

Inguinal hernia repair in day surgery: the role of MAC (Monitored Anesthesia Care) with remifentanyl

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SUMMARY: Inguinal hernia repair in day surgery: the role of MAC (Monitored Anesthesia Care) with remifentanyl.

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Background. *The extension of indications for procedures in a Day Surgery (DS) setting has led to changes in the anesthetic and surgical treatment of Inguinal Hernias (IH). According to the recommendations of the European Hernia Society, the treatment of IH in DS units should be performed under Monitored Anesthesia Care (MAC).*

Patients and methods. *960 patients underwent IH repairs over a period of 24 months. The patients were randomly divided into two groups: R (remifentanyl) and F (fentanyl); the group F was considered as a control group. The exclusion criteria in both groups were: morbid obesity (BMI>40 or BMI>35 in association with high blood pressure or diabetes); coagulopathy; OSAS (obstructive sleep apnea syndrome) with AHI >10; cardiovascular, respiratory, renal, hepatic or metabolic disease; history of substances abuse; GERD-related esophagitis (ga-*

stro-esophageal reflux disease); chronic analgesic use; allergy to local anesthetic and ASA>III. Patients reported their level of pain on a verbal numeric scale (VNS), with scores ranging from 0 to 10. For each patient systolic and diastolic blood pressure (SBP and DBP), mean arterial pressure (MAP), heart rate (HR) and peripheral oxygen saturation (SpO₂) were recorded. The results are presented as the mean value ± standard deviations; statistical analysis was performed using Student's t-test.

Results. *Amongst the 960 procedures, complications or side effects related to the anesthetic techniques didn't occur; no procedure-related complications requiring mechanical ventilation support were reported. Our research focused on evaluating remifentanyl effectiveness in pain control and its impact on hemodynamic stability and respiratory function. There was a significant difference between the two groups with regard to the VNS.*

Conclusions. *Remifentanyl, is an excellent drug for pain control during intra-operative procedures, that allows an optimal hemodynamic stability for IH repairs in a DS setting, due to its pharmacokinetic and pharmacodynamic properties and few adverse effects.*

KEY WORDS: Inguinal hernia - Monitored Anesthesia Care – Remifentanyl.

Introduction

The extension of indications for procedures in a day surgery setting (DS) has determined a large number of changes in the anesthesiological management and surgical treatment of Inguinal Hernias (IH), since the European Hernia Society confirmed that the treatment of IH in DS is safe, valid and cost-effective, independently of the type of surgical hernia repair (1). Furthermore, elderly ASA III patients are also suitable for this procedure, after an accurate assessment of individual health conditions

(2). As a matter of fact, DS should be considered for all types of patients after rating individual characteristics and comorbidities (3-6). According to the European Hernia Society recommendations, the treatment of IH in DS should be performed under Monitored Anesthesia Care (MAC). This technique is a planned procedure during which the patients undergo local anesthesia together with analgesic and sedative procedures, in order to achieve a safe sedation together with anxiety and pain control (7, 8). In our experience, MAC has been done by analgesia and sedation in addition to local anesthesia.

Our research focused on opioid drugs characterized by high efficiency and ultra-fast recovery, since the context-sensitive half-time (CSHT) is very short: approximately 3 minutes (9, 10). Moreover, MAC allows the patients to be discharged very soon.

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This study's purpose was to determine the efficacy of remifentanyl and its analgesic role in the intra-operative pain management during IH repair, performed in a DS regimen. We evaluated the effect of the drug on intra-operative pain control, safety of handling and timing of discharge.

Patients and methods

From January 2013 to December 2015, 960 consecutive patients underwent IH repairs at the "F. Durante" Day Surgery Department, "Umberto Primo" Academic Hospital in Rome.

The patients were divided into two groups, depending on the treatment they received during the IH repair: group R received remifentanyl, whereas group F fentanyl; group F was considered the control group. No control group without opioids was considered, as it was not deemed appropriate for this intervention. Criteria for inclusion in the study included ASA grade I – III, age < 18 years, non-complicated and unilateral IH, no allergy to local anesthetic drugs and morphine-like substances.

Exclusion criteria included morbid obesity (BMI ≥ 40 or BMI ≥ 35 in association with high blood pressure or diabetes), confirmed or suspected coagu-

lopathy; OSAS (obstructive sleep apnea syndrome) with AHI ≥ 10; history of substances abuse, psychiatric disorders, GERD (gastro-esophageal reflux disease)-related esophagitis, chronic analgesic use, allergy to local anesthetic and ASA > III.

Patients regretting surgical treatment, even if they met all the inclusion criteria, were excluded from the trial. Patients demography and baseline characteristics are reported in Table 1.

Premedication was not administered to any patient, because it could delay the recovery and the discharge.

