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ORIGINAL RESEARCH

The quality and continuity of systemic postoperative analgesia: a single center two-stage follow-up study

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Abstract

The aim of two prospective 1-month follow-up studies was to assess and compare the quality and continuity of postoperative systemic analgesia in Departments of Anaesthesiology and Surgery I and II, as well as adherence to prescribed plan of analgesia with respect to the effect of postoperative analgesia guidelines adopted in 2018. The studies included 94 (2016) and 80 (2018) patients who were operated under general anaesthesia, transferred to post-anaesthetic care unit (PACU), then to surgical wards and received systemic analgesia postoperatively. Comparison was based on adherence to postoperative analgesia plan during patient transfer. Recommendations for multimodal postoperative analgesia were given by the anaesthesiologist in 35.1% (ketoprofen + opioid) and 40.4% (paracetamol + opioid) in 2016 *vs.* 91.3% of cases in 2018, $p < 0.001$. Comparing 2016 to 2018, adherence to planned analgesia in PACU, % of cases was 35.1% *vs.* 92.5% for paracetamol ($p < 0.001$), 30.9% *vs.* 80% for ketoprofen ($p < 0.001$) and 75.5% *vs.* 72.5% for pethidine ($p = 0.649$). Adherence to planned analgesia after transfer to Department of Surgery I, % of cases was 3.3% *vs.* 80% for paracetamol ($p < 0.001$), 1.7% *vs.* 22% for ketoprofen ($p < 0.001$) and 61.7% *vs.* 20% for pethidine ($p < 0.001$). Adherence to planned analgesia after transfer to Department of Surgery II, % of cases was 0% *vs.* 10% for paracetamol ($p = 0.059$), 61.8% *vs.* 73.3% for ketoprofen ($p = 0.325$) and 29.4% *vs.* 13.3% for pethidine ($p = 0.12$), respectively. In conclusion, patients receive recommended systemic analgesia in PACU. Implementation of guidelines in Department of Surgery I resulted in 42% reduction of opioid and 76% increase of paracetamol use. Adherence to recommended analgesia in Department of Surgery II remains low.

Keywords

Postoperative; Analgesia; Surgery; Guidelines; Audit; Follow-up

1. Introduction

Treatment of postoperative pain remains a widely discussed and up-to-date topic. Even more, effective, procedure specific postoperative analgesia is one of the main cornerstones in Enhanced Recovery after Surgery (ERAS) programs. The main goal of pain management is to reduce or even eliminate pain with minimal side effects [1]. Opioids are the most commonly used analgesics for post-operative pain relief immediately after surgery [2]. Although highly effective in the treatment of moderate to severe pain, their use is limited by dose-related adverse effects such as postoperative nausea and vomiting, urinary retention, pruritus, bowel obstruction and respiratory depression. Even more, prolonged postoperative use of opioids can lead to addiction [3]. The risk of opioid-related serious side effects promotes the search for other methods for pain relief. Systemic non-opioid analgesia may reduce the demand for opioids for pain management. Non-opioid analgesics such as paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), both non-selective cyclooxygenase inhibitors and selective Cyclooxygenase 2 (COX2) inhibitors are commonly used in combination with opioid analgesics as part of multimodal analgesia following major surgery [4]. Paracetamol is the most commonly prescribed medication for the treatment of acute pain characterized by reduction of opioid consumption by about 30% and it can be used to complement opioids alone or in combination with other non-opioid analgesics [5].

High quality postoperative analgesia is complex and can be achieved in several steps. The best option of postoperative analgesia is to plan and tailor it according to the general guidelines, specific patient and type of surgery. Management of postoperative analgesia should be started in the recovery area or even in the operating room and be followed in the surgical unit and at home. Even more, the effects of pain management should be monitored and adjusted to the patient's needs. Audit of postoperative analgesia comes as the next

step and could be used for quality improvement of postoperative patient care. However, during patient transfer from one department to another, adherence to the prescribed analgesic plan is frequently lost. This can lead to inadequate analgesia and increased risk of drug overdosage or side effects if the analgesics are given violating safety requirements.

In order to analyze and improve the quality of analgesia in adult patients following surgery we performed a two-stage follow-up study. The first stage prospective follow-up study was carried out in 2016 and aimed to clarify the existing pain management practices in the Postanaesthetic Care Unit (PACU) of the Department of Anaesthesiology and two Departments of Surgery [6]. Results of this audit led to a broad interdisciplinary discussion and development of the institutional guidelines of multimodal postoperative analgesia in 2018.

The aim of the second stage prospective follow-up study was to assess the quality and continuity of systemic postoperative analgesia in the PACU and the two departments of surgery with respect to the adherence to the institutional guidelines adopted in 2018, and to compare these results with the results of 2016 follow-up study.

2. Methods

2.1 Study protocols and ethical approval

The study was performed in November 1–30, 2016. The study included data of patients who had experienced elective surgery under general anaesthesia and were transferred to PACU followed by transfer to Departments of Surgery I and II. For ethical reasons, Departments of Surgery were coded as Departments of Surgery I and II; only the authors of the manuscript were familiar what particular departments were coded.

