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Original Research Article

Drug utilization pattern of analgesics after a surgical procedure in a tertiary care hospital: a prospective observational single centre cohort study

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ABSTRACT

Background: the study aimed to understand the prescription pattern of analgesics used in the post-operative period after a general surgical procedure in a tertiary care hospital in India and estimate the severity of post-operative pain up to 48 hours. Such a study was not done in this institute of recent hence it was carried out.
Methods: 266 adults of either gender were recruited and prescription pattern analyzed over a period of 1 year beginning January 2021 to December 2021 from the post-operative general surgery wards of a tertiary care hospital in India. Patient interview and records were used to collect data. Follow ups at 4, 24 and 48 hours were undertaken to assess pain according to the visual analogue scale (VAS) that was analyzed using the Friedman's test followed by the post hoc Dunn's test.
Results: an average of 1.52±0.58 analgesics were prescribed per patient. Paracetamol was most commonly used followed by tramadol and diclofenac. All analgesics prescribed were a part of the national list of essential medicines. Effective pain management is feasible as seen by the significant ($p<0.0001$) reduction in average pain score from 4.75±1.35 to 3.05±1.18 at 24 hours and further to 2.16±1.04 at 48 hours.
Conclusions: Use of analgesics prescribed from a standardized list is effective in majority of patients.

Keywords: Pain, Analgesics, NSAID's, Drug utilization, Visual analogue scale

INTRODUCTION

Drug utilization is "the marketing, distribution, prescription and use of drugs in society, with special emphasis on the resulting medical, social and economic consequences."[1] Pain is defined as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage.'[2] It encompasses multiple domains including but not restricted to the affect of a person. The intensity of pain experienced is different for each individual even while facing similar stimuli. This is so because it goes beyond the tangible to include personality and culture which may bring about a variety of responses and therefore when a patient complains of pain it must not be taken lightly or ignored on the basis of pre-defined notions. Pain is a subjective symptom.[3] It's generation involves highly complex mechanisms which are tightly integrated at different levels - central as well as peripheral. Post-operative pain is one of the most common outcomes of any surgical procedure and demands appropriate attention and efficient management. Undertreated severe pain may lead to several complications related to major systems like cardiovascular, respiratory, gastrointestinal,

musculoskeletal and also psychological. Opium, its semisynthetic and synthetic derivatives have proved to be the most effective analgesics in the immediate postoperative period.[4] A step down approach from injectable to oral opioids and ultimately to non-steroidal anti-inflammatory drugs (NSAID's) is promoted currently.[5] Analgesics with the least tolerance and dependence potential should be used keeping in mind their safety profile. The end point of effective pain management is to provide relief to patients and hasten the recovery process. Multimodal analgesia advocates the use of several different classes of analgesics and different routes of administration which can produce a synergistic action. This also helps to reduce the effective doses of the individual drugs and their adverse effects.

NSAID's efficiently manage pain associated with minor surgical procedures and trauma with minimum tissue destruction. Their mechanism of action is through the inhibition of the cyclooxygenase (COX) enzyme, responsible for the synthesis of prostaglandins. Prostaglandins along with other mediators have a role to play in the generation of pain, fever and inflammation. They are also gastro protective and thus blocking their actions results in peptic ulcer disease and gastrointestinal hemorrhage, the most common side effects of this class of drugs. Renal dysfunction, altered liver function and platelet dysfunction may also be seen. Although they are less potent than opioids, they can act as opioid sparing agents.

Opioids act on central and peripheral opioid receptors to bring about analgesia and are unique as they reduce not only the sensory but the affective component of pain as well. In contrast, non-opioid analgesic drugs are more effective in relieving inflammation associated sensory component of pain but are incapable of mitigating its affective arm. To maximize therapeutic benefit and decrease adverse effects, periodic assessment of the manner in which drugs are being prescribed, dispensed and used enable timely and rational modifications to be made. There is always scope through continuous research to identify more effective and safer drugs. Previous drug utilization studies on post-operative analgesia all conceded the use of multimodal analgesia to be the most efficacious and safest method. Such studies were reported by Vallano et al Balasubramanian et al, Arshad et al, Chaudhari et al, Sen et al.[5-9] Each of these studies, although they differed in population demographics, duration, site and year in which they were conducted, all had a similar purpose. They wished to determine the pattern of analgesic usage so as to contribute to rational prescription and improve pain management.

