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Original Article

The role of clinical pharmacists in multidisciplinary teams for postoperative pain management in lumbar spine surgery: A prospective study

[El papel de los farmacéuticos clínicos en equipos multidisciplinarios para el manejo del dolor postoperatorio en cirugía de columna lumbar: Un estudio prospectivo]

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Abstract

Context: The role of clinical pharmacists in a multidisciplinary team (MDT) related to pain management is still limited in Vietnamese hospitals.

Aims: To evaluate the impact of clinical pharmacists within a multidisciplinary team (MDT) on postoperative pain management, focusing on the optimization of analgesic usage, drug safety, fentanyl consumption, and pain scores.

Methods: Conducted at a tertiary hospital in Vietnam, this before-and-after study involved lumbar spine surgery patients. The intervention group received pharmacist-led MDT care, focusing on adherence to clinical pathways, minimizing adverse drug reactions (ADRs), and managing fentanyl use and pain levels using the Verbal Analogue Scale (VAS).

Results: Eighty patients participated, split evenly between intervention and control groups. The intervention group showed significant improvements in analgesic compliance (97.5% vs. 80.0%, p=0.04) and a higher usage of nefopam over gabapentinoids. Although reductions in fentanyl dose and pain scores were observed, these changes were not statistically significant.

Conclusions: Clinical pharmacists effectively enhanced pain management and drug safety within the MDT framework. Further research is necessary to more definitively ascertain the impact on pain scores.

Keywords: clinical pharmacist; fentanyl dose; multidisciplinary team; pain management.

Resumen

Contexto: El papel de los farmacéuticos clínicos en un equipo multidisciplinario (EMD) relacionado con el manejo del dolor aún es limitado en los hospitales vietnamitas.

Objetivos: Evaluar el impacto de los farmacéuticos clínicos dentro de un equipo multidisciplinario (EMD) en el manejo del dolor postoperatorio, centrándose en la optimización del uso de analgésicos, la seguridad farmacológica, el consumo de fentanilo y las puntuaciones de dolor.

Métodos: Realizado en un hospital terciario de Vietnam, este estudio de antes y después incluyó a pacientes sometidos a cirugía de columna lumbar. El grupo de intervención recibió atención EMD dirigida por farmacéuticos, centrándose en la adherencia a las vías clínicas, la minimización de las reacciones adversas a medicamentos (RAM) y el manejo del consumo de fentanilo y los niveles de dolor mediante la Escala Verbal Analógica (EVA).

Resultados: Participaron ochenta pacientes, divididos equitativamente entre los grupos de intervención y control. El grupo de intervención mostró mejoras significativas en el cumplimiento del tratamiento analgésico (97,5 % frente al 80,0 %, p=0,04) y un mayor uso de nefopam en comparación con gabapentinoides. Si bien se observaron reducciones en la dosis de fentanilo y en las puntuaciones de dolor, estos cambios no fueron estadísticamente significativos.

Conclusiones: Los farmacéuticos clínicos mejoraron eficazmente el manejo del dolor y la seguridad farmacológica en el marco del EMD. Se necesitan más investigaciones para determinar con mayor precisión el impacto en las puntuaciones de dolor.

Palabras Clave: dosis de fentanilo; equipo multidisciplinario; farmacéutico clínico; manejo del dolor.

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Abbreviations: ADRs: adverse drug reactions; ASA: American Society of Anesthesiologists; BMI: body mass index; CG: control group; CPs: clinical pharmacists; GI: Gastrointestinal; IG: intervention group; MDT: multidisciplinary team; NSAIDs: Non-steroidal anti-inflammatory drugs; POD: postoperative days; PCA: Patient-controlled analgesia; VAS: Verbal Analogue Scale.

INTRODUCTION

Unrelieved postoperative pain is a global issue that leads to poor patient outcomes, particularly in developing countries like Vietnam. Inadequate management of postoperative pain is linked to a range of adverse effects, including post-surgical complications, chronic pain, diminished quality of life, extended recovery periods, increased opioid consumption, and higher healthcare costs (Eisenach and Brennan, 2018; Raja et al., 2020). Despite its prevalence, where over 80% of patients report acute pain post-surgery and a significant majority rate their pain as moderate to severe, less than half receive adequate pain management (Eisenach and Brennan, 2018; Gan, 2017; Raja et al., 2020).

