULAR DICLOFENAC – A COMPARATIVE STUDY

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ABSTRACT: BACKGROUND: The search for an ideal drug for postoperative analgesia is ongoing. Diclofenac is commonly used drug for this purpose in different routes. **AIMS:** To compare the efficacy of transdermal diclofenac with intramuscular diclofenac for postoperative analgesia. **SETTINGS AND DESIGN:** This prospective comparative study was conducted in the department of anaesthesiology in a medical college & general hospital. **METHODS AND MATERIALS:** The study subjects were 200 patients of both sexes between 18-50 years of age who were scheduled for elective laparoscopic, gynaecological & orthopaedic surgeries on limb. They divided into two groups. Group I received intramuscular injection of diclofenac sodium (75mg) & Group II received transdermal diclofenac diethylamine patch (200mg per 75 sq.cm) postoperatively. The outcome measures were pain intensity, changes in vital parameters, requirement for rescue analgesia & adverse effects. **STATISTICAL ANALYSIS:** Parametric data were analysed by using student t-test (unpaired). Non parametric data were analysed by using test of association (chi-square test). **RESULTS:** The mean pain score was significantly high in intramuscular diclofenac group (Group I) in laparoscopic & gynaecological surgeries ($P = 0.002$). Though the mean pain score was different among two groups in orthopaedic surgeries it was not statistically significant ($P = 0.377$). There were no significant differences in vital parameters & adverse reactions in between two groups. The requirement of rescue analgesia was significantly more in intramuscular diclofenac group (Group I). **CONCLUSIONS:** Transdermal diclofenac is more effective in reducing the intensity of postoperative pain following laparoscopic & gynaecological surgeries but the effect is similar to intramuscular diclofenac in orthopedic limb surgeries. **KEY-WORDS:** Postoperative pain, Analgesia, Diclofenac, Transdermal patch & Intramuscular Injections.

INTRODUCTION: One of the most common symptoms for which a patient seeks medical advice is pain. The International Association for the study of pain has defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage”.⁽¹⁾ Postoperative pain is a unique and common form of acute pain. Although ample evidence indicates that an efficacious postoperative pain treatment reduces patient morbidity and patient outcome, recent studies

ORIGINAL ARTICLE

demonstrate that about 50–70% of patients experience moderate to severe pain after surgery indicating that postoperative pain remains poorly treated. ⁽²⁾ The management of postoperative pain is an essential and integral part of the care given to the patient that assumes an important role in transition from the recovery unit to the home environment.

Any method of postoperative analgesia must meet three basic criteria. It must be effective, safe and predictable. The commonest hospital practice had been to prescribe fixed parenteral dose of a non-steroidal anti-inflammatory drug or an opioid, to be given at fixed time intervals, with the administration of the same being delegated to a nurse. This method of pain relief had a lot of short comings. Besides the discomfort of repeated injections, it may produce undesirable side effects like nausea & vomiting.

Opioids have been administered for hundreds of years to allay anxiety & to reduce the pain associated with surgery. Problems with incomplete amnesia, histamine release, prolonged postoperative respiratory depression, increased blood volume requirement secondary to vasodilatation & hypotension diminished the popularity of earlier opioids as a sole analgesic agent. ⁽³⁾ However with the discovery of newer opioids, these continue to occupy an important place in the field of postoperative pain management.

Now a days apart from the traditional opioid analgesics, use of parenteral and oral NSAIDS is becoming more popular. ⁽⁴⁾ Among NSAIDS, the drug diclofenac is being used widely for postoperative analgesia by the anaesthesiologists. ^(5 & 6)

Diclofenac is an analgesic-antipyretic-antiinflammatory drug. It inhibits prostaglandin synthesis by inhibiting cyclooxygenase enzyme. Though we have been using parenteral diclofenac (Intramuscular) most often, suppository & intravenous use is also possible. It can be administrated by Transdermal route also. The advantages of this route are painless, non-irritant, increased bioavailability & it can be applied for 24 hours. ⁽⁷⁾ Though transdermal route has its own advantages there are no studies to compare this route along with intramuscular route.

