Original Article

Clinical pharmacist intervention in Appendectomy - Dexmedetomidine as an adjunct therapy

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ABSTRACT

This research was performed by a clinical pharmacist to determine the efficacy of dexmedetomidine as an alternative therapy in laparoscopic appendectomy surgery for acute and short-lived analgesic appendicitis and to focus on the consistency of pharmacotherapy and patient safety. A randomized, double-blind, prospective analysis of 2 groups allocated to the fentanyl [GF] and fentanyl dexmedetomidine [GF-D] groups. Propofol, Sevoflurane, Atracurium, and intraoperative fentanyl bolus were administered to the patient, followed by an infusion of maintenance dose of 0.2 µg/kg/h for the two grades. GF patients were given placebo, however, while patients with GF-D received both dexmedetomidine and fentanyl as an infusion (0.5 µg/kg/h).

The requirements for postoperative analgesics and the need for initial postoperative analgesics, consistency of hemodynamic parameters, side effects of nausea and vomiting, and food tolerance have been controlled. GF-D showed lower side effects and food resistance compared to GF: pain score, morphine consumption, nausea, and vomiting ($p<0.05$), When GF was compared to GF-D, the period for the first postoperative morphine was shorter in GF ($p<0.05$). The addition of dexmedetomidine to appendectomy surgery is strongly recommended; clinical pharmacist involvement has improved patient safety and avoids any adverse drug reaction.

Keywords: Appendectomy surgery, Dexmedetomidine, Nausea and vomiting, Hemodynamic stability, Postoperative analgesics, Food tolerance

Introduction

Appendectomy is done laparoscopically, owing to the advancement of endoscopic surgery, and general anesthesia is much more desired [1, 2].

The most common concerns after surgery are nausea and vomiting side effects, food tolerance and pain after surgery [3-8].

Dexmedetomidine is an analgesic, anxiolytic, and sedative alpha-2 adrenergic receptor agonist [9, 10]. Other desirable effects of this agent include the reduction of criteria for other anesthetics and analgesics, neuroprotection, minimal respiratory depression, and reduction of anxiety in emergencies. On the other hand, it has been confirmed that dexmedetomidine is associated with cardiovascular stabilizing effects [11, 12].

Making it an ideal adjuvant for anesthetics and emergency treatment, reducing anesthetic and analgesic requirements will predispose the patient to consciousness.

It decreases sympathetic activity and decreases anesthesia stress responses, enhances respiratory stability, decreases the need for analgesics, provides early postoperative recovery, and elevated hemodynamic stability [13-16].

There have been no studies on the use of dexmedetomidine in general anesthesia for emergency laparoscopic appendectomy.

In this analysis, using the visual analog scale (VAS) score, We looked at how long it took for patients to need analgesics for the first time after surgery and how much morphine they took in total.

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Besides, we have studied food resistance and the side effects of nausea and vomiting.

A clinical pharmacist, who developed the experimental protocol for the procedure, conducted this research [1, 2, 15, 17, 18].

Materials and Methods

The Human Investigation Section of the Institutional Review Board of the Specialty Hospital, Amman/Jordan gave the official permission for our investigation.

Patient Selection

Each patient (aged 16 to 34 years old) who was enrolled in this study presenting for laparoscopic appendectomy surgery gave written informed consent. This research adheres to the principles of the Declaration of Helsinki. Initially, patients were examined for various clinical criteria, such as the extent of the complaint, the history of the patient, age, and gender.

A prospective double-blind condition was performed with 100 adult patients, 18 patients were removed from the primary study because they did not meet the inclusion criteria, and the remaining 82 were evenly divided into 2 classes (41 each between 16-34 years of age, regardless of gender and age. For the two classes, the existing standardized surgical procedures were treated by the same surgical, anesthetic, and nursing teams for laparoscopic appendectomy surgery [19].

We included adult patients with emergency appendicitis who were categorized as ASA I and II according to the physical status classification scheme of the American Society of Anesthesiologists, after the pre-operative test, they were free of any systemic diseases, could understand the use of the patient-controlled analgesia procedure, and were considered eligible and appropriate for laparoscopic surgery.