Advancements in Vietnamese healthcare have increased the frequency of surgical procedures, yet patient-centered perioperative care remains deficient. Common issues include perceptions of unsafe anesthesia and the occurrence of multiple postoperative symptoms, with a substantial percentage of patients experiencing severe pain shortly after surgery and no pain relief within the first day (Soejima et al., 2010). These issues often stem from inadequate knowledge, negative attitudes, and passive approaches to pain management among healthcare providers (Nguyen et al., 2021) and patients alike (Vu et al., 2023). Additionally, the limited availability of opioids in Vietnam, unlike in developed countries with initiatives to curb opioid use (Barlas, 2017), exacerbates under-treatment of pain due to prescribers' inexperience and reluctance.

The multidisciplinary team (MDT) approach is increasingly recognized as effective for managing pain (Staudt, 2022). In developed countries, clinical pharmacists (CPs) play a crucial role within MDTs, contributing significantly to pain management (Bansal and Morris, 2019; Mathew et al., 2016). However, the integration of CPs in pain management MDTs is not yet comprehensive globally, and particularly in Vietnam, gaps remain in fully utilizing their potential (Dong et al., 2022; Gavaza and Vickery, 2018; Qin et al., 2023; Shrestha et al., 2023). This study evaluates the role of CPs in an MDT, focusing on optimizing analgesic use, drug safety, fentanyl consumption, and pain scores through standardized processes and a clinical pathway in a Vietnamese hospital setting.

MATERIAL AND METHODS

Study design and participants

This pre- and post-intervention study was conducted at Nguyen Tri Phuong Hospital, one of the largest public tertiary hospitals in Ho Chi Minh City, Vietnam. Participants in the historical control group (CG) received routine care and underwent surgery from December 2021 to February 2022. The intervention group (IG), managed by an MDT including CPs, underwent surgery from May to July 2022.

Eligibility and exclusion criteria

Participants were eligible if they were 18 years or older, underwent elective lumbar spinal fusion surgeries, and were treated in the Neurosurgery Department. Exclusion criteria included patients with systemic diseases requiring special perioperative care, communication barriers with healthcare providers, those lost to follow-up, or who declined participation.

Sample size calculation

The sample size was determined based on a review of thirty-one trials with pain scores ranging from 14–69 mm on the Verbal Analogue Scale (VAS) (Geisler et al., 2022). Assuming a mean VAS score of 5 cm on the first postoperative day, a clinically important difference of 1.5 points, and a standard deviation of 3.2 (Brusko et al., 2019), a total of 36 patients per group was required to achieve a power of 90% with a significance level of 0.05 and an anticipated dropout rate of 20%.

MDT establishment and pharmacist interventions

The MDT for acute perioperative pain management was established following a literature review (Chou et al., 2016; De Andrés et al., 2015; Venkatraman et al., 2021; Waelkens et al., 2021; Yang et al., 2020) and consultations with local healthcare professionals. Interventions included preoperative, intraoperative, and postoperative pharmacological management based on a developed clinical pathway, with adjustments made based on ongoing assessments, including pain history, gastrointestinal (GI) function, respiratory status, and potential adverse drug reactions. Details of the protocols and interventions are outlined in Fig. S1.

Control group

The CG received standard pain management without CPs involvement, with drugs administered based on clinical experience rather than a standardized protocol. Pharmacists provided prescription reviews primarily for antibiotics.

Outcome measures

Primary outcomes were assessed using the VAS for pain at 24 hours, 48 hours, and at discharge. Secondary outcomes included optimization of analgesic use, management of adverse drug reactions (ADRs), and fentanyl consumption. ADR severity was classified using the Naranjo algorithm (Naranjo et al., 1981).

Data collection

Data were collected from interviews and medical records by two CPs for patients in both the CG and IG. The baseline data included patient age, sex, body mass index (BMI), number of motion segments treated, American Society of Anesthesiologists (ASA) classification, surgery duration, and intraoperative blood transfusion details. The ASA grading system, which categorizes preoperative comorbid conditions on a scale from 1 to 6 (Committee on Economics, 2020), was utilized to assess and assign the ASA class for each patient.

Ethics approval

The study received ethical approval from the Nguyen Tri Phuong Hospital Ethics Committee on November 11, 2021 (Approval No. 1547/NTP-CD). Oral informed consent was obtained from participants during each encounter, and all personal data was de-identified. Persons who did not consent still received treatment per the study protocol and guidelines, but were excluded from all analyses.

Statistical analysis

Data analysis was conducted using Statistical Package for the Social Sciences (SPSS) version 20.0. The Shapiro-Wilk test determined the appropriateness of parametric versus nonparametric tests for the baseline and outcome variables. The Mann–Whitney U test evaluated differences in total fentanyl consumption on postoperative days (POD), VAS scores, and other non-normally distributed variables between the groups. Daily average fentanyl consumption was analyzed using the Independent Samples T Test. Categorical variables were assessed using the Chi-squared test. A p-value of less than 0.05 was deemed statistically significant.