The 1-month prospective follow-up study was carried out in the PACU, Departments of Surgery I and II, in November 1–30, 2018. The prospective analysis included patients after general anaesthesia who were operated in Departments of Surgery I and II, were treated in PACU after surgery and then in surgical wards and received systemic analgesia for postoperative pain relief. According to the guidelines adopted in 2018, patients were prescribed to receive intravenous paracetamol 1 g $\times$ 4, intravenous ketoprofen 100 mg $\times$ 2–3 and opioid (pethidine 12.5–50 mg or other) in bolus doses for rescue analgesia. The first doses of paracetamol and ketoprofen were given in the operating room before the end of surgery, and the time of analgesic prescription was stated in the anaesthesia records. The following doses and timing of analgesics were written on patient care records in PACU and Departments of Surgery.

Patient data including demographic characteristics, type of surgery, pain intensity, type and dosage of systemic analgesics along with side effects were collected in both studies every 24 h per patient until discharge from hospital or up to 72 h after surgery if patients remained hospitalized.

Patients unwilling to participate, having allergy or contraindications for the use of recommended analgesics (paracetamol, ketoprofen, pethidine), those with incomplete postoperative care information in patient records and receiving regional analgesia for postoperative pain relief were excluded from the study. The flow charts of both studies are shown in Fig. 1 and Fig. 2.

2.2 Collection of patient data

Data such as patient's age, sex, ASA class, type of anaesthesia, type of surgery, duration of stay in PACU, pain intensity over 24 h, requirements of analgesics, cumulative doses of analgesics in PACU, at 24 and 72 h after transfer from PACU to Surgical Units, potential systemic analgesics related side effects and postoperative complications were collected from medical records. The analysis also included postoperative analgesia protocols.

Information on pain intensity and analgesic consumption along with other parameters were collected by the investigators every 24 h. Pain intensity was to be assessed by means of Visual analogue scale (VAS) scale ranging 0–10 scores where 0 meant no pain and 10—worst imaginable pain, and VAS score >5 was regarded as unacceptable requiring supplementary rescue analgesics. Pain intensity was assessed and recorded every hour during the patient stay in PACU which covers a period of up to 24 h and at the moment of patient transfer to Departments of Surgery to be followed by further pain assessment in Departments of Surgery.

Side effects: nausea, dizziness, arterial hypotension, allergy, pruritus *etc*. were recorded at 24 h intervals both in PACU and Departments of Surgery. The investigators did not interfere with prescription of any analgesics or other medications and did not influence medical treatment or perioperative care in any way throughout the study.

2.3 Assessment of the quality and continuity of analgesia

Continuity of postoperative analgesia was defined as adherence to the recommended plan of postoperative analgesia as prescribed by the attending anaesthesiologist in terms of the medication, dosage, method of use and administration at predefined hours.

Analysis of adherence to the recommended plan of postoperative systemic analgesia was based on: the number of cases having a plan of analgesia given by the attending anaesthesiologist (the rate of prescription of postoperative systemic analgesia plan), the number of cases with continuity of the recommended analgesia in PACU and after patient transfer to the Departments of Surgery, and the number of cases with deviations from the recommended plan.

The results if the 2018 follow-up were compared to the results of the previous 2016 follow-up which was performed using the same patient selection criteria and methodology. The second study was expected to reveal an opioid-sparing effect of implemented multimodal analgesia, and a reduction of 25% in opioid use was regarded as clinically significant [7]. The results of the two consequent studies were compared with respect to:

- postoperative pain intensity,
- the rate of prescription of postoperative systemic analgesia plan,
- adherence to the prescribed plan of systemic analgesia,

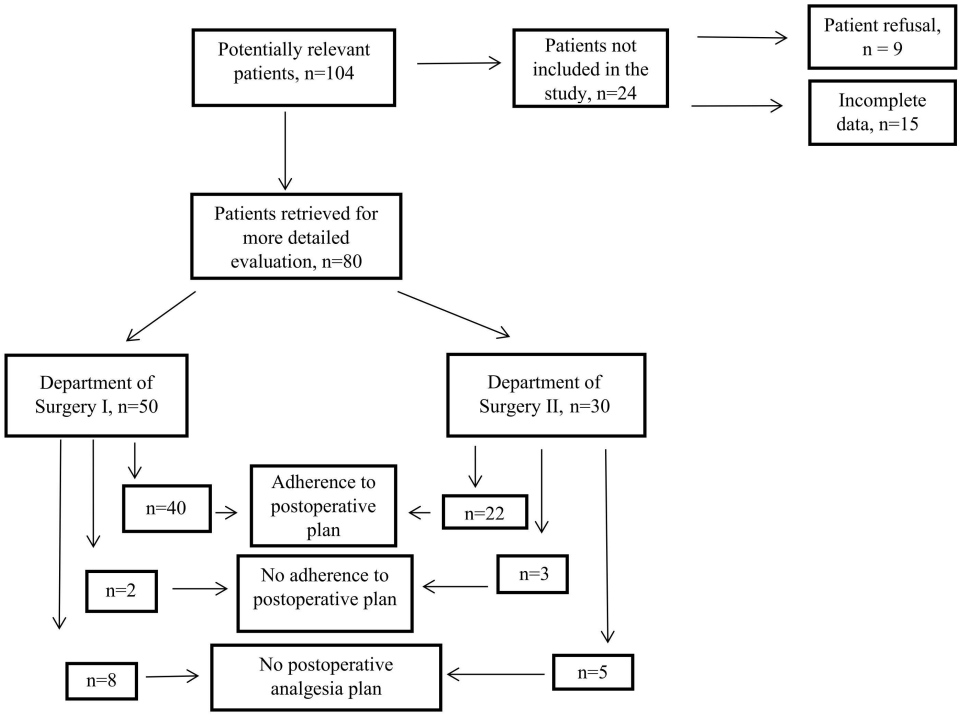

FIGURE 1. The flow chart of the 2016 study. n—number of cases.