The present study was undertaken in patients undergoing elective laparoscopic, gynaecological & orthopaedic surgeries on limbs, under general & regional anaesthesia with the objective to evaluate the efficiency of transdermal diclofenac patch with intramuscular diclofenac for post-operative analgesia.

MATERIALS & METHODS: This prospective comparative study was carried out in a medical college & general hospital after the approval from the institutional ethical committee. The clinical study was carried out on 200 patients belonging to American Society of Anaesthesiologists (ASA) group-I & II of both sexes between 18-50 years of age who were scheduled for elective laparoscopic surgeries, gynaecological surgeries & orthopaedic procedures on limb. Patients of ASA group-III & IV, history of acid peptic disease, asthma, urticaria and hypersensitivity to any components of patch or injection were excluded from the study. The patients were divided randomly in following manner:

- Laparoscopic surgeries - Group I consisting of 30 patients (L-I).
- Group II consisting of 30 patients (L-II).
- Gynaecological surgeries - Group I consisting of 30 patients (G-I).
- Group II consisting of 30 patients (G-II).
- Orthopedics procedure - Group I consisting of 40 patients (O-I).

ORIGINAL ARTICLE

- Group II consisting of 40 patients (O-II).

Patients were received for preanaesthetic check up on the previous day of surgery. Detailed history was taken & thorough physical examination was done. Investigations were checked. The patients were explained about the procedure, purpose, risks & complications of the study & how to interpret visual analogue scale (VAS) postoperatively. Informed written consent was obtained. For the purpose of study 60 cases of laparoscopic cholecystectomy, 60 cases of abdominal hysterectomy & 80 cases of open reduction and internal fixation in both upper & lower limb for fracture of long bones were selected. All patients were premedicated with tablet diazepam (10mg) previous night and one & half hour before surgery. On the day of surgery patients were brought to the operation theatre half an hour before the procedure. Intra venous line was secured with an 18 gauge intravenous cannula. Then Monitors (Pulse oximetry, N.I.B.P. & E.C.G.) were attached. Baseline pulse rate, blood pressure, respiratory rate & O₂ saturation values were recorded. Surgeries under spinal anaesthesia were done with plain 0.5% heavy bupivacaine. Patients operated under general anaesthesia were administered 1.5 micro grams/kg body weight of fentanyl for intraoperative analgesia.

In the postoperative ward, Group I patients received first dose of 75 mg diclofenac sodium (3ml) by intramuscular route 30 minutes following surgery & second dose was repeated 12 hours after the first dose. Patients in Group II received transdermal diclofenac diethylamine patch of 200mg per 75sq.cm for 24 hours postoperatively. Postoperatively pulse rate, assessment of intensity of pain by VAS, mean arterial pressure (MAP), SpO₂ & respiratory rate were recorded & was repeated for the next 24 hours every 2nd hourly. Patients with VAS of 6 or more were administered injection Tramadol Hydrochloride 50 mg. slow I.V as rescue analgesia. Hypotension was said to be significant if MAP was less by 30% of preoperative value & was treated with intravenous fluids & vasopressor drugs. Simultaneously 100% O₂ was administered through face mask. Bradycardia was considered when PR was below 50 beats per minute and treated with injection Atropine sulphate intravenous 0.6 mg increments. Respiratory Rate of <10 was considered significant & O₂ supplementation was given. In case of nausea & vomiting, first hypotension was ruled out & then antiemetic injection was given. Any other reactions or complications were also noted.

Data were expressed as mean, standard deviation, standard error of mean & percentage. Parametric data were analysed by using student t-test (unpaired) and non parametric data were analysed by using test of association (chi-square test). 'P' value less than 0.05 was considered as significant.