RESULTS

Study population

A total of 80 patients participated in the study, with 40 in the CG and 40 in the IG. No significant differences were found in baseline demographic and clinical characteristics between the groups (Table 1).

Rate of compliance with standard practice

Compliance with the prescribed analgesic protocols was significantly higher in the IG than in the CG, with 97.5% of IG patients adhering to the protocols compared to 80.0% in the CG (p=0.04) (Table 2).

Analgesics consumption

The use of gabapentinoid and/or eperisone was significantly lower in the IG (30.0%) compared to the CG (67.5%, p=0.001). Conversely, nefopam usage was significantly higher in the IG (92.5%) than in the CG (70.0%, p=0.01).

Fentanyl consumption

The IG exhibited a non-significant reduction in mean daily fentanyl dose compared to the CG (564.6 ± 88.4 μg vs. 597.5 ± 123.9 μg; p=0.2). Although the duration of fentanyl use was longer in the IG (median 4.0 days) than in the CG (median 3.0 days, p=0.06), the total fentanyl dose increase in the IG was not statistically significant (2250 μg vs 1800 μg; p=0.2) (Table 2).

Pain scores

Pain scores on postoperative day 1 and at discharge were lower in the IG compared to the CG, although these differences were not statistically significant (Day 1: 5.7 vs 6.4, p=0.36; Discharge: 1.8 vs 2.3, p=0.08) (Table 3).

Adverse drug reactions (ADRs)

A total of 46 ADRs were detected in the IG compared to 40 in the CG. The most common ADR was constipation, accounting for 87.5% in the IG and 82.5% in the CG. Other ADRs included vomiting/nausea, hallucinations, fatigue/dyspnea, palpitations/tachycardia, and confusion. ADR occurrence was particularly higher among patients taking gabapentinoid/eperisone with fentanyl, with an odds ratio of 9.333 (95% CI: [1.8-47.2], p=0.006) (Table 4). Pain levels were also higher in patients with ADRs, with significant differences noted on postoperative days 1 and 2 (Day 1: 7.8 vs. 5.03, p=0.04; Day 2: 6.6 vs. 4.4, p=0.04).

Table 1. Patient characteristics.

Variable	Total (n = 80)	Control group (n = 40)	Intervention group (n = 40)	p-value	Test
Age (years), median (min-max)	59 (23 – 83)	58 (31 – 76)	63 (23 – 83)	0.2	Mann-Whitney
Gender (female), N (%)	45 (56.3%)	18 (45.0%)	27 (67.5%)	0.4	X^2
Height (cm), mean ± SD	160 ± 7.7	160 ± 8.2	159 ± 6.7	0.3	Independent samples t-test
Weight *(kg),* mean ± SD	60 ± 8.8	60.3 ± 10.1	58.1 ± 8.9	0.6	
Number of motion segments of the lumbar spine treated, N (%)					
1	26 (32.5 %)	16 (40.0%)	10 (25.0%)	0.4	
2	28 (35.0 %)	14 (35.0%)	14 (35.0%)		
≥ 3	26 (32.5 %)	10 (25.0%)	16 (40.0%)		
ASA grade, N (%)					
1	15 (18.8 %)	9 (22.5%)	6 (15.0%)	0.5	
2	51 (63.7 %)	23 (57.5%)	28 (70.0%)		
3	14 (17.5 %)	8 (20.0%)	6 (15.0 %)		
Duration of surgery (minutes), mean (min–max)	168 (60 - 390)	156 (60 - 390)	180 (60 - 318)	0.6	Mann-Whitney
Blood transfusion (yes), N (%)	29 (36.3%)	13 (32.5%)	16 (40.0%)	0.5	X^2
(p<0.05)					

Table 2. Comparison of analgesics consumption between control and intervention groups.