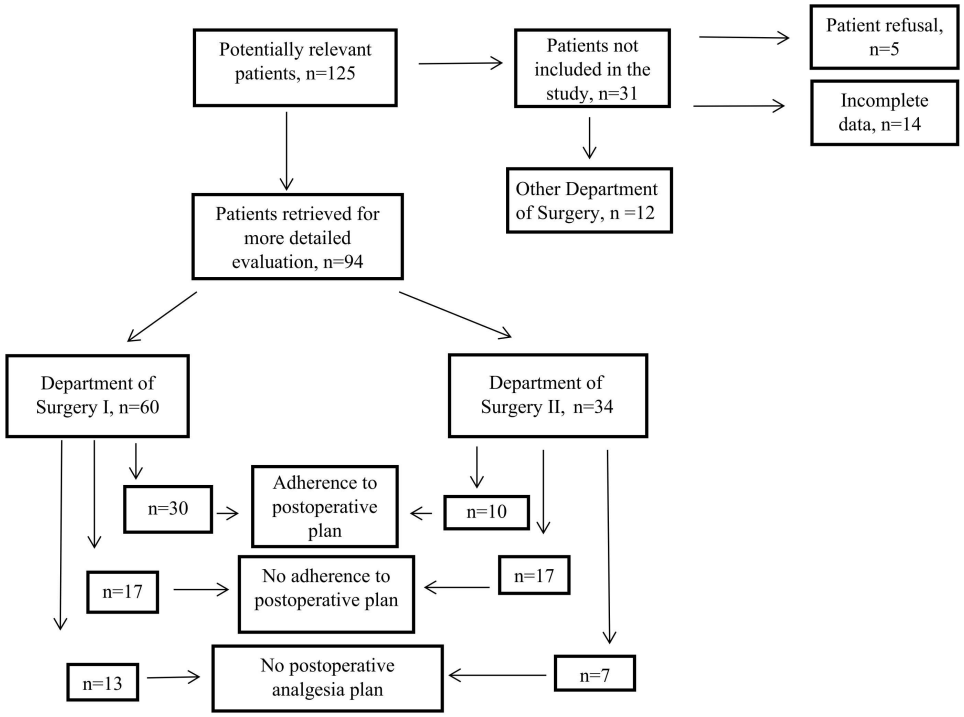

FIGURE 2. The flow chart of the 2018 study. n—number of cases.

- the rate of analgesics-related side effects.

2.4 Statistical Analysis

Statistical analysis was performed with Microsoft Excel 2010 and IBM SPSS Statistics (Statistical package for social sciences) version 22 (IBM Corp., Armonk, NY, USA). Data of the study are presented as number (%) of cases, mean (SD), median (interquartile range, IQR), and scores on a scale where appropriate. Comparisons between groups were made using a two-sample *t*-test for data with normal distribution, the Mann-Whitney U test for data with abnormal distribution and chi square test where appropriate. The threshold for statistical significance was $p < 0.05$.

3. Results

Patient demographic data of the 2016 and 2018 studies are presented in Table 1. Studies were comparable with respect to all demographic data except that there were statistically

significantly more cases of laparoscopic cholecystectomies in 2018.

Median (IQR) pain intensity over the first 24 h was 1.2 (0.1–2.0) *vs.* 1.0 (0.4–2.3) in 2016 *vs.* 2018, respectively, $p = 0.5$. It was assessed in PACU in 88.3 *vs.* 97.5% of cases in 2016 *vs.* 2018, respectively ($p = 0.039$). Pain scores were unavailable in surgery units (SUs) in both studies.

Pattern of systemic postoperative analgesia as prescribed in PACU and followed in Departments of Surgery is presented in Table 2. The most common medications used in PACU were paracetamol, ketoprofen and pethidine. According to the 2016 study, a combination of opioid and non-opioid analgesics was prescribed by the attending anaesthesiologist and given in PACU in <40% of cases; prescribed treatment was continued in Departments of Surgery mostly in <5% of cases (Table 2). Adherence to the prescribed opioid was higher, ranging from 76% of cases in PACU to 62% or 29% of cases in Departments of Surgery (Table 2). In 2018, the recommendations of postoperative analgesia by the attending anaesthesiologist to the staff of PACU were given in approximately 50% more of cases compared to 2016 and reached 91.3%. A statistically significant improvement in adherence to the guidelines can be noted for non-opioid analgesics in PACU (increased use by 60%) and in Department of Surgery I (increased use of paracetamol by 76% along with increased use of ketoprofen by 20%), in particular. In addition, the use of opioid pethidine decreased in Department of Surgery I by 42% (Table 2).