RESULTS: There was no significant difference in mean age of two different sub groups in each categories of surgery (Tab.1). In gynaecological group all patients were females where as in laparoscopic and orthopaedic group the sex distribution was comparable (Tab.1). The mean body weight was comparable in between both groups in different categories of surgery (Tab.1). The mean pain score was significantly different among two groups in laparoscopic & gynaecological surgeries (P = 0.002). It was low in Transdermal group (Group II). Though the mean pain score was different among two groups in orthopaedic surgeries (P = 0.377) it was not statistically significant (Fig.1). The difference in mean pulse rate was not significant in between two groups among

ORIGINAL ARTICLE

laparoscopic ($P = 0.287$), gynaecological ($P = 0.819$) & orthopedic surgeries ($P = 0.957$) (Fig.2). Similarly, the difference in mean MAP, oxygen saturation & respiratory rate was not statistically significant in between two groups among different categories of surgeries ($P > 0.05$) (Fig.2). Whereas the mean of the number of times the rescue analgesia required during post operative period in both the groups in the laparoscopic ($P = 0.023$), gynaecological ($P = 0.050$) & orthopaedic surgeries ($P = 0.003$) were statistically significant (Fig.3). Adverse effects like nausea and vomiting in both the groups in laparoscopic, gynaecological & orthopaedic surgeries was not statistically significant in between two groups ($P > 0.05$) (Fig.4).

DISCUSSION: Postoperative pain may result in psychological, physiological, neuroendocrine, respiratory and cardiovascular problems ultimately increasing the risk of postoperative morbidity and mortality. Effective control of postoperative pain remains one of the most important & pressing issues in the field of anaesthesia. NSAIDS are being very widely used either alone or in combination with opioids for postoperative analgesia.

The mean age of both groups was almost similar. Paediatrics and geriatrics age group patients were excluded from the study because the evaluation of pain score is difficult in them. The sex distribution & mean weight of patients in both groups were similar. So, the demographic profile of both the groups in different categories of surgeries was comparable.

The mean pain score as measured by VAS was high in group I (L-I=2.33; G-I=2.43; O-I=2.53) as compared with group II (L-II=2.00; G-II=2.00; O-II=2.42). But the pain score was significantly higher in laparoscopic ($P=0.002$) and gynaecological ($P=0.00$) surgeries. In orthopaedic surgeries, though the pain score was high in group I, it was not statistically significant ($P=0.377$). It indicates that the transdermal diclofenac patch was more effective for postoperative analgesia in laparoscopic and gynaecological surgeries where as it was not so effective in orthopaedic procedures. It may be due to the fact that the intensity of pain is more severe in orthopaedic procedures.

Other studies found similar results like our findings. F. Alessandri & Colleagues ⁽⁸⁾ found that transdermal diclofenac administration seems a valid help to standard analgesic treatment in postoperative pain control and could also to reduce the period of hospitalization of patients who undergo laparoscopic benign gynaecologic surgery. Funk L. & Colleagues ⁽⁹⁾ concluded that diclofenac patches provides significantly better pain relief compared to tablets in the early postoperative period following arthroscopic shoulder surgery. Anil Agrawal & Colleagues ⁽¹⁰⁾ compared the efficacy of transdermal diclofenac patch with eutectic mixture of local anaesthetics (EMLA) for venous cannulation pain. They concluded that transdermal diclofenac patch and EMLA are equally effective in reducing venous cannulation pain, but signs of erythema, induration and edema are less frequently observed with the transdermal diclofenac patch. H.G. Predel & Colleagues ⁽¹¹⁾ carried out a randomized, placebo controlled, double blind multicentric study in 120 patients with traumatic blunt soft tissue injuries. They found that the diclofenac patch was significantly more effective than placebo ($P<0.0001$). Bruhlmann P. & Colleagues ⁽¹²⁾ in a randomized, double blinded, controlled clinical trial found that topical diclofenac patch is more effective in patients with knee osteoarthritis. Galer B.S. & Colleagues ⁽¹³⁾ in a multicentric controlled clinical trial found that topical diclofenac patch relieves minor sport injuries effectively.