Hernia repair was performed according to the open Lichtenstein technique for primitive inguinal hernia, with only mesh placement. In 50% of the cases the mesh was fixed with fibrin glue. The different surgical technique received (fibrin glue vs. suture) by the patients does not affect the outcome in terms of intensity of pain, because no difference is generally reported in the immediate postoperative phase, as the advantages with the use of fibrin glue are evident at medium to long term (11). Recurrent hernias were excluded from the study.

In group R, analgo-sedation was achieved with a continuous infusion of remifentanyl (0,25-1 μg.kg⁻¹.min⁻¹) from the first minute (skin incision) until the end of suturing of the superficial layers. Remifen-

TABLE 1 - STUDY POPULATION.

		Group R	%	Group F	%
Tot Pats.	960	548		412	
Male		464	84,67%	352	85,44%
Female		84	15,33%	60	17,05%
ASA					
	I	317	57,85%	176	42,72%
	II	213	38,87%	222	53,88%
	III	22	4,01%	14	3,33%
Hernia					
	DX	281	51,28%	227	55,00%
	SX	271	0,494526	185	45,00%
Age mean, years.		55,51 ± 14,26		52,32 ± 12,77	
Weight mean, Kg		72,64 ± 10,91		77,12 ± 0,98	

tanil was diluted in a concentration of $10\mu\text{g}\cdot\text{kg}^{-1}$. This concentration is considered safe, since even in the event of an accidental overdose, the possibility of apnea and chest stiffness is excluded.

The dose was modified in a range of $0.01\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ to $0.13\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ during the procedure, according to the intensity of the pain perceived from the patient and to the modification of the cardiovascular and respiratory parameters. Supplemental oxygen was administered to all the patients during the treatment period. Acetaminophen ($15\text{mg}\cdot\text{kg}^{-1}$) was administered at a slow infusion velocity, 20 minutes before the end of the surgical procedure, to provide sufficient analgesia in the early recovery phase. Ondansetron at a dose of $50\mu\text{g}\cdot\text{kg}^{-1}$, was also administered, in order to prevent nausea and vomiting.

In group F, analgesia and sedation were obtained by administering fentanyl as an intravenous bolus according to patient's pain, the duration of the surgical procedure and the modification of circulatory function. Supplemental oxygen was administered to all the patients during the treatment period. In order to prevent nausea and vomiting, $50\mu\text{g}\cdot\text{kg}^{-1}$ of ondansetron were also administered. For post-operative analgesia, acetaminophen ($15\text{mg}\cdot\text{kg}^{-1}$) and ketorolac (30mg) was used.

During the surgical procedure, continuous monitoring of vital signs was performed every 5 minutes via assessment of electrocardiogram (ECG), heart rate (HR), non invasive blood pressure (NIBP), EtCO₂ and peripheral oxygen saturation (SpO₂). EtCO₂ was measured through nasal cannula and a conventional sidestream capnometer with $200\text{ml}\cdot\text{min}^{-1}$ aspiration flow rate. Monitoring and administered drugs were reported on the anesthetic paper.

Peripheral oxygen saturation (SpO₂) and EtCO₂ were considered as the main indicators of respiratory depression. An oxygen saturation $<94\%$ and EtCO₂ $>35\text{mmHg}$ would require a rapid intervention, such as stopping the remifentanyl infusion, starting oxygen administration, stimulating with voice, touch or pain the patient. The anesthetist was ready for a tracheal intubation procedure in refractory cases.

Mepivacaine 2% was administered as local anesthetic.

Patients expressed their level of pain on a verbal numeric scale (VNS), with scores from 0 to 10 (0=no pain, 10=maximum pain) at different times of the procedure: T₀ venipuncture; T₁ incision of the deep layers; T₂ traction of the spermatic cord (in males); T₃ fixation of the mesh; T₄ end of intervention; T₅ discharge and T₆ 24 hours later. This latter parameter was assessed by phone interview.

The results were expressed as the mean value (MV) \pm standard deviation (SD). Statistical analysis was done with the Student's t-test.

Results

All the IH repairs were successful and no patient required the conversion to general anesthesia during surgery. All the patients were evaluated through Aldrete scoring system for the measurement of recovery after anesthesia, in order to guarantee a safe discharge from the recovery room. None of the 960 patients had complications, side effects related to the anesthetic technique or procedure-related complications that required mechanical ventilation. There were no deaths in this series.

Group R

Five hundred- fourty -eight patients, 464 males of a mean age of 55.51 ± 14.26 years were enrolled. Overall, 279 right IHs and 269 left IHs were treated. Three hundred-seventeen patients were ASA I, 210 were ASA II and 21 were ASA III. Conscious sedation was obtained with a continuous remifentanyl infusion during the surgical procedure; the dose was adjusted according to the VNS, however the mean dose of remifentanyl infusion was $0.052 \pm 0.008\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. The remifentanyl total dose mean value was $329.12 \pm 147.42\mu\text{g}$, according to the weight of the patients. The IH repair procedures were performed by different surgeons and the mean value of the surgical procedure duration was 55.94 ± 26.89 minutes.