In addition to the presented data we determined the cumulative doses of the medication in PACU and in Surgical Units at 24 and 72 h after postoperative admission and adherence to postoperative analgesia recommendations given by the attending anaesthesiologist (Table 2). A more detailed comparison of the choice of systemic analgesia in Departments of Surgery I and II over time, *i.e.* 2016 *vs.* 2018 revealed the level of adherence to recommendations of postoperative analgesia in PACU and after transfer to Departments of Surgery.

Cumulative doses, 2016 *vs.* 2018 in PACU were comparable for ketoprofen and pethidine, statistically significant reduction of 0.5 g for paracetamol was found. Cumulative doses, 2016 *vs*. 2018 in Surgical Units were comparable at both 24 and 72 h time intervals for ketoprofen; however, an increased dose for paracetamol and a decreased dose for pethidine were found in 2018 (Table 2). Doses of all analgesics were not exceeding safe limits.

A more detailed profile of systemic analgesia in Department of Surgery I is presented in Table 3 and Fig. 3 (See also **Supplementary Fig. 1**).

The range of analgesics and comparison of 2016 *vs*. 2018 in Department of Surgery II are shown in Tables 2 and 4, and Fig. 2 (See also **Supplementary Fig. 2**). Although statistically insignificant, there is a trend towards increased use of paracetamol by 10% and decreased use of opioid pethidine by approximately 16%, as well.

A separate comparison of the analgesic medications used in Departments of Surgery I and II over 1 month in 2016 has revealed that opioid pethidine was given in approximately 30% more cases in Department of Surgery I while ketoprofen was continued in only small increment compared to continuation of ketoprofen in Department of Surgery II in >60% of cases (Fig. 3).

TABLE 1. Demographic Characteristics.

Variable	Year, 2016	Year, 2018
Age, years	63.7 (14.7)	67.4 (13.8)
Total no of patients	94	80
Male	55 (58.5%)	42 (52.5 %)
Female	39 (41.5%)	38 (47.5%)
	ASA	
I	7 (7.5%)	11 (13.8%)
II	23 (24.5%)	19 (23.8%)
III	46 (48.9%)	30 (37.5%)
IV	18 (19.1%)	20 (25.0%)
	ANAESTHESIA	
Endotracheal	83 (88.3%)	69 (86.3%)
Laryngeal mask	11 (11.7%)	11 (13.8%)
	SURGERY	
Colorectal surgery	33 (35.1%)	23 (28.8%)
Inguinal hernia repair	5 (5.3%)	6 (7.5%)
Cholecystectomy*	4 (4.3%)	11 (13.8%)
Thyroid surgery	12 (12.8%)	4 (5.0%)
Nephrectomy	7 (7.4%)	3 (3.8%)
Renal resection	7 (7.4%)	7 (8.8%)
Radical prostatectomy	8 (8.5%)	5 (6.3%)
Transurethral surgery	7 (7.4%)	6 (7.5%)
Other	11 (11.7%)	17 (21.3%)
PACU stay, hrs	8 (8.3)	7.2 (7.2)

*PACU: Postanesthesia care unit. Values are mean (SD) or no (%) of cases of total number of patients. *p = 0.02.*

Comparing the systemic analgesia in the Departments of Surgery I and II in 2018, we can see a different analgesic profile (Fig. 4). The use of paracetamol in Department of Surgery I was higher by 70% of cases. However, ketoprofen was continued after transfer from PACU in only 22% of cases, compared to 73% of continued use in Department of Surgery II.

A more detailed analysis of the changes in prescription of the 3 most popular analgesics over time (2016 *vs.* 2018) in the two Departments of Surgery revealed the positive impact of the institutional pain management guidelines adopted in 2018 in the Department of Surgery I: the use of paracetamol had increased by 76% and the use of pethidine had decreased by more than 40%, respectively. On the contrary, only insignificant changes in the pattern of postoperative analgesia over time could be noted in Department of Surgery II (Table 2, Fig. 4). The use of pethidine remained comparable in both departments: it was continued in approximately <20% of cases.

Switching to other systemic non-opioid analgesics other than prescribed in PACU like ketorolac, dexketoprofen and diclofenac remains popular after the patient transfer to Departments of Surgery. To note, comparison of analgesic profile in Departments of Surgery I and II in 2016 and 2018 has revealed

TABLE 2. Pattern of Systemic Postoperative Analgesia: 2016 *vs.* 2018.

Variable	Recommendation	Given in PACU	Doses in PACU	Given in SU I	Given in SU II	Doses in Sus 24 h	Doses in Sus 72 h
Paracetamol	40.4 *vs.* 91.3	35.1 *vs.* 92.5	2.4 (0.9) *vs.* 1.9 (1.1) g	3.3 *vs.* 80.0	0.0 *vs.* 10.0	0.04 (0.3) *vs.* 1.45 (1.5) g	0.04 (0.3) *vs.* 3.8 (4.2) g
	$p < 0.001$*	$p < 0.001$*	$p = 0.039$*	$p < 0.001$*	$p = 0.059$	$p < 0.001$*	$p < 0.001$*
Ketoprofen	35.1 *vs.* 91.3	30.9 *vs.* 80.0	151.8 (66.4) vs. 143.1 (49.9) mg	1.7 *vs.* 22.0	61.8 *vs.*73.3	84.0 (226.9) *vs.* 93.8 (127.6) mg	142.6 (251.7) *vs.* 228.8 (327.3) mg
	$p < 0.001$*	$p < 0.001$*	$p = 0.519$	$p < 0.001$*	$p = 0.325$	$p = 0.735$	$p = 0.057$
Pethidine	76.6 *vs.* 91.3	75.5 *vs.* 72.5	96.8 (76.3) *vs.* 83.0 (39.6) mg	61.7 *vs.* 20.0	29.4 *vs.* 13.3	35.6 (39.9) *vs.* 18.1 (45.2) mg	93.6 (107.1) *vs.* 53.8 (134.9) mg
	$p = 0.010$*	$p = 0.649$	$p = 0.191$	$p < 0.001$*	$p = 0.120$	$p = 0.007$*	$p = 0.031$*