ORIGINAL ARTICLE

The difference in mean pulse rate & mean arterial pressure was not found to be statistically significant in laparoscopic ($P = 0.287$ & 0.159), gynaecologic ($P = 0.819$ & 0.976) & orthopaedic surgeries ($P = 0.957$ & 0.828). Similar findings observed by others studies. Aziza Mohammad Hussain & Colleagues⁽¹⁴⁾ compared the changes of mean pulse rate & mean arterial pressure in post hysterectomy patients in between placebo and diclofenac. They concluded that the change in mean pulse rate & mean arterial pressure is not statistically significant in both the groups. Zahid Ahmed Hashmi & Colleagues⁽¹⁵⁾ concluded that the change in mean pulse rate & mean arterial pressure is not statistically significant in postoperative cases using diclofenac and ketorolac.

The difference in mean oxygen saturation & respiratory rate was not found to be statistically significant in laparoscopic ($P = 0.480$ & 0.731), gynaecologic ($P = 0.740$ & 0.458) & orthopaedic surgeries ($P = 0.538$ & 0.869). Zahid Ahmed Hashmi & Colleagues⁽¹⁵⁾ concluded that the change in mean respiratory rate is not statistically significant in postoperative cases using diclofenac and ketorolac. Paivi Laurilla Nee⁽¹⁶⁾ observed the changes in oxygen saturation & mean respiratory rate in postoperative joint surgery in between ketoprofen, diclofenac & ketorolac. He concluded that the changes are not statistically significant. J G Klant⁽¹⁷⁾ concluded that the changes in oxygen saturation in postoperative cases are not significant statistically.

The difference in mean of the number of times rescue analgesia required was found to be statistically significant in laparoscopic & gynaecologic surgeries & highly significant in orthopaedic surgeries ($P = 0.003$). Other studies in this aspect reported similar findings. F. Alessandri & Colleagues⁽⁸⁾ found that 35% of patients required rescue analgesia in transdermal diclofenac group where as 71.7% of patients required rescue analgesia in placebo group ($p < 0.001$) in patients undergoing laparoscopic surgery for benign gynaecologic conditions. Funk L. & Colleagues⁽⁹⁾ found that the requirement of rescue analgesia is not statistically different in two groups of patients in the early postoperative period following arthroscopic shoulder surgery in between transdermal diclofenac patches and diclofenac tablets. Anil Mehtani et al⁽¹⁸⁾ found that the requirement of rescue analgesia was less in diclofenac & acetaminophen group when compared with placebo for postoperative analgesia. E Zohar & colleagues⁽¹⁹⁾ compared the requirement of rescue analgesia in postoperative period in patients following total abdominal hysterectomy with bilateral salpingo-oophorectomy. There was no difference in both the groups. Fredman et al⁽²⁰⁾ found that the requirement of rescue analgesia was more in post laparoscopy cholecystectomy patients in diclofenac group when compared with ketorolac.

The percentage of patients had adverse effects in group-I was (L-I = 13.33%; G-I = 10%; O-I = 5%) & group-II was (L-II = 10%; G-II = 6.66%; O-II = 7.5%). The difference in the finding was not found to be statistically significant in laparoscopic ($P = 0.687$), gynaecologic ($P = 0.640$) & orthopaedic surgeries ($P = 0.644$). Aziza Mohammad Hussain & Colleagues⁽¹⁴⁾ compared the occurrence of adverse effects like nausea and vomiting in post hysterectomy patients in between placebo and diclofenac. They concluded that occurrence of nausea & vomiting was similar both the groups. Paivi Laurilla Nee⁽¹⁶⁾ observed the incidence of nausea & vomiting in postoperative joint surgery in between ketoprofen, diclofenac & ketorolac. He concluded that the incidences are not statistically significant in between the three groups. In our study only few patients had local reaction to transdermal diclofenac patch but the findings were not significant. Anil Agrawal & colleagues⁽¹⁰⁾ found that the signs of erythema, induration & edema are less frequently observed with the transdermal diclofenac patch. Funk L. & Colleagues⁽⁹⁾ found that the incidence of side

ORIGINAL ARTICLE

effects is not statistically different in two groups of patients in the early postoperative period following arthroscopic shoulder surgery in between transdermal diclofenac patches and diclofenac tablets. Other findings like auscultation of chest & other adverse effects do not have any significant findings in both groups.