Objectives

Objectives of current study were to investigate the prescription pattern of analgesic drugs used in the post-operative period after a general surgical procedure in a tertiary care hospital in India, To determine whether the drugs being used comply with those listed in the National list of essential medicines and to estimate the severity of post-operative pain up to 48 hours. To the best of our knowledge such a study has not been done in this institute in recent years hence this study was conducted to plug the gap.

METHODS

The study was conducted as a prospective observational single center study at Topiwala National medical college & B. Y. L Nair Ch. Hospital, Mumbai, Maharashtra. The first patient was recruited on the 11th of January 2021 while the last on the 24th of December 2021. A sample size of 266 was arrived upon by estimating the patients undergoing operations on a daily basis and use of an online sample size calculator.[11] Convenient sampling was used.

Inclusion criteria

Inclusion criteria were; post-operative general surgery patients admitted for up to 48 hours and 18 years and above of all genders.

Exclusion criteria

Exclusion criteria were; Patients not willing to give consent, Pregnant women, mentally challenged patients, terminally ill patients, Patients with a known history of allergy to analgesics and Patients undergoing laparoscopic surgeries.

Patients were explained the study details and consent was taken. Interview and case records were used to obtain all relevant information. This included demographic data that was analyzed as a percentage of male and female patients and age as mean±SD (standard deviation).

Co-morbidities and operation conducted was summarized as a percentage, the mean number of analgesics, class of analgesics prescribed, their frequency, dose and route of administration, whether monotherapy or polypharmacy was used, whether generic or brand name was being used, any fixed dose combinations and whether analgesics were being prescribed from National List of Essential Medicines were all detailed as a percentage. Any analgesic or anesthetic administered intra-operatively was also noted along with any adverse reaction experienced depicted as a percentage.

Pain rating using the visual analogue scale[12] was determined on three occasions at 4 hours, 24 hours and 48 hours post-operatively keeping in mind the patient's level of consciousness and ability to communicate appropriately. The values lie on a horizontal straight line measuring 10 cm ranging from 0-10 where 0 is no pain and 10 is excruciating. The results were shown as mean±SD. Friedman's test or repeated measures ANOVA as appropriate, followed by post hoc Dunn's test was used for comparison.

RESULTS

Demographics

The average age of the study populace was 47.23±14.41. Patients ranged from 18-76 years of age. Most patients were found in the age group between 50-59 years (25.19%). The age group with least number of patients was 70-79 years (4.14%).

With respect to gender majority of the patients were male (62%) as compared to female (38%). The male to female ratio was 1.66:1.

Table 1: Severity of pain using visual analogue scale (n=266).

Average pain score according to visual analogue scale at different time intervals (mean±SD)			
4 hours	24 hours	48 hours	P value
4.75±1.35, (median-5) (IQR: 4-6)	3.05±1.18*, (median-3) (IQR: 2-4)	2.16±1.04*, (median-2) (IQR: 1-3)	<0.0001, (Friedman's test)

*p<0.0001 using post hoc Dunn's test for inter-comparison between 4 and 24, 4 and 48 and 24 and 48 hours

Table 2: Distribution of total analgesics prescribed.

Name of analgesic	Number of patients receiving the analgesic	% total analgesic prescribed	% patients receiving the analgesic
Paracetamol	263	65.26	98.87
Diclofenac	52	12.90	19.55
Tramadol	88	21.84	33.08
Total	403	100	-----

Table 3: Percentage of monotherapy /polypharmacy with respect to analgesics agents (n=266).

Category	Drug name	N	%
Single analgesic	Paracetamol	154	57.89
	Diclofenac	3	1.13
Two analgesics	Paracetamol + Diclofenac	38	14.29
	Paracetamol + Tramadol	60	22.56
Three analgesics	Paracetamol + Diclofenac + Tramadol	11	4.14

Table 4: Frequency of administration of analgesic agents (n=403).