On the other side, the findings were excluded from pregnant women and patients with serious medical conditions requiring intensive treatment such as (hemodynamic dysfunction, cirrhosis, and chronic medical or mental illness, and coagulation disorders), patients taking chronic narcotic analgesics, or hyper-sensitivities to any drug.

Before and during surgery, the following data was obtained and reported from patients: gender, age, body mass index, Heart Rate (HR) and Mean Arterial Blood Pressure (MAP).

Details of patient age, BMI, HR, and MAP before and after the operation for the two groups are shown in **Table 1**.

Clinical Pharmacist's Role

Before the procedure, a clinical pharmacist, who developed the experimental protocol, played a pivotal educational role in various phases of the surgery to ease the concerns and apprehensions of patients and to mitigate the effects of this painful surgical experience, they tracked all prescription medicine especially for certain medications that are considered to affect blood clotting.

The clinical pharmacist reviewed the guidelines for storage and the expiry date of all drugs. Drug allergy, side effects, drug-drug reactions, legibility, scheduling, compatibility, drug reconciliation, dosage estimation, dilution, and time of infusion were tested and the findings were analyzed for patients.

They demonstrated how to use the face pain scale to the patients. Ascertain that patients have received the required morphine as a postoperative analgesic, if necessary.

During their hospital stay, they supported the patients with simple case details and drug treatment pre-, intra-, and post-operatively.

They taught patients how to use the 100 visual analog scale score before surgery (VAS).

They were also responsible for evaluating patients who were recovering a day after surgery for prescription management of pain medications.

In both the main and the secondary endpoints, they played an investigational function.

Technique of Anesthesia

After the patient was sedated with 0.25 mg/kg midazolam, the following medications were administered to the operating room upon arrival: propofol 2 mg/kg as an induction intravenous bolus, followed by 0.6 mg/kg atracurium and a combination of sevoflurane/nitrous oxide. Bolus injection of fentanyl (1 μg/kg) accompanied by (0.2 μg/kg/h) fentanyl infusion.

However, GF-D patients received dexmedetomidine (0.5 μg/kg bolus injection and 0.2 μg/kg/h maintenance dose) for 24 hours immediately following surgery.

At the same volume and flow rate as for the dexmedetomidine infusion, the GF- was given 0.9 percent normal saline infusion as a placebo.

We conducted a perioperative quantitative measurement and analgesic evaluation, blindly gathering data. For all patients, hemodynamic measures such as Heart Rate (HR) and mean arterial pressure MAP were recorded. The postoperative pain was recorded using the Visual Analog Scale (VAS) score in the Post-Anesthesia Care Unit (PACU).

The severity of postoperative pain was measured using the VAS / zero score (no pain) to ten score system (the highest measurable pain). If the pain level was higher than 4, morphine was given until the pain was relieved.

Morphine infusion pumps are used to inject 1 mg/mL/h of morphine solution.

The overall demand for morphine, VAS scores, and nausea and vomiting were all reported and tracked.

Statistical Analysis

To perform all statistical analyses, SPSS (version 19) was used. All data was interpreted and analyzed using the Student's t-test as mean ± SD, and ($p<0.005$) was found to be statistically significant. For contrast, the $\chi 2$ (categorical) test was used to analyze the symptoms of nausea and vomiting.

Results and Discussion

Patient Selection

A total of 18 patients who did not fit in the inclusion criteria were excluded from the study, the remaining 82 patients were all included and did not show any further reason to be excluded.

The two experimental groups were found to be comparable in terms of gender, age, BMI, HR, and MAP. No statistically significant variations were found between the two groups **(Table 1)**.

Table 1. Demographic Characteristics of Patients, Baseline HR, and MAP

	GF(n=41)	GF-D(n=41)	P-value
Sex (m/f)	20/21	21/20	0.986 NS
BMI	23.2 ±2.6	23.3 ±2.5	0.905 NS
Age	25.5 ±4.4	25.1 ±4.8	0.355 NS
HR before	70.3 ±4	70.9 ±3.6	0.340 NS
MAP before	78.3 ± 1.3	78.2 ±1.2	0.795 NS

Abbreviations: NS: Not Significant, MAP: Mean Arterial Blood Pressure, HR: Heart Rate, GF: Fentanyl Group, GF-D: Fentanyl- Dexmedetomidine Group

Hemodynamic (MAP, HR) measurements, on the other hand, were standard and showed no noticeable discrepancies between the two classes (MAP [p=0.265] and HR [p=0.932]) after the procedure.