Variable	Control group (n = 40)	Intervention group (n = 40)	p-value	Test
Analgesics				
Intra-operative corticosteroid, N (%)	27 (67.5%)	32 (80.0%)	0.1	X2
Paracetamol, N (%)	40 (100.0%)	40 (100.0%)	-	
NSAIDs, N (%)	4 (10.0%)	2 (5.0%)	0.7	
Nefopam, N (%)	28 (70.0%)	37 (92.5%)	**0.01**	
Gabapentinoids, N (%)	26 (65.0%)	9 (22.5%)	**< 0.001**	
Eperisone, N (%)	6 (15.0%)	7 (17.5%)	0.8	
Gapabentinoids and/or epersisone, N (%)	27 (67.5%)	12 (30.0%)	**0.001**	
Fentanyl, N (%)	40 (100.0%)	40 (100.0%)	-	
Pain management regimen				
A regimen (Fentanyl + Paracetamol + NSAID), N (%)	4 (10.0%)	2 (5.0%)	0.7	
B regimen (Fentanyl + paracetamol+ nefopam), N (%)	28 (70.0%)	37 (92.5%)	**0.01**	
Use A or B regimen, N (%)	32 (80.0%)	39 (97.5%)	**0.04**	
Fentanyl consumption				
Mean daily fentanyl dose (mcg), mean ± SD	597.5 ± 123.9	564.6 ± 88.4	0.2	Independent samples t-test
Number of days of using fentanyl (day), median (min-max)	3.0 (1.5-7.5)	4.0 (1.0-8.0)	0.06	Mann-Whitney
Total fentanyl dose (mcg), median (min-max)	1800 (800 - 6500)	2250 (700 - 4700)	0.2	
(p<0.05)				

Table 3: Postoperative pain scores in patients after lumbar spine surgery.

Pain at rest score (VAS)	**Control group (n = 40)**	**Intervention group (n = 40)**	**p-value**	**Test**
24h after	6.4 ± 3.0	5.7 ± 3.5	0.36	Mann-Whitney
48h after	5.0 ± 2.3	5.0 ± 2.8	0.7	
Discharge	2.3 ± 1.5	1.8 ± 1.1	0.08	
(p<0.05)				

Table 4. Characteristics of patients with and without adverse drug reactions.

Characteristics	**Patients with ADRs (n = 10)**	**Patients without ADRs (n = 30)**	**p-value**	**Test**
Age (years) mean ± SD	64.4 ± 6.7	57.97 ± 14.2	0.06	Independent samples t-test
Gender				
Female, N (%)	8 (80.0 %)	19 (63.3 %)	0.3	χ2
Male, N (%)	2 (20.0 %)	11 (36.6 %)		
Height (cm) mean ± SD	157.8 ± 5.4	159.37 ± 7.3	0.8	Independent samples t-test
Weight (kg) mean ± SD	61.0 ± 7.2	58.2 ± 8.7	0.4	
ASA grade				
1, N (%)	1 (10.0 %)	5 (16.7 %)	0.9	χ2
2, N (%)	7 (70.0 %)	21 (70.0 %)		
≥ 3, N (%)	2 (20.0 %)	4 (13.3 %)		
Corticosteroid intra-operation				
Yes, N (%)	9 (90.0 %)	23 (76.7 %)	0.7	
No, N (%)	1 (10.0 %)	7 (23.3 %)		
Pain management regimen				
A regimen, N (%)	1 (10.0 %)	1 (3.3 %)	0.6	
B regimen, N (%)	9 (90.0 %)	28 (93.3 %)		
Gabapentinnoids/eperisone				
Yes, N (%)	7 (70.0 %)	6 (20.0 %)	**0.006**	
No, N (%)	3 (30.0 %)	24 (80.0 %)		
(p<0.05)				

DISCUSSION

Rate of compliance with standard practice

In Vietnam, the integration of clinical pharmacy into healthcare facilities has not been fully realized, focusing primarily on non-patient-specific activities. According to a 2022 national survey of 560 hospitals, patient-oriented activities remain insufficiently developed (Dong et al., 2022). Although the MDT approach has proven effective in antimicrobial stewardship programs (Huong et al., 2021; Son et al., 2017), its adoption for pain management in Vietnamese hospitals is rare, particularly in settings lacking local anesthetic-based regional analgesic techniques.

This study highlighted significant improvements in the standardization of pain management, including a more comprehensive evaluation of pain, selection of appropriate analgesic regimens, and tailoring of anal-

gesic doses based on patient responses. Additionally, the management of ADRs was standardized, and the frequency of medication preparation was minimized. CPs were instrumental in standardizing drug administration through educational initiatives for physicians, medication reviews, and targeted interventions.

Multimodal analgesic regimen

The adoption of a multimodal analgesic approach has become standard practice for managing postoperative pain. During the intervention phase, CPs engaged in discussions with physicians about combining various analgesic medications and employing multimodal therapies, thus moving beyond traditional reliance on one or two types of analgesics (Chou et al., 2016; Waelkens et al., 2021). This collaborative effort resulted in an increased usage of prescribed A or B analgesic regimens, with rates rising from 80.0% in the control group to 97.5% in the intervention group. CPs conducted regular patient follow-ups to ensure accurate dosing for optimal efficacy and safety, with most pharmacists' recommendations being accepted after discussions with physicians (Fig. S2).