The transdermal diclofenac patch is non-invasive, less painful and non-irritant than intramuscular diclofenac. In laparoscopic and gynaecological surgeries, the pain scores and rescue analgesia requirement is less with transdermal diclofenac than intramuscular diclofenac for 24 hours postoperative analgesia. In orthopaedic limb surgeries, although pain scores are high but requirement of rescue analgesia is less with transdermal diclofenac. However as, the number of cases are less in the study, further study is required with large number of cases and at multiple centres to correlate our findings.

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ORIGINAL ARTICLE

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ORIGINAL ARTICLE

Table 1: Demographic profile of patients (n=200)

Parameter	Laparoscopic surgery (n=60)		Gynaecological Surgery (n=60)		Orthopaedic Surgery (n=80)	
	Group-I (n=30)	Group-II (n=30)	Group-I (n=30)	Group-II (n=30)	Group-I (n=40)	Group-II (n=80)
Age in yrs. (Mean±SD)	31.43±7.15	31.86±6.97	36.76±7.12	36.96±6.37	33.8±7.94	34.07±7.73
Sex						
Male	16(53%)	15(50%)	0	0	33(82%)	32(80%)
Female	14(47%)	15(50%)	30(100%)	30(100%)	07(18%)	08(20%)
Body weight in Kg. (Mean±SD)	50.33±5.35	49.93±4.87	49.2±3.98	48.36±4.18	52.42±3.95	52.05±4.35