However, the following parameters showed a significant difference between the two groups (p<0.05): VAS score, time to first postoperative request of analgesia in PACU, food tolerance, and total morphine consumption during the first 24 hours after the surgery,

There was a significantly reduced VAS value in the GF-D compared to the GF (P=0.002). The morphine demands in the GF-D were significantly lower than those in the GF-D (p=0.001), while the first patient query to analgesia in PACU was significantly lower in the GF-D in comparison with the GF-D (p=0.001), and patients in the GF-D returned to bowel function more rapidly than patients in the GF-D (p=0.001) **(Table 2)**.

Table 2. HR, MAP, VAS score, Time to First Request for Analgesia, the Cumulative Requested Doses of Morphine, and Food Tolerance.

	GF (n=41)	GFD (n=41)	P-value
Time to First Request for Analgesia in PACU (Minutes)	15.6±1.8	23.5±1.2	0.012
Morphine/Dos24	60±1.4	45.2±2.2	0.001
Vas	6±1.2	4±0.8	0.002
HR After	70.1 ±3.7	70.7 ±4	0.932 NS
MAP After	78 ±1.1	78.2 ±1.2	0.265 NS
Food Tolerance/hr.	4.5±0.4	2.3± 0.2	0.001

Note: Data are expressed as a mean value.

Abbreviations GF: fentanyl group; GF-D: fentanyl-dexmedetomidine group; MAP: mean arterial pressure; VAS: visual analog scale; HR: heart rate, S/NS stand for significant/non-significant.

Patients in the GF-D reported lesser nausea and vomiting episodes than patients in the GF, and the association between these variables was important (P=0.008). Owing to any complications from the study, none of the patients were excluded.

GF-D patients experienced fewer nausea episodes and vomiting than the GF patients, the relation between these variables was significant (P=0.008) **(Table 3)**. No patient was removed from the study because of any complications.

Table 3. Nausea and Vomiting in GF-D vs GF over the First 24-hour Postoperative Period.

	GF	GF-D	p-Value
N-V n (%)	29(70.7)	17(41.4)	0.008 S

Abbreviations: S: Significant, N-V: Nausea and Vomiting, GF: Fentanyl Group, GF-D, Fentanyl-Dexmedetomidine Group

Worldwide, "surgical" literature on clinical pharmacist interventions is still minimal. This study applied an experiment in pharmaceutical intervention to surgery for an appendectomy. More pharmacist involvement during surgery in combination with anesthesiologists has been indicated by earlier research [20]. Recent experiments have introduced a surgical room clinical pharmacy intervention program [1, 2].

Chaoliang Tang et al. have tested dexmedetomidine in perioperative acute pain control [21]. The results indicate that the addition of dexmedetomidine to anesthetics is a promising new way to increase its efficacy. In comparison to Chaoliang Tang, we had the same results about postoperative use of analgesics and hemodynamic stability.

As an adjuvant to sevoflurane and fentanyl-based anesthesia, low-dose dexmedetomidine could provide lower anesthetics and opioid use and stable hemodynamics, without adversely having an effect on the recovery profile in patients undergoing supratentorial neurosurgery Prathapadas et al. [22].

Improved hemodynamic regulation compared to fentanyl was observed with dexmedetomidine. A study was conducted by Kim et al. which concluded that dexmedetomidine in conjunction with fentanyl-based IV-PCA substantially enhanced postoperative analgesia in patients undergoing open gastrectomy without hemodynamic instability, which was comparable to thoracic E-PCA [23]. Lehnen et al. and Cepeda

et al. suggested that vomiting and nausea are the most common opioids side effects during surgery [24, 25].