Analgesics consumption

The study observed a shift in analgesic practices, with decreased use of gabapentinoids due to their side effects, such as sedation and respiratory depression, and an increased reliance on nefopam over Non-steroidal anti-inflammatory drugs (NSAIDs), minimizing potential cardiovascular and gastrointestinal risks. Despite these changes, the reduction in pain scores and daily fentanyl doses were not statistically significant. This could be attributed to the complexity of surgeries and limited adjustments in fentanyl dosing, constrained by hospital resources. Moreover, the lack of available Patient-controlled analgesia (PCA) pumps led to reliance on less optimal continuous opioid infusions.

Fentanyl use and pain score

In this study, both the average daily fentanyl dose and the pain scores recorded on the first POD 1 and at discharge were lower in the IG than in the CG, although the differences were not statistically significant. Several factors may explain these outcomes. First, the IG had a higher proportion of patients undergoing surgeries involving three or more motion segments of the lumbar spine—40.0% compared to 25.0% in the CG. Such surgeries are considered significant risk factors for poor postoperative pain control, as identified by Yang et al. (2020). Second, the adjustment of the fentanyl dose was performed once daily, constrained by limited hospital staffing, despite recommendations for more frequent assessments to maintain a VAS score under four (Chou et al., 2016; De Andrés et al., 2015). Third, the absence of PCA pumps in our facility necessitated the use of continuous opioid infusions, although PCA is the recommended practice for managing pain after spine surgery (Chou et al., 2016; Waelkens et al., 2021).

Furthermore, although the mean daily dose of fentanyl was reduced, the IG required fentanyl for more extended periods compared to the CG. Consequently, the total fentanyl dose administered during the postoperative period was higher in the IG, yet this increase was not statistically significant. The extended duration of opioid use in the IG, where more patients underwent multilevel spine surgery, aligns with findings from Mathiesen et al. (2013), who reported the use of morphine for up to six days in similar surgical cases. Many patients in the IG experienced significant pain, with VAS scores between 7 and 8 on POD 4 and 5, necessitating ongoing fentanyl administration.

ADR management

CPs played a key role in preventing, detecting, and managing opioid-induced ADRs during the study. Notably, the variety of ADRs was greater in the IG compared to the CG, likely due to more rigorous monitoring by CPs. During direct patient interviews, CPs identified symptoms such as hallucinations and palpitations/tachycardia. Additionally, CPs actively engaged in ward rounds, offering guidance and recommendations on ADR management to physicians.

The study revealed that combining gabapentinoids or eperisone with fentanyl led to a higher rate of ADRs compared to using these agents separately. This increase can be attributed to drug interactions between central nervous system depressants and opioid agonists, suggesting that such depressants should be introduced cautiously following the discontinuation of fentanyl to mitigate risks (Drugs.com, 2025).

Opioid-induced constipation was the most frequently observed adverse event, affecting approximately 80% of patients in the IG, which is higher than the typical incidence range of 40% to 60% (Larkin et al., 2018). Factors such as limited mobility and a suboptimal diet during hospitalization likely exacerbated this condition. This is in line with findings from a study in France, which reported an 85.7% prevalence of constipation among cancer patients on chronic opioid therapy (Abramowitz et al., 2013). Additionally, the incidence of nausea and vomiting decreased from 15.0% in the CG to 7.5% in the IG, potentially due to increased use of intraoperative corticosteroids for nausea and vomiting prophylaxis (Gan et al., 2020).

The predominantly reactive nature of ADR identification in this context highlights the challenges posed by limited resources and systemic overload in the healthcare system. Nevertheless, this study's focus on documenting opioid-associated ADRs provides valuable insights, contrasting with the prevailing data in Vietnam's national database, which predominantly records reactions to antibiotics or NSAIDs.

Limitations

The study's before-and-after design inherently carries risks of bias, potentially influencing the results. Additionally, the subjective nature of pain assessment and the non-inclusion of factors like preoperative opioid use and mental health status may have affected the outcome measures. Future studies could benefit from more robust designs and broader data collection to mitigate these limitations.

