A preliminary assessment of vital-signs-integrated patient-assisted intravenous opioid analgesia (VPIA) for postsurgical pain

Ban Leong SNG (✉ sng.ban.leong@singhealth.com.sg)
KK Women's and Children's Hospital

Daryl Jian'an Tan
KK Women's and Children's Hospital

Chin Wen TAN
KK Women's and Children's Hospital

Nian-Lin Reena HAN
KK Women's and Children's Hospital

Rehena SULTANA
Duke-NUS Medical School

Alex Tiong Heng SIA
KK Women's and Children's Hospital

Research article

Keywords: infusion pump, postoperative pain, vital sign monitoring, oxygen desaturation.

DOI: https://doi.org/10.21203/rs.2.11609/v5

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

Background: We developed a Vital-signs-integrated Patient-assisted Intravenous opioid Analgesia (VPIA) analgesic infusion pump, a closed-loop vital signs monitoring and drug delivery system which embodied in a novel algorithm that took into account patients' vital signs (oxygen saturation, heart rate). The system aimed to allow responsive titration of personalized pain relief to optimize pain relief and reduce the risk of respiratory depression. Moreover, the system would be important to enable continuous monitoring of patients during delivery of opioid analgesia.

Methods: Nineteen patients who underwent elective gynecological surgery with postoperative patient controlled analgesia (PCA) with morphine were recruited. The subjects were followed up from their admission to the recovery room/ ward for at least 24 hours until assessment of patient satisfaction on the VPIA analgesic infusion pump.

Results: The primary outcome measure of incidence of oxygen desaturation showed all patients had at least one episode of oxygen desaturation (<95%) during the study period. Only 6 (31.6%) patients had oxygen desaturation that persisted for more than 5 minutes. The median percentage time spent during treatment that oxygen saturation fell below 95% was 1.9%. Fourteen (73.7%) out of 19 patients encountered safety pause, due to transient oxygen desaturation or bradycardia. The patients’ median [IQR] pain scores at rest and at movement after post-op 24 hours were 0.0 [2.0] and 3.0 [2.0], respectively. The average morphine consumption in the first 24 hours was 12.5 ± 7.1mg. All patients were satisfied with their experience with the VPIA analgesic infusion pump.

Conclusions: The use of VPIA analgesic infusion pump, when integrated with continuous vital sign monitor and variable lockout algorithm, was able to provide pain relief with good patient satisfaction.

Keywords: infusion pump, postoperative pain, vital sign monitoring, oxygen desaturation.

Trial registration: This study was registered on clinicaltrials.gov registry (NCT02804022) on 28 Feb 2016.

Background

More than 230 million major surgeries are performed annually in the world that could result in moderate to severe post-surgical pain [1]. Patient-controlled analgesia (PCA) with an opioid pump is often the commonly used technique to relief pain. Opioids adverse effects such as nausea, vomiting, sedation and respiratory depression may occur especially in high risk patients. The risk of opioid-induced respiratory depression was significantly increased in the patients with advanced age, respiratory disease and obstructive sleep apnoea [2, 3], leading to the increased length of stay and overall costs [4]. Intermittent monitoring measures were highly labor intensive, yet not reliably recognized opioid-induced respiratory depression in the postoperative period [5]. According to Anaesthesia Patient Safety Foundation, patients having vital signs charted every 4 hours were usually left unmonitored >90% of the time. Since these patients were commonly administered with supplemental oxygen, this might eventually complicate the
monitoring by masking hypoventilation, causing the signs of respiratory depression to be recognized only in its later stage [6].

Our overall aim was to develop a Vital-signs-integrated Patient-assisted Intravenous opioid Analgesia (VPIA) analgesic infusion pump with closed-loop vital signs monitoring and drug delivery system which embodied a novel algorithm that accounted for patients’ vital signs (oxygen saturation, heart rate). In this preliminary study, our primary aim was to investigate the incidence of oxygen desaturation (defined as oxygen saturation <95% in a patient for more than 60 seconds) in post-operative patients using our VPIA analgesic infusion pump. The side effects of opioid administration (nausea, vomiting and sedation), patients’ satisfaction and vital signs monitoring data were also evaluated.