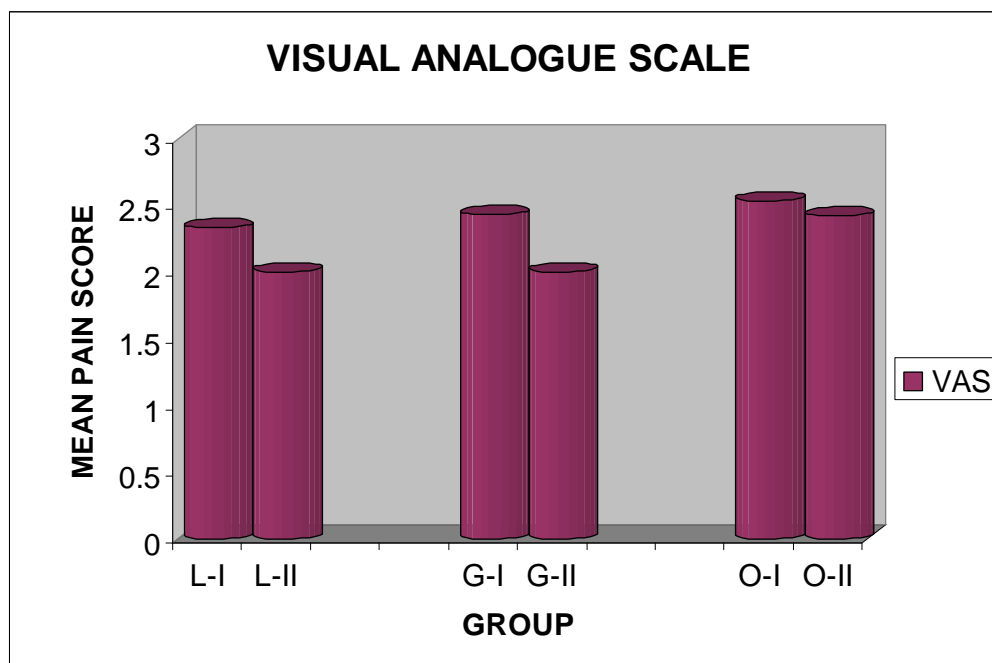


Figure 1: Column chart showing mean pain score of patients in different groups

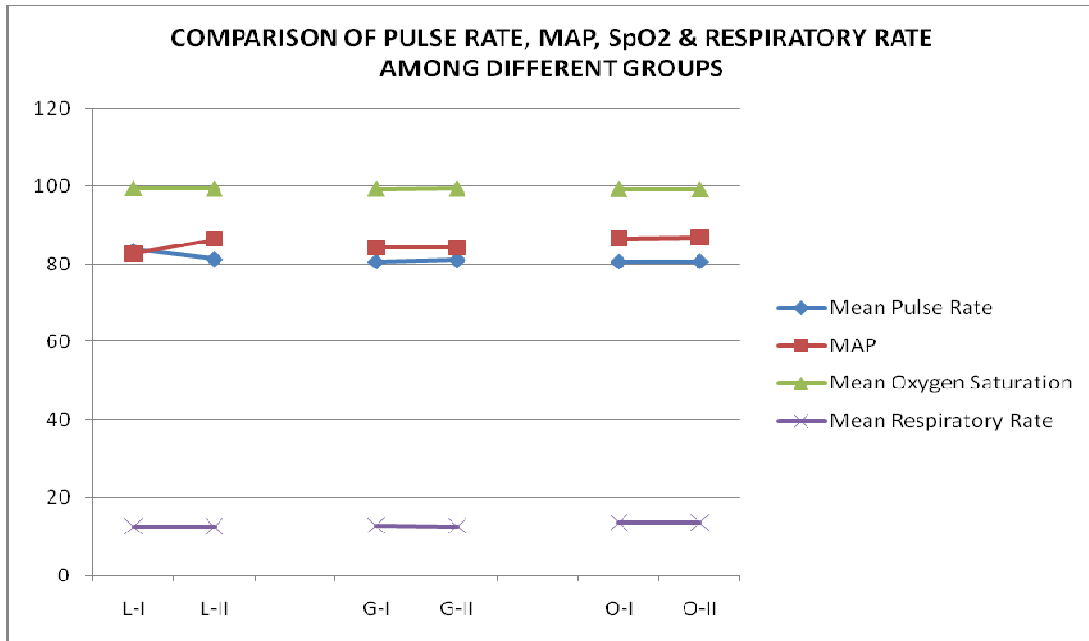


Figure 2: Line chart showing comparison of pulse rate, mean arterial pressure (MAP), SpO₂ & respiratory rate among different groups of patients.