*Values are % of cases or mean (SD). Recommendation—as recommended by the attending anaesthesiologist, given—the mean dose given during the stay in a certain department. PACU—postanaesthesia care unit, SU—surgical unit (department of surgery). Doses in SUs 24 h—cumulative doses of analgesics in surgical units over 24 h after postoperative admission. Doses in SUs 72 h—cumulative doses of analgesics over 72 h after postoperative admission. *$p < 0.05$, 2016 vs. 2018 studies.*

that the pain management plan was likely to be changed not only in terms of the particular analgesics but from the hourly timing of prescription into "medication under request", as well. Diclofenac was selected for postoperative analgesia 10 times more frequently compared to paracetamol in the Department of Surgery I in 2016, but its use decreased by 22% in 2018 (Table 3). Diclofenac was selected by the Department of Surgery II for 3% of patients in 2016. It was not prescribed for any patient in 2018. (Table 4). Ketorolac remained a popular systemic analgesic in Department of Surgery I both in 2016 and 2018 (Table 3). Ketoprofen was chosen more frequently in Department of Surgery II than ketorolac, 2016 *vs.* 2018. Dexketoprofen for postoperative analgesia remained popular in Department of Surgery II, 2016 *vs.* 2018 (Table 4).

Postoperative side effects which are presumed to be analgesic related are presented in Table 5. According to the 2016 survey, 17/94 (17%) patients experienced postoperative side effects. The most common of them were nausea and vomiting (Table 5). According to the 2018 study, 4/80 (5%) patients experienced one postoperative side effect—nausea. Data of postoperative side effects were not evaluated or registered for 10/94 (11%) *vs.* 10/80 (13%) patients in 2016 *vs.* 2018, respectively.

TABLE 3. Profile of Systemic Analgesia in Department of Surgery I: 2016 *vs.* 2018.

Variable	Given, 2016	Given, 2018	*p* value
Paracetamol	2/60 (3.3)	40/50 (80)	$p < 0.0001$
Ketoprofen	1/60 (1.7)	11/50 (22)	$p < 0.0001$
Pethidine	37/60 (61.7)	10/50 (20)	$p < 0.0001$
Ketorolac	26/60 (43.3)	26/50 (52)	$p = 0.3654$
Diclofenac	18/60 (30)	4/50 (8)	$p = 0.0421$

Values are no/of total number (%) of cases when medication was given.

TABLE 4. Profile of Systemic Analgesia in Department of Surgery II: 2016 *vs.* 2018.

Variable	Given, 2016	Given, 2018	*p* value
Paracetamol	0/34 (0.0)	3/30 (10.0)	$p = 0.059$
Ketoprofen	21/34 (61.8)	22/30 (73.3)	$p = 0.325$
Pethidine	10/34 (29.4)	4/30 (13.3)	$p = 0.123$
Dexketoprofen	5/34 (14.7)	6/30 (20.0)	$p = 0.575$
Ketorolac	6/34 (17.6)	3/30 (10.0)	$p = 0.387$
Diclofenac	1/34 (2.9)	0/30 (0.0)	$p = 0.344$

Values are no/of total number (%) of cases when medication was given.

4. Discussion

The main finding of our current study is that guidelines of postoperative pain management adopted in the Departments of Anaesthesiology and Surgery I after our first survey had a positive effect on continuity of systemic analgesia in the process of patient transfer from one department to another. This resulted in prescription and administration of analgesics at certain time points but not under patient request leading to statistically significant reduction of opioid consumption and increase in the administration of paracetamol and ketoprofen. The Department of Surgery II did not implement the suggested guidelines into daily practice, and this led to only a slight increase in the administration of systemic paracetamol and ketoprofen.

However, pain intensity is still poorly monitored in both Departments of Surgery, and the practice raises the question about the adequacy of postoperative analgesia. Discussion