Name of analgesic	Frequency of administration (per day)			
	Once	**Twice**	**Thrice**	**SOS**
Paracetamol	1	30	228	4
Diclofenac	0	9	20	23
Tramadol	23	15	47	3

Clinical data

The most common operative procedure was hernia repair (15.79%). The least common operative procedures were hemorrhoidectomy (0.38%), debridement of upper limb (0.38%), esophageal foreign body removal (0.38%) and gastrectomy (0.38%). In our study population 128 patients in total had co-morbidities. Diabetes mellitus (37.57%) and hypertension (28.90%) were the most commonly seen. The results of pain measurement according to visual analogue scale are depicted in (Table 1).

Prescription analysis

All 266 patients received analgesics. Overall 403 analgesics were prescribed to 266 patients. The average number of analgesics prescribed was 1.52±0.58. The most commonly prescribed analgesic was paracetamol which contributed to 65% of the total analgesics prescribed. It was prescribed to 98.87% of the total patients. The distribution of analgesics prescribed is reflected in (Table 2). The non-opioids paracetamol and diclofenac were used most often (78%) as compared to the opioid tramadol (22%). Generic name was used for prescribing the major proportion of analgesics (87%) while brand name (13%) was used much less frequently. The brand name used was Dynapar for the drug diclofenac. Analgesics were prescribed intravenously (78.66%), far exceeding oral prescription (21.34%). Paracetamol was prescribed both orally and intravenously whereas diclofenac and tramadol were prescribed exclusively by intravenous route. Mono-therapy (59%) predominated over poly-pharmacy (41%).

The distribution for the same is seen in (Table 3). The statistics for frequency of administration can be viewed in (Table 4). The oral dose used for paracetamol was 500mg while intravenous administration saw it doubled to 1 gm. Diclofenac was used at a dose of 75 mg in 100 ml normal saline (NS) and that of tramadol was 50 mg in 100 ml NS. All the analgesics prescribed were a part of the National list of essential medicines. No fixed dose drug combinations were used and no adverse reactions were experienced by the patients.

Table 5: Percentage of drugs used as intraoperative anesthesia and analgesia (n=835).

Type of anesthesia	Purpose of use	N	%
General anesthesia Number of patients receiving general anesthesia is 146 (54.89%)	**Inducing agents**		
	Propofol	125	14.97
	Ketamine	11	1.32
	Sodium Thiopental	18	2.16
	Etomidate	9	1.08
	Maintenance agents		
	Sevoflurane	75	8.98
	Isoflurane	32	3.83
	Desflurane	19	2.28
	Nitrous Oxide	3	0.36
	Skeletal muscle relaxants		
	Scoline	123	14.73
	Atracurium	6	0.72
	Vecuronium	3	0.36
	Cisatracurium	2	0.24
	Reversal agents		
	Neostigmine	114	13.65
	Glycopyrrolate	114	13.65
Regional anesthesia Number of patients receiving regional anesthesia is 120 (45.11%)	**Regional block**		
	Bupivacaine	120	14.37
	Buprenorphine	22	2.63
	Fentanyl	14	1.68
	Morphine	2	0.24
Intraoperative analgesia	**Analgesic**		
	Tramadol	23	2.75

DISCUSSION

Pain is one of the most common complains for which patients report to the hospital. Currently there is an abundance and variety of analgesics at the disposal of the prescriber. This study delves into the patterns of prescription with respect to analgesics followed by medical professionals in a tertiary care setting. In our study three analgesic were prescribed; namely paracetamol, tramadol and diclofenac. For procedures where minimal post-operative pain can be expected, paracetamol proved to be a sufficiently effective analgesic while minimizing adverse drug reactions, especially administered as an intravenous infusion. During longer procedures it was either used in combination with tramadol or diclofenac thereby reducing the dose of the second analgesic. This in turn reduced the adverse drug reaction that may have occurred by using another analgesic alone. The analgesics used in this study were readily available in the hospital. In contrast another study showed that the most common analgesic used was tramadol and then paracetamol.[9] This would be in accordance with the step down approach in the WHO analgesic ladder where opioid medications are used in the immediate post-operative period to manage more severe pain gradually titrating the dose and changing to NSAID usage when pain eventually receded.[10-12]