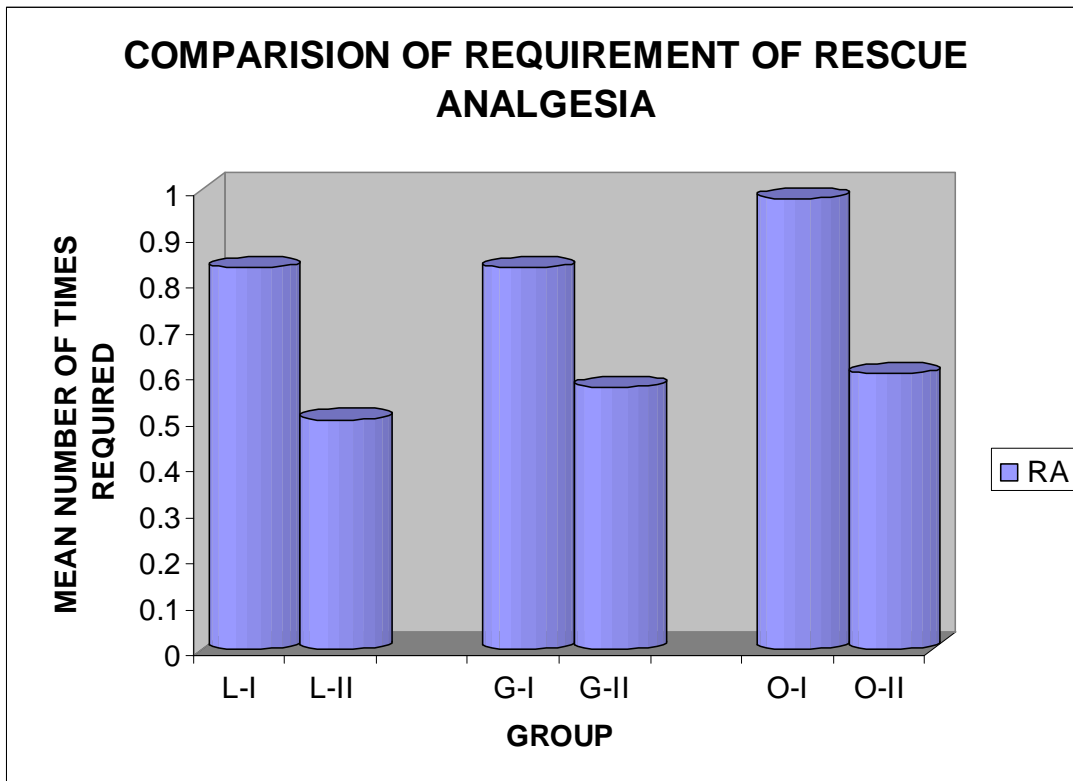


Figure 3: Column chart showing requirement of rescue analgesia of patients in different groups

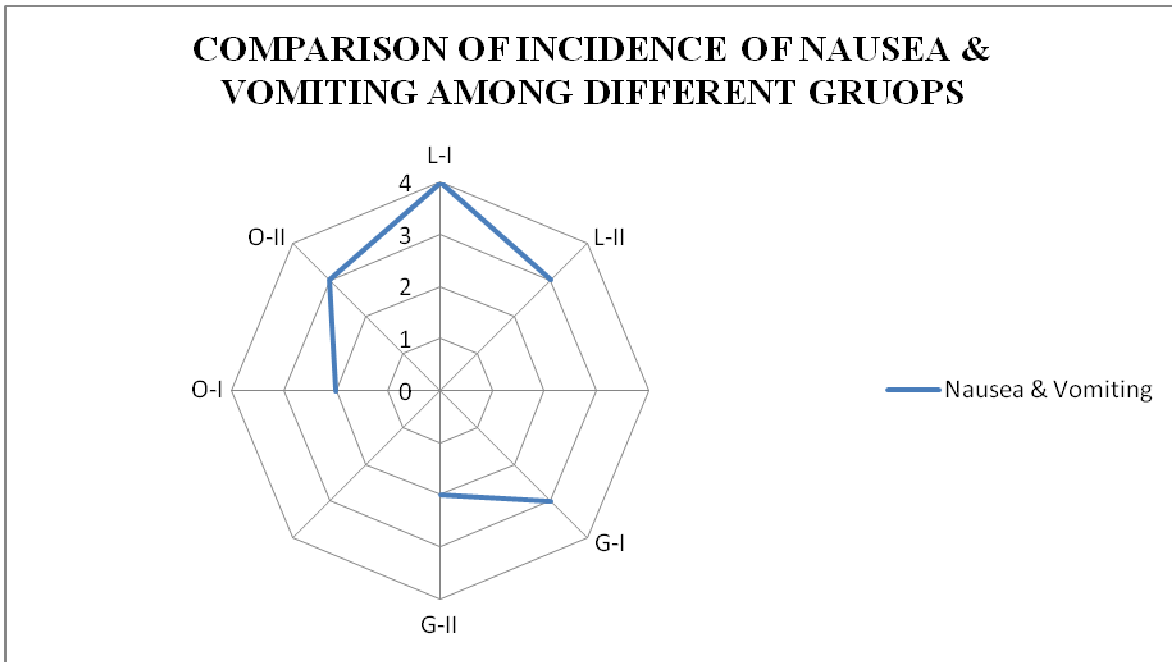


Figure 4: Radar chart showing adverse effects of patients in different groups