**Methods**

We recruited female patients aged 21 to 70 years old with American Society of Anesthesiologists (ASA) status I or II, undergoing elective surgery and intending to use postoperative PCA with morphine for postoperative analgesia. The exclusion criteria were the patients with allergies to morphine, history of significant respiratory disease or obstructive sleep apnea, unwilling to wear oxygen saturation monitoring devices throughout the study duration, pregnancy and unable to comprehend the use of PCA. The recruitment was performed either in the pre-operative assessment clinic or on the same day of surgery if they had not attended pre-operative assessment clinic. An information brochure describing the use of VPIA analgesic infusion pump for post-operative analgesia, including potential side effects and complications was provided to the patients.

**Setting up of Infusion Pump**

The detailed VPIA variable lockout algorithm was illustrated in Figure 2. The bolus lockout interval was empirically set at 7 minutes, and was adjusted automatically according to the patient successful demands and the patient safety in the event of abnormal vital signs monitoring. The monitoring data was performed by taking average epochs of 15 seconds to summarize the vital signs. Missing vital signs were dropped from the analysis. However, if there was no available vital sign for the whole duration of each epoch, a safety pause would be triggered. The VPIA variable lockout algorithm reassessed for the recovery of the patient’s’ vital signs at the end of the safety lockout period. If the patient’s vital signs did not recover to the safe levels, the pump automatically raised the on-board alarm. Conversely, if the patient’s vital signs recovered beyond the threshold limits by the end of the safety lockout period, the lockout interval would be prolonged. If at any time, there were critically abnormal vital sign parameters, the system would trigger the “emergency safety stop” function to cease the patient’s boluses. The system would be manually restarted by a clinician or a nurse after reviewing the patient.

All patients had established intravenous access before surgery. The patients were instructed on the use of the VPIA analgesic infusion pump prior to the study and educated to press the demand button whenever they needed pain relief. While in the recovery room after surgery, the VPIA analgesic infusion pump was secured with a 50 ml syringe filled with 1 mg/ml morphine that was connected to the patient’s intravenous
The patient’s oxygen saturation and heart rate was continuously monitored by the VPIA analgesic system at least for 24 hours after surgery.

**Data Collection**

We collected and analyzed three sets of data: (1) patient demographic, surgical and anesthetic characteristics; (2) VPIA analgesic infusion pump data including opioid consumption, patient demands, successful demands, pattern of demands, oxygen saturation and heart rate; and (3) VPIA analgesic infusion pump user feedback survey that was conducted at the end of the study.

Following the initiation of VPIA analgesic infusion pump, attending nurses who were educated on the usage and side effects of morphine therapy would monitor the patient at regular intervals and document pain scores (0-10 numeric rating scale), blood pressure, heart rate, oxygen saturation and sedation score (0 for “awake, alert”, 1 for “occasionally drowsy, easy to rouse, responds to calling”, 2 for “occasionally drowsy, difficult to rouse, responds to shaking only”; 3 for “unresponsive and unarousable—defined as no response to voice or physical stimulation”; D for “distressed – defined as awake and in great pain”). Side effects such as nausea and vomiting were also recorded.

An independent observer would assess the patient during the period she was placed on the VPIA analgesic infusion pump. The patient’s overall satisfaction (numerical score between 0-100%) with the postoperative analgesia provided, the feedback on pain relief effectiveness and any side effect from the therapy were also gathered. Once the indications for PCA opioid for pain management were deemed unnecessary by the patient’s primary care team, the VPIA analgesic infusion pump was disconnected.