CONCLUSION

Vietnamese clinical pharmacists demonstrated the ability to effectively integrate into multidisciplinary teams, enhancing pain management through optimized analgesic use and improved patient safety. To further solidify these benefits, it is imperative to refine and standardize clinical practices and medication pathways. Future research should aim to substantiate these findings and evaluate the sustained impact on patient pain outcomes.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTION:

Contribution	Nguyen HT	Pham NK	Le DT	Nguyen DN	Vo NT	Nguyen CV	Pham TA	Vo HT
Concepts or ideas	x							x
Design	x							x
Definition of intellectual content	x	x	x	x	x	x	x	x
Literature search	x							x
Experimental studies	x	x	x	x	x	x	x	x
Data acquisition	x	x	x	x	x	x	x	x
Data analysis	x	x	x	x	x	x	x	x
Statistical analysis	x	x	x	x	x	x	x	x
Manuscript preparation	x	x	x	x	x	x	x	x
Manuscript editing	x	x	x	x	x	x	x	x
Manuscript review	x	x	x	x	x	x	x	x

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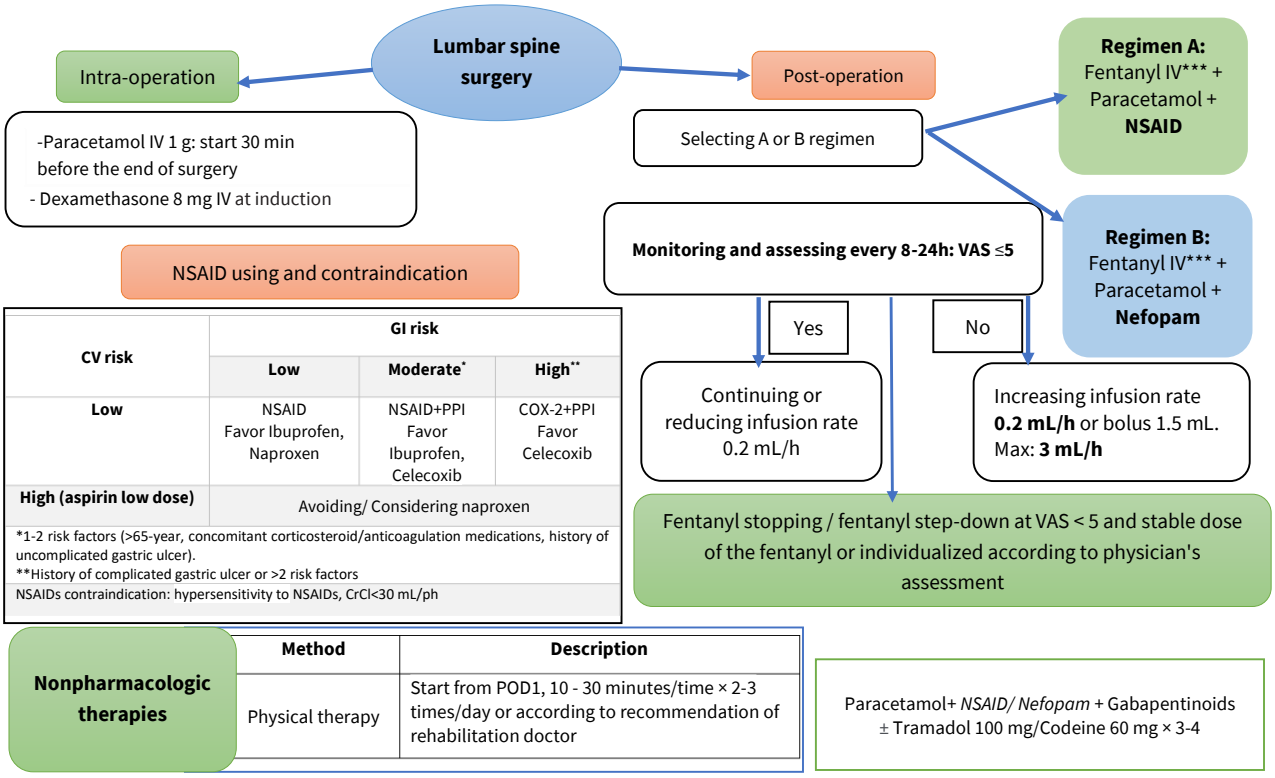
Supplementary data

Responsibilities	Flowchart	Form/ Appendix
Doctors	Patients *are* admitted to the neurosurgical ward for intervention procedures	
Neurosurgery nurses	Informing anesthesiologist and clinical pharmacists	
Attending doctors/ Anesthesiologists/ clinical pharmacists	- Anesthesiologist: preanaesthetic assessment - Attending doctors: perioperative assessment - Clinical pharmacists*:* interviewing of medication history and preoperative assessment of pain	Clinical pharmacists: Filling in a form (**Appendix 1.1)** and discuss with attending doctors
Doctors	- Attending doctors: ordering pain medication pre and post-operation - Anesthesiologists: ordering pain medication intra-operation	According to "**Protocol for pain management after spine surgery**"
Anaesthesia nurses	*Modifying* the dosage of fentanyl to ensure VAS ≤ 5	Filling in a form (**Appendix 1.2)**
Anesthesiologists	Carrying out a physician's order, monitoring and assessement	According to "**Protocol for pain management after spine surgery**"
Neurosurgery nurses	Receiving and evaluating transferred patients	Informing attending/duty doctors Filling in a form (**Appendix 1.2)**
MDT	**Care Coordination**	**-** MDT with patient rounds on POD 1, POD 2 and discharge date - The attending *doctor* will *make decisions* - The nurses fill in a form (**Appendix 1.2)** - Clinical pharmacists provide drug information, monitor adverse events, detect drug related problems and and recommend pharmacological interventions
DISCHARGE		