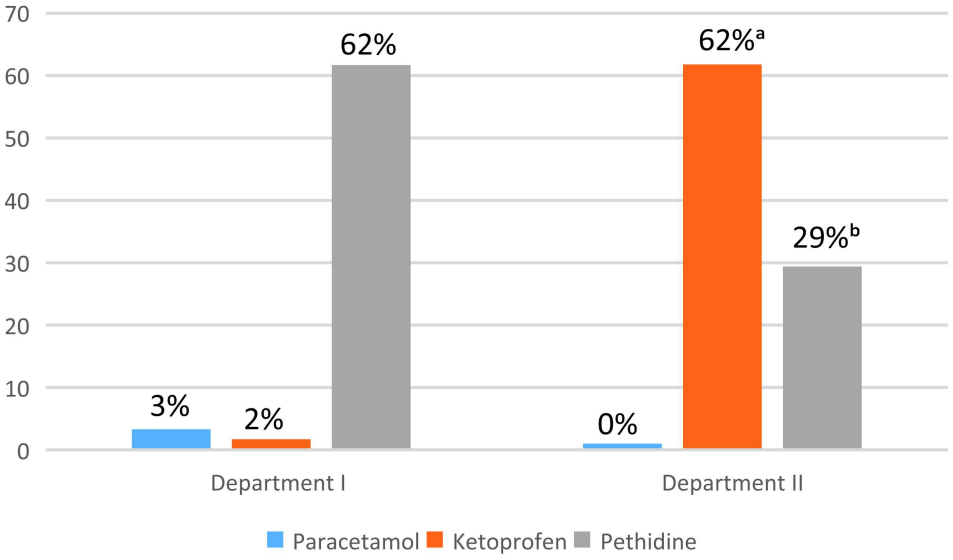

FIGURE 3. Analgesic Pattern in Departments of Surgery I *vs.* II in 2016. Values are % of total cases. $^{a}p < 0.05$ ketoprofen; $^{b}p < 0.05$ pethidine in Departments of Surgery I *vs.* II, 2016.

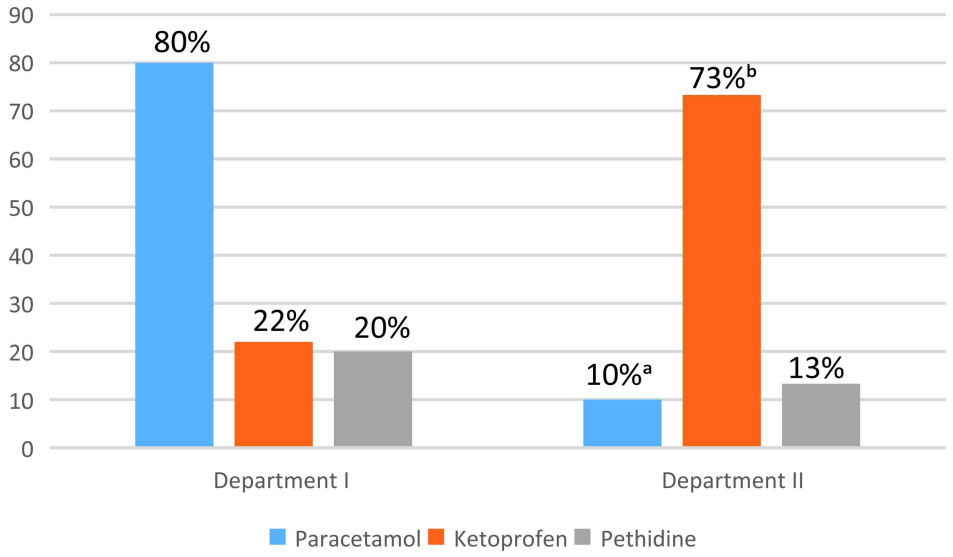

FIGURE 4. Analgesic Pattern in Departments of Surgery I *vs.* II in 2018. Values are % of total cases. $^{a}p < 0.05$ paracetamol; $^{b}p < 0.05$ ketoprofen in Departments of Surgery I *vs.* II, 2018.

with the surgical teams after the second study revealed that pain intensity was evaluated on a verbal 0–10 numeric rating scale (NRS) rather than VAS but this was done at irregular intervals ("when the patient complains about pain" or "when the nurse has time"). However, the value of pain intensity was not recorded in any available medical documents making assessment of the quality of analgesia difficult. Reduction of the use of opioids and implementation of balanced multimodal analgesia must go in line with continuous assessment of postoperative pain preventing not only opioid overdosage but providing adequate analgesia, as well. Opioids are still the mainstay of treatment of acute postoperative pain after major surgery when other methods of postoperative analgesia are not applied. Inappropriate pain assessment or misinterpretation can lead to inadequate pain relief, impaired patient mobility, wound healing, respiratory complications and other harmful outcomes [8–10]. On the other hand, pain intensity should be monitored with validated and reliable tools and treatment should be based not only on certain numbers on a scale. Proper pain assessment should include location, nature, intensity and must be context-sensitive (type of surgery, psycho-social factors) [11–13].

Unfortunately, data supporting positive effect of routine pain assessment on patient outcomes is lacking [14]. Institutions trying to implement pain monitoring into routine practice report inconsistencies in the frequency and nature of pain assessment [15, 16]. Guidelines for the use of opioids in children released in 2019 by the Society of Pediatric Anaesthesia have rated the available data proving necessity of pain assessment and analgesic efficacy as moderate, level B evidence [17]. However, it is hard to imagine another option for safe patient care.

TABLE 5. Postoperative side effects in PACU and Departments of Surgery, 2016 *vs.* 2018.

Postoperative side effects	Year, 2016	Year, 2018	*p*, 2016 *vs.* 2018
Nausea	11 (11.7)	4 (5.0)	$p = 0.26$
Vomiting	3 (3.2)	0 (0.0)	NA
Arterial hypotension	2 (2.1)	0 (0.0)	NA
Stomach pain	1 (1.1)	0 (0.0)	NA
Pruritus	0 (0.0)	0 (0.0)	NA
Total	17 (18.1)	4 (5.0)	$p = 0.01$

Values are no of cases (%) of total number of patients. NA—not applicable.