**Sample size calculation and statistical analysis**

The primary outcome measure of the study was the incidence of oxygen desaturation (defined as oxygen saturation < 95% in a patient for more than 60 seconds) in the patients using the VPIA analgesic infusion pump. The secondary outcome measures were bradycardia, sedation, nausea/vomiting, pain scores, total consumption of morphine, patient’s satisfaction score. Patient’s oxygen saturation and heart rate were measured every minute for at least 24 hours. Assuming that a patient had < 3% oxygen desaturation, 0.005 width of interval and 95% confidence interval, we would require 18,000 oxygen saturation readings. Each patient would provide at least 1200 readings. Therefore, the study was adequately powered for 18 patients with 1200 readings (= 18 X 1200 ~ 21,600) for both primary and secondary aims.

The patient demographics, surgical and anesthetic characteristics were summarized as frequency with corresponding proportion, as mean ± standard deviation (SD) or median [range], whichever applicable. The incidence rate and 95% confidence intervals (CI) of binary outcomes (such as desaturation, bradycardia) were estimated based on the exact method by Wilson [7], which demonstrated to have good statistical properties even for small number of subjects and/or extreme probabilities [8, 9]. Significance level was set at 0.05 and all tests were two-tailed. SAS version 9.3 software (SAS Institute; Cary, North Carolina, USA) was used for the analysis.
Results

Nineteen patients were recruited for this study over a 6-month period (January 2017 to June 2017), with their baseline and demographic characteristics shown in Table 1. The mean age of patients was 51.5 ± 8.8 years (range 36 - 66 years), the average body mass index (BMI) was 24.7 ± 4.4 kg/m². All patients recruited went through scheduled open surgery, with the majority (n=15) under total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAHBSO). The rest were open myomectomy (n=2) and salpingo-oophorectomy (n=2). Intraoperative morphine and fentanyl was administered with a mean dosage of 8.7 ± 1.3 mg and 102.0 ± 35.3 µg respectively.

The patients were offered pain relief via VPIA analgesic infusion pump once they were transferred to the Post-Anesthesia Care Unit (PACU). The primary outcome measure of incidence of oxygen desaturation (Table 2) showed that all patients had at least one episode of oxygen saturation (SpO₂) below 95% transiently during the study period. Only 13 (68.4%, 95%CI 46.0% - 84.6%) patients had oxygen desaturations that persisted for more than 60 seconds. However, only 8 (42.1%, 95%CI 23.1% - 63.7%) and 6 (31.6%, 95%CI 15.4% - 54.0%) patients had persisted oxygen desaturation for 3 and 5 minutes, respectively. The median total time spent and the percentage of time that SpO₂ fell below 95% was 35.3 minutes and 1.9%, respectively. During the 1st 4 hours post-surgery, the median time period and the percentage of time that SpO₂ fell below 95% was 2.08 minutes and 0.87%, respectively; whereas the median time spent and the percentage of time that SpO₂ fell below 95% was 26.8 min and 1.4%, respectively after 4 hours until the removal of VPIA infusion pump.

All patients had at least one episode of heart rate (HR) <60/min with 3 (15.8%, 95%CI 5.5% - 37.6%) patients experiencing their HR < 60/min for longer than 60 seconds duration (Table 2). The median time period and the percentage of time that HR fell below 60/min was 1.2 minutes and 0.13%, respectively. Only 1 (5.3%, 95%CI 1.0% - 24.6%) patient had HR <60 for both 3 and 5 minutes. There was no clinically significant respiratory event of note.

Fourteen out of 19 (73.7%) patients encountered the safety pauses, whereas ten (52.6%) patients had experienced an emergency safety stop during the study period. The median [range] number of safety pause was 5 [1 - 21]. The reasons for the safety pause included either the occurrence of oxygen desaturation or bradycardia. Eleven (57.9%) patients had the safety pause due to SpO₂ < 95% but all had HR > 60/min during the episode. Six (31.6%) patients had HR < 60/min but all had SpO₂ > 95% during the episode. There were 2 (10.6%) patients experiencing oxygen desaturation <90% for more than one minute. The median number of demands of bolus was 21 per patient. Post-operative side effects included nausea / vomiting (6/19) and pruritus (1/19).