Figure 1S. Flowchart of an MTD. Standard operating procedure of pain management of an MTD.



***** FENTANYL DOSING**

Choosing a dosage regimen of 0.3 µg/kg/h or 0.4 µg/kg/h depending on the physician's assessment or based on *risk factors* for severe *postoperative pain*: CAPPS score ≥ 9 or spinal *fusion* with ≥3 risk factors: female sex, <70 year, preoperative daily use of opioid medication (tramadol, fentanyl, …), surgery involving ≥3 motion segments.

0.3 µg/kg/h	**Weight (kg)**					
	40	50	60	70	80	90
Fentanyl 100 µg/2 mL (ampoules)	4	5	6	7	8	9
Diluted volume (mL)	50					
Initial dose (mL/h)	2					
Bolus (mL)	1.5					
Increased/ decreased dose (mL/h)	0.2					
Maximal dose (mL/h)	3					

0.4 µg/kg/h	**Weight (kg)**					
	40	50	60	70	80	90
Fentanyl 100 µg/2 mL (ampoules)	4	5	6	7	8	9
Diluted volume (mL)	50					
Initial dose (mL/h)	2					
Bolus (mL)	1.5					
Increased/ decreased dose (mL/h)	0.2					
Maximal dose (mL/h)	3					

Figure S2. Protocol for pain management after spine surgery.

Appendix 1.1. Medication history record and preoperative assessment of pain.

NTP 1903	**MEDICATION HISTORY RECORD AND PREOPERATIVE ASSESSMENT OF PAIN**
	OVERVIEW INFORMATION
Full name:_____ Birthday:_____ Ward:_____ BMI:_____ Day of admission: _____ *Interview date*:_____ Doctor:_____ Pharmacist:_____	□Pregnancy □Lactation □Smoking:……..package/day □Alcohol:……..mL/day Reason for admission:_____ Allergic (factors and description):_____ Medical history:_____ Surgical history:_____ Diagnosis:_____

MEDICATION HISTORY

Drug	Administration/ frequency	Duration	Last dose	Plan	Note	Source*
Other (functional foods, herbal…)						
*: (1): Patient, (2): Documentation (3): Patients' relatives						

ASSESSMENT

GI function: □Normal □Abnormal:_____ Respiratory function: □Normal □ Abnormal:_____ + *VAS* at move/ rest:____/____. Response to pain medication: □ Yes □ No + *Anxious:* □ A lot □ Little □ No + *Sleeping*: ____hours per night + *Eating:* □Good □ Normal □ Little □Other:_____	**Abnormal test** **CAPPS score**

Appendix 1.2. Monitoring and assessement.

NTP 1903	**MONITORING AND ASSESSEMENT**											Full name: Birthday: Sex: Ward:						
Recording the corresponding number	Day/month																	
	Hour, minute																	
Identify/ Assess																		
VAS of the incision																		
VAS of the back																		
Move/rest VAS of other side (if any)																		
Sedation (1) Alert (2) Slightly drowsy, easy to rouse (3) Frequently dowsy (4) Difficult to awaken or unresponsive																		
Shortness of breath (1) Yes (2) No (3) Other (detail)																		
Nause/Vomiting (1) Yes (2) No (3) Other (detail)																		
Constipation (1) Yes (2) No (3) Other (detail)																		
Note																		
Nurses																		

Appendix 2. Drug-related problems (DRP) and clinical pharmacist's interventions.