In order to assess the severity of post-operative pain experienced by our patients the visual analogue scale was used. Our study showed a diminishing trend. The 4 hour average pain score in our study was bearable. This suggests effective pain management. A different study discussed reasons for "inappropriate prevention of post-operative pain" with contrasting results.[6] NSAID's were used more often than opioids in our study. A similar result is reflected in other recent studies.[6,9] However an older study used morphine sulphate most commonly which is an opioid analgesic.[13] This study was conducted in 1994 on surgical intensive care unit patients and would explain the contrasting results. Opioids are rarely used post-operatively nowadays, in commonly carried out procedures with proper use of intraoperative anesthesia. They are known to cause respiratory depression (not common at clinical doses), dependence and sedation among other adverse drug reactions. The use of NSAID's in greater abundance, as seen in this study may provide an opioid sparing effect.[14]

Gastrointestinal side effects are common among the non-selective NSAID's. However no adverse drug reactions were recorded in this study. Similar results were also seen in other studies done.[5,15] This suggest that non-selective NSAID's are relatively safe for short term use, though it does not exclude long term reactions. The simultaneous administration of anti-emetics and proton pump inhibitors routinely after the operations would also explain the lack of post-operative nausea and vomiting as well as gastrointestinal side effects that administration of NSAID's would have otherwise brought about. The use of paracetamol most commonly, which does not exhibit the gastrointestinal side effects seen in conventional NSAID's, could explain the lack of adverse drug reactions. In this study the use of generic names in drug prescription predominated over that of brand names. Similar results were obtained elsewhere.[16] However, some studies did exhibit opposing results.[17] Prescribing by generic name should be encouraged as they are internationally accepted and used in scientific publications.[18] They help in rational drug therapy as cost can be minimized, while standardizing safety and efficacy. Maximum number of analgesics were prescribed intravenously. Similar results are seen in other studies.[6,9] This is an expected result as pain in the immediate post-operative period tends to be a unanimous complain that needs to be effectively managed in the shortest time possible. They act more quickly and effectively as the bioavailability of the drug is greatly increased compared to orally administered drugs.

All the analgesics that were prescribed in our study were a part of the National List of Essential Medicines. Essential Medicines are those that satisfy the "priority health care needs of the population."[19] This list is generated considering disease prevalence, efficacy, safety and cost-effectiveness of the medicines. Those that appear in this list are intended to be available in adequate amounts, appropriate dosage forms and strengths with assured quality. They must be available in such a way that an individual or community can afford. Another study[7] had similarly high percentage of drugs prescribed from the NLEM while most carried out across India showed opposing results with much lower values for drugs prescribed from NLEM.[16,17,20-22]

The procedure that patients underwent play a role in the 4 hour post-operative pain score. In general, longer and more complex operations such as exploratory laparotomy and colon surgeries would require the use of intra-operative analgesia in order to have effective pain management and an uncomplicated postoperative period. Tramadol was used for this purpose. Propofol was the most commonly used inducing agent due to its rapid action and short distribution half-life of 2-4 min.[23] A similar result was seen in another study.[24] Sevoflurane dominated among the maintenance agents as "rapid changes in depth" of anesthesia could be achieved, a desirable quality among maintenance agents from the viewpoint of an anesthetist.[23] It is also pleasant to administer as it is not pungent. Succinylcholine was the predominantly used skeletal muscle relaxant as it produced "rapid, complete and predictable paralysis with spontaneous recovery in ~5 min."[25] Glycopyrrolate and neostigmine administered as a single injectable was the reversal agent of choice. It was used to hasten recovery at the end of an operation by reversing the residual block which can cause weakness, hypoventilation and hypoxia in the recovery room.[25] However neostigmine has a tendency to cause hypotension and bronchospasm due to its muscarinic action – this is prevented by the addition of glycopyrrolate. Bupivacaine was used most frequently among the local anesthetics. Another study showed that Bupivacaine was the most commonly used local anesthetic which is higher than seen in our study. The reason for this, despite its cardio toxicity is that it is an effective and long-acting amide local anesthetic.[26]

Limitations

Medication and pain felt were only recorded up to 48 hours post-operatively and any changes beyond that was not assessed. Pain is a subjective symptom. Quantifying it may bring in bias as one patient may complain of severe pain after a given procedure while another may just brush it aside as acceptable after the same procedure.

CONCLUSION

Effective pain management is a feasible reality as highlighted even with the use of simple antipyretic analgesics like paracetamol as long as the judicious use of opioids is not withheld when needed. Administering drugs from the National List of Essential Medicines only adds on to the standardization and quality maintenance which in turn improves patient satisfaction by minimizing the pain experienced.

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