The average morphine consumption during the stay was 3.6 ± 3.0 mg (Table 3), whereas the last pain score before sending to ward was 3 [0 - 6]. Minimal to moderate sedation was observed in 15 patients, whereas 4 other patients exhibited no sedation, having a median of overall sedation scoring of 1 [0 - 2]. Only one patient showed nausea or vomiting during this period. At 12 hours post-surgery, the pain score
at rest and movement in 19 patients was 2 [0 - 6] and 5 [0 -10], respectively (Table 3). At 24 hours postsurgery, patients had pain scores of 0 [0 - 7] and 3 [0 - 8] at rest and movement, respectively. The average morphine consumption in the first 24 hours was 12.5 ± 7.1 mg.

User feedback received on VPIA analgesic infusion pump showed that all patients agreed that the pump was safe and effective to use, although they remained neutral on the mobility of the pole where the pump was mounted onto (Table 4).

**Discussion**

The results of this preliminary assessment on our novel VPIA analgesic infusion pump suggested that the use of this drug delivery system, when integrated with continuous physiological monitoring and a variable lockout algorithm, was able to provide pain relief with good patient satisfaction in post-operative acute pain management. No significant adverse event was observed in this study.

Several studies evaluated the incidence of oxygen desaturation after different types of analgesia, but few analyzed the oxygen saturation continuously for 24-60 hours after surgery [10]. Our results showed that all patients had at least one episode of oxygen desaturation (SpO$_2$ < 95%) transiently, whereas only 13 (68.4%) patients had persistent oxygen desaturations more than 60 seconds. Moreover, only 8 (42.1%) and 6 (31.6%) patients had persisted oxygen desaturation for 3 and 5 minutes, respectively. It was important to understand the percentage of time spent with oxygen desaturation. Motamed et al [11] demonstrated that the time spent with SpO$_2$ <95% was about 65% and 40% during 1st and 2nd postoperative night, respectively. This was much higher than our results that showed the median time period and percentage of time spent with SpO$_2$ < 95% was 35.3 minutes and 1.9%, respectively. The reason behind this might due to our novel VPIA analgesic infusion system that integrated with continuous vital sign monitor and a variable lockout algorithm.

Hospital practice of intermittent vital signs monitoring with opioid delivery became an increasing concern. More than 75% of patients with moderate to severe sleep apnea were undiagnosed and conventional risk stratification for heightened post-op monitoring could potentially miss the patients at increased risk of respiratory depression [12]. Respiratory depression was reported in up to 5% patients with the use of PCA opioids [5, 13]. A retrospective study on Chinese patients receiving PCA intravenous morphine showed that the incidence of respiratory depression (as defined by SpO$_2$ < 90% for longer than one minute) was 1.62%. The present study showed a higher incidence due to the difference in the definition of oxygen desaturation and the continuous monitoring system because conventional intermittent routine monitoring could under-diagnose the events of oxygen desaturation [14]. Early recognition and the detection of risk of opioid-induced respiratory depression by continuous monitoring vital signs could mitigate the chance of patients’ increased length of stay, the risk of hospital-acquired infections and the increased costs [15].
This study concentrated on varying the duration of the lockout interval as a safety mechanism. This safety of margin allowed an interval to be long enough for the drugs to take effect in the patients from the present bolus dose before the next bolus was delivered. There was no recommended optimal lockout interval, hence this would need to be individualized to the patient’s pain relief and safety requirements [16]. Our results showed that the morphine consumption was 12.5 mg in 24 hours after surgery which was comparable with other groups. Chou et al. found that the average morphine consumption of 40 mg in postoperative 48 hours in 80 patients that underwent total abdominal hysterectomy and later [17]. Another study on patients after total knee arthroplasty showed an average morphine consumption of 27 mg in 48 hours, indicating the different opioid consumptions across various surgical procedures [18].

We also gathered the patient-centered outcomes through the patients’ feedback on the device setup (patient handset, pole stand) and their overall treatment experiences (the interference with treatment, the safety and the effectiveness). The overall feedback was positive but the patients remained neutral on the reduced mobility of the pump due to the integration of the vital signs monitor. Future design of a more portable setup would be desirable.