Our studies did not aim to find out possible reasons why pain intensity was not monitored in surgical departments. We can only presume that it was due to insufficient education, work overload and lack of motivation of the nursing staff. Implementation of guidelines into clinical setting faces a broad spectrum of challenges. Cabana *et al.* [18] (1999) have found 293 potential barriers to physician guideline adherence. The barriers can be divided into big groups: awareness, familiarity, agreement, self-efficacy, outcome expectancy, ability to overcome inertia, and absence of external obstacles to perform recommendations [18]. Adoption of clinical guidelines consists of 2 categories: primary strategies involving creation, mailing and publication, and secondary interventional strategies to reinforce the guidelines [18]. Emond *et al.* [19] (2020) have found that obstacles for implementation of patient safety guidelines in the perioperative setting in the Netherlands were: time barrier (16% of the total number of barriers), emergency patients (8%), inefficient Information Technology (IT) structure (4%) and workload (3%). Van Gulik *et al.* [20] have found that adherence is especially poor in terms of nonscheduled, flowchart-guided interventions. Joint efforts are needed to make the guidelines of postoperative pain management work in real-time clinical practice.

Most authors point out that the use of several different medications to treat post-operative pain reduces the potential side effects of opioid and non-opioid class medications, and the importance of multimodal analgesia is increasingly being discussed worldwide. Centrally acting analgesics morphine and its synthetic derivatives can cause side effects such as nausea, vomiting and respiratory depression [21]. Although most studies report these side effects as the most common, patients are also more likely to experience delirium, increased risk of injury, cardiovascular pathologies, pneumonia and prolonged hospital stay [22]. Takkouche *et al.* [23] (2007) found that those exposed to opioids had a 38% increased risk of fractures. A systematic review of 866 patients using medications (including opioids) that may increase the risk of delirium was published in 2011 [24]. Solomon *et al.* [25] (2010) also reported an increased risk of cardiovascular events by using codeine. Dublin *et al.* [26] (2011) found that nearly 50% of older patients using opioids were at higher risk for pneumonia. In our study, the number of side effects was rather small. We presume the reasons are inaccurate follow-up and registration of patient data in the postoperative period. In 2016, 17% of patients experienced postoperative side effects, the most common of which were nausea, vomiting, arterial hypotension and stomach pains. In 2018 patients experienced one postoperative side effect—nausea. More detailed investigation of opioid- or analgesia-related side effects should be conducted in future studies.

Non-steroidal anti-inflammatory drugs (NSAIDs), acting through a peripheral pain relief mechanism, were introduced in 1950's to reduce opioid use. The date is considered to be the beginning of multimodal analgesia [27]. Ketoprofen has a short half-life, a simple metabolism, and a broad therapeutic window, and does not accumulate with multiple doses [28]. These features contribute to a rapid onset of action, flexible dosing, and a reliable tolerance profile. In our study, ketoprofen use in Department of Surgery I increased by 20% in 2018, compared to 2016. However, it is also important to note that its use in Department of Surgery II has increased only slightly compared to 2016.

A very favourable tolerability ratio has made paracetamol one the most common medications in postoperative multimodal analgesia regimens [29]. According to our 2018 study, the use of paracetamol for postoperative analgesia increased by 77%, compared to 2016, while the need for opioids decreased by almost 42%. However, while the use of paracetamol in the surgical units increased, the need for opioids in the PACU remained similar and could be related to the high pain intensity during the first postoperative hours. Graff and Grosh (2016) from Anesthesia Patient Safety Foundation suggest that opioids still have a critical role in acute postoperative pain management, especially for procedures where a primary regional, neuraxial, or local infiltration is not possible [30].

Many studies also recommend the use of multimodal analgesia in combination with epidural, spinal and local anesthesia [31]. Cochrane review analyzed randomized controlled trials comparing patients after abdominal surgery with different methods of postoperative analgesia and found that epidural analgesia was more effective in relieving pain compared to patient-controlled intravenous analgesia during the first 72 h after surgery [32]. The interest in transverse abdominal plane block (TAP), as an effective method of postoperative analgesia, has been growing over the past decade, as well. Brady *et al.* [33] demonstrated in 2012 that TAP blockade is safe and effective in reduction of intraoperative and postoperative pain intensity and opioid requirements in patients after right hemicolectomy.

Analgesic adjuvants have been shown to be effective in relieving postoperative pain, as well. Koh *et al.* [34] (2019) proved that treatment of patients with central sensitization caused by chronic pain before and after knee arthroplasty with duloxetine resulted in better postoperative pain management and faster postoperative recovery. Weibel *et al.* [35] (2016) stated that a combination with lidocaine reduced the need for opioids during laparoscopic abdominal surgery by about 30%, with lower postoperative pain at 24 h and reduced length of hospital stay by approximately 8 hours. Caumo *et al.* [36] (2009) demonstrated the efficacy of clonidine in the manage-

ment of postoperative pain. Patients treated with clonidine preoperatively experienced less postoperative pain, resulting in a 30% reduction in opioid demand.