The effects of ketamine on morphine intake and the side effects that come with it after tonsillectomy, such as nausea and vomiting, have been investigated in previous research. Their findings showed that the overall intake of morphine and its side effects were greatly reduced [4]. On the other hand, when dexmedetomidine was used for various procedures, opioid use was decreased during the intraoperative phase and in the PACU [5, 15, 26]. In the current study, dexmedetomidine affected morphine intake and side effects in appendectomy surgery at all stages the same way. Shenhui et al. reported on a meta-analysis trial that dexmedetomidine was superior to placebo in terms of post-anesthesia nausea and vomiting, but not to any other anesthetic agents, and this efficacy could be linked to decreased intraoperative opioid intake [26]. Such findings were close to the current results. Our analysis showed a substantial decrease in the analgesic agents' intake in the GF-D relative to the postoperative GF **(Tables 2 and 3)**. Turgut et al. stated that additional analgesia was needed earlier than in the GF-D in patients in the GF [27].

Dexmedetomidine may be used safely to relieve pain, which as is evident from previous research, can help to lower intraoperative opioid requirements [28].

Conclusion

In appendectomy surgery at various levels, the addition of dexmedetomidine to fentanyl could be a supplementary therapy to retain hemodynamic levels and make sure that there is postoperative analgesic regulation while it reduces postoperative morphine intake, minimizing food tolerance period, vomiting side effects and minimizing nausea. Clinical pharmacists' methods play an important role in recovering and optimizing the total appendectomy surgery effects.

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References

1. Semm K. Endoscopic appendectomy. Endoscopy. 1983;15(2):59-64. 10.1055/s-2007-1021466.
2. Bajwa SJ, Kulshrestha A. Anaesthesia for laparoscopic surgery: General vs regional anaesthesia. J Minim Access Surg. 2016 Jan;12(1):4-9.
3. Hadi BA, Daas R, Zelko R. A randomized, controlled trial of clinical pharmacist intervention in microdiscectomy surgery–low dose intravenous ketamine as an adjunct to standard therapy. Saudi Pharm J. 2013;21(2):169-75. doi:10.1016/j.jsps.2012.08.002
4. Hadi BA, Sbeitan SM. Clinical pharmacy intervention post-tonsillectomy: a randomized control trial. Int J Clin Pharm. 2015;37(1):133-8. doi:10.1007/s11096-014-0051-6
5. Hadi BA, Sbeitan SM, Shakya AK. Dexmedetomidine infusion prevents significant postoperative pain in the first 24 hrs after myomectomy laparoscopic surgery. Acta Pol Pharm Drug Res. 2018;75(1):183-8.
6. Kim HO, Kang M, Lee SR, Jung KU, Kim H, Chun HK. Patient-Controlled Nutrition After Abdominal Surgery: Novel Concept Contrary to Surgical Dogma. Ann Coloproctol. 2018 Oct; 34(5):253-8.
7. Nuzhnaya KV, Mishvelov AE, Osadchiy SS, Tsoma MV, AM RS KK, Rodin IA, et al. Computer simulation and navigation in surgical operations. Pharmacophore. 2019;10(4):43-8.
8. Elkatatny AA, Ramadan M, Gouda AH, Hamdy TM, Fahmy RS, El Emady MF, et al. Surgical Outcome of Spinal Meningioma, Single Institute Experience. Pharmacophore. 2019;10(2):7-17.
9. Illiandri O. Anaesthetic Management with Dexmedetomidine for Intraoperative Awake Test in Correction of Scoliosis; a Case Report. Int J Pharm Res Allied Sci. 2019;8(1):198-201.
10. Aantaa R, Scheinin M. Alpha2-adrenergic agents in anaesthesia. Acta Anaesthesiol Scand. 1993 Jul;37(5):433-48.
11. Wijeysundera DN, Naik JS, Beattie WS. Beattie, Alpha-2 adrenergic agonists to prevent perioperative cardiovascular complications: a meta-analysis. Am J Med. 2003;114(9):742-52.
12. El-Sayed MG, Ahmed FM. Efficacy of the perineural combination of dexamethasone with nalbuphine on duration of analgesia following supraclavicular brachial plexus block. Arch Pharm Pract. 2020;11(2):81-6.
13. Walwyn WM, Chen W, Kim H, Minasyan A, Ennes HS, McRoberts JA, et al. Sustained Suppression of Hyperalgesia during Latent Sensitization by μ-, δ-, and κ-opioid receptors and α2A Adrenergic Receptors: role of Constitutive Activity. J Neurosci. 2016;36(1):204-21. doi:10.1523/JNEUROSCI.1751-15.2016