This preliminary study was an initial assessment of our newly developed VPIA analgesic infusion pump. The limitations of this study would include the small number of subjects conducted in only gynecological surgeries. The larger trials in patients with different demography, medical comorbidities and surgical procedures would need to be investigated. This system could be more refined with higher risk patients in future. The physical design of the pump would be reduced to enable great mobility on the patient transfer. The artefact interference with the algorithms could led to false alerts in the present system. Hence, future study plans will include refining new vital signs sensors, incorporating a respiratory rate monitoring and better integration with the delivery system to ensure better data capture.

**Conclusions**

In conclusion, this preliminary assessment on the VPIA analgesic infusion pump system has found that this novel pump was able to detect and automatically respond to oxygen desaturation and bradycardia by instituting safety pause, and to provide pain relief with good patient satisfaction in post-operative acute pain management. Larger studies with adequate number of subjects would be needed to evaluate the efficiency of this drug delivery system.

**Abbreviations**

ASA: American Society of Anesthesiologists; BMI: Body mass index; CI: Confidence intervals; IQR: Interquartile range; PACU: Post-Anesthesia Care Unit; PCA: Patient controlled analgesia; SD: Standard deviation; SpO2: Oxygen saturation; TAHBSO: Total Abdominal Hysterectomy and Bilateral Salpingo-oophorectomy; VAS: Visual analogue scale; VPIA: Vital-signs-integrated Patient-assisted Intravenous opioid Analgesia.
Declarations

Ethical approval and consent to participate

This study was approved by the SingHealth Centralized Institutional Review Board, Singapore (SingHealth CIRB Ref: 2015/3062), and registered on Clinicaltrials.gov (NCT02804022). Written informed consent was obtained from all participants prior to start of the study. This work was conducted in accordance with the Declaration of Helsinki.

Consent to publish

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

Ban Leong Sng is an associate editor of BMC Anesthesiology. Ban Leong Sng and Alex Sia Tiong Heng have filed a patent related to this work (SG 10201801161P, filed 12 Feb 2018, Singapore). Alex Sia Tiong Heng has intellectual property ownership and is the founding scientific director of Innovfusion Pte Ltd. All other authors reports no conflicts of interest in this work.

Funding

This work was supported by the funding from the National Health Innovation Centre Innovation to Develop (I2D) grant (Grant no. NHIC-I2D-1409017). The aforementioned sponsor had no involvement in the study activities.

Authors’ contributions

All authors (BLS, DJT, CWT, NLRH, RS, ATHS) contributed to the study design, data analysis and discussion, drafting and/or revising the manuscript. All authors approved the final version of the manuscript, and agree to be accountable for all aspects of this work.

Acknowledgments

We would like to thank Miss Agnes Teo (Senior Clinical Research Coordinator) and Miss Denise Anne (Clinical Research Coordinator) for their administrative support in this work. The design and layout of the algorithm was performed by Innovfusion Pte Ltd, Singapore.

References
1. Weiser TG, Regenbogen SE, Thompson KD, Haynes AB, Lipsitz SR, Berry WR, et al. An estimation of the global volume of surgery: a modelling strategy based on available data. The Lancet. 2008;372(9633):139-44. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2014;120(1):97-109.

2. Maddox RR, Williams CK, Oglesby H, Butler B, Colclasure B. Clinical experience with patient-controlled analgesia using continuous respiratory monitoring and a smart infusion system. American journal of health-system pharmacy. 2006;63(2):157-64.

3. Schein JR, Hicks RW, Nelson WW, Sikirica V, Doyle DJ. Patient-controlled analgesia-related medication errors in the postoperative period. Drug safety. 2009;32(7):549-59.

4. Etches RC. Respiratory depression associated with patient-controlled analgesia: a review of eight cases. Canadian journal of anaesthesia. 1994;41(2):125.

5. Paul JE, Buckley N, McLean RF, Antoni K, Musson D, Kampf M, et al. Hamilton Acute Pain Service Safety Study Using Root Cause Analysis to Reduce the Incidence of Adverse Events.