DRPs	Frequency	CPIs	Code of VMOH	
			DRP	CPI
Did not use A or B regimen according to the published protocol (only use paracetamol+ fentanyl)	1	Decreasing of fentanyl dosage and combining a variety of analgesic medications as well as multimodal therapies	T1.99	C1.2
Did not use intraoperative corticosteroid according to the published protocol	5	Discussing with the Anesthesia and Resuscitation Department to ensure consensus	T1.99	C1.2
Patient had dyspnea while eperisone was being added to B regimen	1	Discussing with a doctor about drug interaction between fentanyl and eperisone, considering to avoid combination or decrease fentanyl dosage if combination is needed	T7.1	C1.1
The fentanyl *infusion rate did not match with doctor's orders*	5	Discussing with the doctors/nurses to review and *correct*	T2.99	C1.3
Etoricoxib was used in patient with ischemic heart disease	1	Discussing with a doctor that it would increase the risk of cardiovascular events => change to other analgesic	T1.5	C1.4
Patient developed agitation while it was using B regimen, doctor decided to stop fentanyl although VAS=8	1	Discussing with a doctor about reinitiating fentanyl at the dosage 50% reduced	T7.1	C1.2
Patient developed confusion while it was using B regimen	1	Discussing with a doctor about 50% reduction of the fentanyl dosage	T7.1	C1.3

Appendix 3. Adverse drug reactions.

Ordinal number	Sex	Age range	Weight (kg)	Comorbidities	Allergy history	Describe reaction	Timing	Fentanyl dosage	Concomitant medication	Seriousness of the reaction	Categorization of ADR	Treatment	Outcomes
1	Female	50-60	45	No	No	Fatigue, dyspnea, SpO2: 94%	In the afternoon of POD3, 2 h after eperisone addition	500 µg/50 mL, 2.2 mL/h	Eperisone 50 mg, celebrex 200 mg, paracetamol 1 g IV	Life threatening	Possible	Supplemental oxygen therapy + decreasing fentanyl infusion rate: 1.5 mL/h	Recovered
2	Female	50-60	70	No	No	Fatigue, Dyspnea	POD1, after increasing fentanyl infusion rate: 2.4 mL/h	700 µg/50 mL, 2.4 mL/h	Nefopam 20 mg IV, paracetamol 1 g IV	Life threatening	Possible	Decreasing fentanyl infusion rate: 2 mL/h	Recovered
3	Male	50-60	66	No	No	Spinning, hallucination	immediately after surgery, max POD1, at the end of first fentanyl 500 µg, and starting of second fentanyl 500 µg	600 µg/50 mL, bolus 1.5 mL, 2.2 mL/h,	Nefopam 20 mg IV, paracetamol 1 g IV, gabapentin 300 mg, eperisone 50 mg	Being not serious	Possible	Diazepam 5 mg, fentanyl stopping, then restart at lower dose, 300 µg/50 mL, 2 mL/h	Recovered
4	Female	70-75	62	No	No	Hallucination	At night of POD1	600 µg/50 mL, 2.2 mL/h	Pregabalin 75 mg, nefopam 20 mg IV, paracetamol 1 g IV	Being not serious	Possible	Fentanyl stopping	Recovered
5	Female	60-65	60	No	No	Tachycardia, palpitation, slightly hallucination	At night of POD1	600 µg/50 mL, 2.2 mL/h	Gabapentin 300 mg, diclofenac 75 mg IV, paracetamol 1 g IV	Being not serious	Possible	No	Recovered after finishing of fentanyl therapy
6	Female	70-75	63	No	No	Palpitation, fatigue, chest pressure, dizziness	POD2	700 µg/50 mL, 2.2 mL/h	Eperisone 50 mg, nefopam 20 mg IV, paracetamol 1 g IV	Life threatening	Possible	Decreasing fentanyl infusion rate: 1.8 mL/h	Symptom reducing -> recovered
7	Male	50-60	62	Hypertension, COPD	No	Alert decreasing, confusion	POD2	600 µg/50 mL, 2.2 mL/h	Nefopam 20 mg IV, paracetamol 1 g IV, theophylline 100 mg, spironolactone 25 mg, losartan 50 mg	Being not serious	Possible	Decreasing fentanyl infusion rate: 1 mL/h Theophylline stopping	Recovered
8	Female	60-65	56	No	No	Vomiting	POD2, after increasing fentanyl infusion rate: 2.6 mL/h	500 µg/50 mL, 2.6 mL/h	Nefopam 20 mg IV, paracetamol 1 g IV	Being not serious	Possible	Decreasing fentanyl infusion rate: 2 mL/h	Symptom reducing -> recovered
9	Female	70-75	62	No	No	Vomiting after eating	POD1	600 µg/50 mL, 2.2 mL/h	Nefopam 20 mg IV, paracetamol IV, eperisone, gabapentin	Being not serious	Possible	No	Recovered after finishing of fentanyl therapy
10	Female	65-70	65	No	No	Nausea	POD1	500 µg/50 mL, 2.4 mL/h		Being not serious	Possible		

Appendix 4. Flowchart of ADRs management.