14. Naaz S, Ozair E. Dexmedetomidine in current anesthesia practice-a review. J Clin Diagn Res. 2014;8(10):GE01–GE04.
15. Hadi BA, Sbeitan SM, Shakya AK. Fentanyl vs fentanyl-dexmedetomidine in lumbar foraminotomy surgery. Ther Clin Risk Manag. 2019;15:885-90.
16. Ghodki PS, Thombre SK, Sardesai SP, Harnagle KD. Dexmedetomidine as an anesthetic adjuvant in laparoscopic surgery: An observational study using entropy monitoring. J Anaesthesiol Clin Pharmacol. 2012 Jul-Sep;28(3):334-8.
17. Miranda TM, Petriccione S, Ferracini FT, Borges Filho WM. Interventions performed by the clinical pharmacist in the emergency department. Einstein (São Paulo). 2012 Mar;10(1):74-8.
18. Hisham M, Sivakumar MN, Veerasekar G. Impact of clinical pharmacist in an Indian Intensive Care Unit. Indian J Crit Care Med. 2016;20(2):78-83.
19. Shahzeer K. Step-by-step guide to performing a laparoscopic appendectomy: For learners. https://www.sages.org/video/step-by-step-guide-to-performing-a-laparoscopic-appendectomy-for-learners/ Accessed April 2020.
20. Marotti SB, Kerridge RK, Grimer MD. A randomized controlled trial of pharmacist medication histories and supplementary prescribing on medication errors in postoperative medications. Anaesth Intensive Care. 2011;39(6):1064-70.
21. Tang C, Xia Z. Dexmedetomidine in perioperative acute pain management: a non-opioid adjuvant analgesic. J Pain Res. 2017;10:1899-1904.
22. Prathapadas U, Hrishi AP, Arulvelan Appavoo SV, Sethuraman M. Effect of Low-Dose Dexmedetomidine on the Anesthetic and Recovery Profile of Sevoflurane-Based Anesthesia in Patients Presenting for Supratentorial Neurosurgeries: A Randomized Double-Blind Placebo-Controlled Trial. J Neurosci Rural Pract. 2020;11(2):267-73.
23. Kim NY, Kwon TD, Bai SJ, Noh SH, Hong JH, Lee H, et al. Effects of dexmedetomidine in combination with fentanyl-based intravenous patient-controlled analgesia on pain attenuation after open gastrectomy in comparison with conventional thoracic epidural and fentanyl-based intravenous patient-controlled analgesia. Int J Med Sci. 2017;14(10):951-60. doi:10.7150/ijms.20347
24. Lehnen N, Heuser F, Sağlam M, Schulz CM, Wagner KJ, Taki M, et al. Opioid-induced nausea involves a vestibular problem preventable by head-rest. PLoS One. 2015;10(8):e0135263. doi:10.1371/journal.pone.0135263
25. Cepeda MS, Farrar JT, Baumgarten M, Boston R, Carr DB, Strom BL. Side effects of opioids during short-term administration: effect of age, gender, and race. Clin Pharmacol Ther. 2003;74(2):102-12. doi:10.1016/S0009-9236(03)00152-8
26. Jin S, Liang DD, Chen C, Zhang M, Wang J. Dexmedetomidine prevent postoperative nausea and vomiting on patients during general anesthesia. Medicine. 2017 Jan;96(1):e5770.
27. Turgut N, Turkmen A, Gokkaya S, Altan A, Hatiboglu MA. Dexmedetomidine-based versus fentanyl-based total intravenous anesthesia for lumbar laminectomy. Minerva Anestesiol. 2008;74(9):469-74.
28. Shukla U, Prabhakar T, Malhotra K, Srivastava D. Dexmedetomidine versus midazolam as adjuvants to intrathecal bupivacaine: a clinical comparison. J Anaesthesiol Clin Pharmacol. 2016;32(2):214-9. doi:10.4103/0970-9185.182105.