Choi *et al*. [37] (2014) found that continuous epidural infusion combined with systemic multimodal analgesia resulted in reduction of 48-hr cumulative opioid consumption following one or two-level lumbar spinal fusion. Kandarian *et al*. [38] (2019) suggested that the use of a multimodal analgesic pathway combining systemic nonopioid medications and regional anesthesia techniques is associated with improved pain scores, lower opioid requirements, shorter hospital stay, and fewer complications for a variety of surgeries. Patients with regional analgesia were excluded from our study because we aimed to demonstrate the efficacy of systemic analgesia and its continuity during the perioperative patient transfer. Analysis of the effects of combined regional and systemic analgesia could be the aim of our following study.

Our analysis of systemic analgesia was mainly focused on 3 medications: paracetamol, ketoprofen and pethidine. They are the mainstay of systemic analgesia in the Department of Anaesthesiology due to available intravenous forms. Pethidine is the most popular systemic opioid in Departments of Surgery in our hospital and this is the reason to start it in Department of Anaesthesiology, as well, so that it could be continued after patient transfer to SUs. However, as demonstrated in Tables 2 and 3, the choice of non-opioid analgesics in Departments of Surgery included but was not limited to the analgesics mentioned above. A study by Parvizi *et al.* [39] (2013) investigating the effects of multimodal analgesia after arthroscopy found that ketorolac was preferred due to better postoperative pain management. A single dose of dexketoprofen trometamol 50 mg given intramuscularly provided faster, better, and longer duration of analgesia in postoperative patients of hernia repair surgery than diclofenac 50 mg, with comparable safety [40]. In another study, a continuous postoperative ropivacaine and ketorolac infusion resulted in better pain control and satisfaction after total hip arthroplasty compared to placebo with saline [41]. In a trial comparing periarticular multimodal drug injection of ropivacaine, ketorolac, and epimorphine with control group (no injection) after total hip arthroplasty, significant improvements in pain scores, opioid consumption, and patient satisfaction were observed over control group [42].

Decision on what particular analgesic should be chosen is not an easy question in clinical practice. Multiple analgesic options are available but the evidence of multi-criteria decision analysis is lacking. A study by Moore (2017) has demonstrated a multicriteria decision analysis model to evaluate 6 over-the counter analgesics in terms of risk and benefit [43]. However, whether this evaluation based on expert opinion, could serve as a solid background for decision making in clinical practice needs further investigation. In addition, switching from systemic opioids and non-opioids to oral forms of analgesic medications to provide adequate analgesia and possibility of faster release from the hospital should be the next step in our postoperative analgesia programs. However, pain assessment with validated and reliable tools and monitoring of adequacy of analgesia are still the cornerstones of all pain management programs and we cannot omit them.

5. Limitations and future perspectives

Our both studies revealed that a major drawback in management of postoperative systemic analgesia after general anaesthesia was the continuing absence of pain intensity registration in surgical departments. Despite a positive effect of the guidelines of postoperative analgesia adopted in one of the surgical departments in terms of significant reduction of the use of opioids and more extensive use of non-opioid analgesics, lack of solid proof about pain intensity in available medical records casts doubt about the reliability of pain management.

In this study, the side effects of analgesia were underestimated and there was no long-term follow-up of the patients. There was no close monitoring of recovery of such important functions as ability of oral intake of food and medications, time to spontaneous urination and defaecation as well as recovery of motor functions. The study included a broad range of surgical interventions suggesting that pain intensity and requirement of analgesia could be different.

To make the program of postoperative pain management more effective, joint efforts are needed to investigate the obstacles of monitoring pain intensity in surgical units, as well as inclusion of pain intensity assessment tools into the perioperative care, improved registration of postoperative complications and development of an individualized pain management plan based on the institution's standards of continued balanced analgesia.

We did not include patients under combined systemic and regional analgesia because this was beyond the scope of the current studies. Nevertheless, development of treatment plans and monitoring of adequacy of combined systemic and regional analgesia should be considered in the future.

6. Conclusions

According to both 2016 and 2018 surveys, the majority of patients during the stay in postanaesthetic care unit, received postoperative systemic analgesia according to the recommendations of the attending anaesthesiologist. The 2018 study revealed that implementation of postoperative analgesia guidelines in Department of Surgery I had positive effect in terms of statistically significantly increase in the use of non-opioid analgesics with reduction of opioid consumption by 42% and improved continuity of multimodal systemic analgesia compared to 2016. Adherence to the recommendations of postoperative systemic analgesia given by the attending anaesthesiologist in Department of Surgery II remained low in 2018 and no positive statistically significant changes compared to 2016 could be found. However, pain intensity is not monitored in both Departments of Surgery, and this raises the question about the adequacy of postoperative analgesia.

AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article and supplementary material.

AUTHOR CONTRIBUTIONS

JG and LJ—designed the research study; LJ and BS—performed the research; DCR—provided help and advice on design and manuscript preparation; LJ and BS—analysed the data; LJ and JG—wrote the manuscript. All authors contribute to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The protocol of the first study was approved by Kaunas Bioethics Committee, No. BEC-MF-489, 06 08 2016. The protocol of the second study was approved by Kaunas Bioethics Committee, No. BEC-MF- 46, 05 11 2018. Written informed consent was obtained from all patients involved in the studies.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.signavitae.com/mre-signavitae/article/1580135563471536128/attachment/Supplementary%20material.pdf.

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