6. Weinger MB, Lee LA. No patient shall be harmed by opioid-induced respiratory depression. APsF Newsletter. 2011;26(2):21-8.

7. Wilson EB. Probable inference, the law of succession, and statistical inference. Journal of the American Statistical Association. 1927;22(158):209-12.

8. Newcombe RG. Interval estimation for the difference between independent proportions: comparison of eleven methods. Statistics in medicine. 1998;17(8):873-90.

9. Brown LD, Cai TT, DasGupta A. Interval estimation for a binomial proportion. Statistical science. 2001:101-17.

10. Madej TH, Whetaley R G, Jackson I.J.B, Hunter D. Hypoxaemia and pain relief after lower abdominal surgery: comparison of extradural and patient controlled analgesia. Br J Anaesth. 1992; 69: 554–557.

11. Motamed C, Spencer A, Farhat F, Bourgain JL, Lasser P, Jayr C. Postoperative hypoxaemia: continuous extradural infusion of bupivacaine and morphine vs patient-controlled analgesia with intravenous morphine. Br J Anaesth. 1998; 80: 742–747.

12. Ankichetty S, Chung F. Considerations for patients with obstructive sleep apnea undergoing ambulatory surgery. Current Opinion in Anesthesiology. 2011;24(6):605-11.

13. Macintyre P, Loadsman J, Scott D. Opioids, ventilation and acute pain management. Anaesthesia and intensive care. 2011;39(4):545-58.

14. Tsui S, Tong W, Irwin M, Ng K, Lo J, Chan W. The efficacy, applicability and side-effects of postoperative intravenous patient-controlled morphine analgesia: an audit of 1233 Chinese patients. Anaesthesia and intensive care. 1996;24(6):658-64.

15. Cohen MJ, Schecter WP. Perioperative pain control: a strategy for management. Surgical Clinics. 2005;85(6):1243-57.
16. Ginsberg B, Gil KM, Muir M, Sullivan F, Williams DA, Glass PS. The influence of lockout intervals and drug selection on patient-controlled analgesia following gynecological surgery. Pain. 1995;62(1):95-100.

17. Chou W-Y, Wang C-H, Liu P-H, Liu C-C, Tseng C-C, Jawan B. Human opioid receptor A118G polymorphism affects intravenous patient-controlled analgesia morphine consumption after total abdominal hysterectomy. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2006;105(2):334-7.

18. Chou WY, Yang LC, Lu HF, Ko JY, Wang CH, Lin SH, et al. Association of μ-opioid receptor gene polymorphism (A118G) with variations in morphine consumption for analgesia after total knee arthroplasty. Acta Anaesthesiologica Scandinavica. 2006;50(7):787-92.

Tables

Table 1 Baseline and demographic characteristics of recruited subjects

| Parameters                  | No. of patients | Mean (SD)/ Percentage |
|-----------------------------|-----------------|-----------------------|
| Age; years                  | 19              | 51.5 (8.8)            |
| Race                        | 19              |                       |
| Chinese                     | 13              | 68.4%                 |
| Indian                      | 3               | 15.8%                 |
| Malay                       | 2               | 10.5%                 |
| Others                      | 1               | 5.3%                  |
| Weight; kg                  | 19              | 62.0 (9.9)            |
| BMI; kg/m²                  | 19              | 24.7 (4.4)            |
| ASA Status                  | 19              |                       |
| I                           | 5               | 26.3%                 |
| II                          | 14              | 73.7%                 |
| Intraoperative morphine (mg)| 19              | 8.7 (1.3)             |
| Intraoperative fentanyl (mcg)| 19            | 102.0 (35.3)          |

SD: Standard deviation.

Table 2 The characteristics of oxygen saturation and heart rate in recruited subjects
| Parameters                          | No. of patients | Percentage % (95% CI) |
|------------------------------------|-----------------|-----------------------|
| **Incidence of oxygen desaturation** |                 |                       |
| At least one episode SpO2 < 95%    | 19              | 100                   |
| SpO2 < 95% persisted for > 60 seconds | 13          | 68.4 (46.0 - 84.6)    |
| SpO2 < 95% persisted for > 3 min    | 8               | 42.1 (23.1 - 63.7)    |
| SpO2 < 95% persisted for > 5 min    | 6               | 31.6 (15.4 - 54.0)    |
| **Post-surgery 0 hours until the removal of pump** |         |                       |
| Total time spent of SpO2 < 95%, min | 35.3 [6.8 - 73.8] |           |
| The % of time of SpO2 < 95%        | 1.9 [0.4 - 4.2] |           |
| **0 - 4 hours post-surgery**       |                 |                       |
| Total time spent of SpO2 < 95%, min | 2.1 [0.2 - 9.2] |           |
| The % of time of SpO2 < 95%        | 0.87 [0.07 - 3.8] |           |
| **> 4 hours post-surgery**         |                 |                       |
| Total time spent of SpO2 < 95%, min | 26.8 [2.7 - 68.8] |           |
| The % of time of SpO2 < 95%        | 1.4 [0.3 - 3.4] |           |
| **Incidence of bradycardia**       |                 |                       |
| At least one episode of HR < 60/min | 19          | 100                   |
| HR < 60/min persisted for > 60 seconds | 3           | 15.8 (5.5 - 37.6)    |
| HR < 60/min persisted for > 3 min | 1           | 5.3 (1.0% - 24.6)    |
| HR < 60/min persisted for > 5 min | 1           | 5.3 (1.0% - 24.6)    |

Table 3 Pain characteristics during Post Anesthesia Care Unit (PACU) and ward stay
| Parameters                                      | No. of patients | Mean (SD) / Median [range] / Percentage |
|------------------------------------------------|----------------|----------------------------------------|
| During PACU stay                               | 19             |                                        |
| Morphine (mg)                                  | 19             | 3.6 (3.0)                              |
| Last pain score before discharge (0-10)        | 19             | 3[0-6]                                 |
| Last sedation score before discharge (0-3)     | 19             | 1[0-2]                                 |
| Nausea/vomiting before discharge (0-3)         | 19             | 0[0-1]                                 |
| During Ward stay                               |                |                                        |
| 12 hours Post-op                               | 19             |                                        |
| Pain score (at rest) (0-10)                    | 19             | 2[0-6]                                 |
| Pain score (movement) (0-10)                   | 19             | 5[0-10]                                |
| Sedation score (0-3)                           | 19             | 0[0-1]                                 |
| Nausea/vomiting (0-3)                          | 18             | 0[0-3]                                 |
| 24 hours Post-op                               | 19             |                                        |
| Pain score (at rest) (0-10)                    | 19             | 0[0-7]                                 |
| Pain score (movement) (0-10)                   | 19             | 3[0-8]                                 |
| Sedation score (0-3)                           | 19             | 0[0-1]                                 |
| Nausea/vomiting (0-3)                          | 19             | 0[0-1]                                 |
| Morphine consumption (24 hours; mg)            | 19             | 12.5 (7.1)                             |

Side effect

- Nausea / vomiting: 6 (31.6%)
- Pruritus: 1 (5.3%)

**Table 4** Post-operative feedback (n=19) on the VPIA analgesic infusion pump

| Parameters                                      | Values [range] |
|------------------------------------------------|----------------|
| Feedback (1-5; 1: Strongly disagree; 5: strongly agree) |                |
| Patient handset button                          | 4 [4-5]        |
| Mobility of pole with mounted pump              | 3 [3-4]        |
| No interference of vital signs monitoring with treatment | 4 [1-5]        |
| Pump safety                                     | 4 [3-5]        |
| Pump effectiveness                              | 4 [3-5]        |
**Figure 1**

An illustration of Vital-signs-integrated Patient-assisted Intravenous opioid Analgesia (VPIA) analgesic infusion pump.

**Figure 2**

The proposed Vital-signs-integrated Patient-assisted Intravenous opioid Analgesia (VPIA) analgesic infusion pump and the variable lockout algorithm.