In crucial moments of the procedure, patients had to describe the intensity of pain through VNS; the mean value for venipuncture pain was 1.8 ± 0.8 ; the mean value during the procedure after remifentanyl infusion was 1.8 ± 0.8 . At the time of discharge, the mean value of the pain intensity was 1.2 ± 1 , while it was 1.7 ± 1.2 at 24 hours after the surgical procedure (Table 2).

The maximum and minimum systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were assessed for each patient; then, the mean values were compared with the baseline values recorded during the pre-operative anesthesiological examination.

In this group, the mean values of these parameters were: maximum SBP 129.44 ± 9.05 mmHg, minimum SBP 115.63 ± 9.66 mmHg; maximum DBP 80.14 ± 7.54 mmHg, minimum DBP 69.2 ± 8.29 mmHg; HR 71.85 ± 9.58 bpm (beats per

TABLE 2 - VNS IN THREE EVALUATION TIMES.

	VNS		
	INTRAPROCEDURAL	DISCHARGE	24H
GROUP R	1,839622642 ± 0,869650442	1,226415094 ± 1,01683935	1,745283019 ± 1,272876912
GROUP F	2.6152645912 ± 0,929655467	2.8245930127 ± 1,10546942	4.5270365492 ± 1,052284932

TABLE 3 - MEAN VALUES COMPARISON.

Mean Value	Group R	Group F
Basal SBP (mmHg)	125.73 ± 17.20	126.10 ± 16.71
SBP (mmHg)	122.53 ± 13.43	123.96 ± 15.77
DBP (mmHg)	74.67 ± 11.12	78.41 ± 12.55
MAP (mmHg)	90.62 ± 11.88	93.59 ± 13.62
Basal HR (bpm)	72.54 ± 11.40	67.95 ± 10.94
HR (bpm)	71.85 ± 9.58	69.48 ± 10.90
SpO ₂ (%)	98.97 ± 0.46	98.69 ± 0.74
Surgery time (min)	85.94 ± 26.89	84.27 ± 22.38
Total dosage (µg)	329.12 ± 147.42	76.10 ± 36.90

minute). The Mean Arterial Pressure (MAP) was 90.62 ± 11.88 mmHg. During the surgical procedure, the peripheral oxygen saturation (SpO₂) values were recorded, with a mean value of 98.97 ± 0.46% (Table 3).

Side effects and/or adverse events, such as post-operative nausea and vomiting (PONV) didn't occur intra- and post-operatively, but in this group PDNV (Post-Discharge Nausea and Vomiting) occurred in 22 patients, a percentage equal to 4%. The PONV risk of each patient was evaluated at preoperative examination through Apfel Score. Post-operatively, PONV impact scale was used to evaluate PONV in patient who had just undergone surgery; a PONV Impact Scale score ≥5 defined clinically important post-operative nausea and vomiting (12).

Group F

The control group (group F) included 412 patients (60 females and 352 males) with a mean age of 52.32 ± 12.77 years; 227 right IHs and 185 left IHs were treated. 176 patients were ASA I, 222 were ASA II and 14 were ASA III. Patients in this group received fentanyl (50 µg.ml⁻¹) in order to control surgical pain, and the mean value of the dosage of fentanyl administration was 76.1 ± 36.9 µg. The mean duration of the procedure was of 84.27 ± 22.38 minutes.

The pain mean value during the surgical procedure was 2.61 ± 0.92, at the time of discharge was 2.8 ± 1.10 and at 24 hours after surgery was 4.5 ± 1.0 (Table 2).

In this group as well, the maximum and minimum systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were assessed for each patient; then, the mean values were compared with the baseline values recorded during the pre-operative anesthesiological examination.

In group F, the mean values of these parameters were: maximum SBP 133.17 ± 11.50 mmHg, minimum SBP 114.76 ± 8.46 mmHg; maximum DBP 85.41 ± 9.02 mmHg, minimum DBP 71.41 ± 7.55 mmHg; HR 69.48 ± 10.90 bpm (beats per minute). The Mean Arterial Pressure (MAP) was 93.59 ± 13.62 mmHg. During the surgical procedure, the peripheral saturation oxygen (SpO₂) values were recorded, with a mean value of 98.69 ± 0.74% (Table 3). Post-operative nausea and vomiting (PONV) didn't occur intra- and post-operatively, but 45 patients (a percentage equal to 11% of the subjects in this group) reported episodes of PDNV. Bradycardia with HR to 45 bpm associated with hypotension (90/60 mmHg) occurred in one patient, who was treated with the administration of 0.5mg of atropine; the patient never lost consciousness and peripheral oxygen saturation remained substantially in the normal range.

Discussion and conclusion

Some studies (13-20) in the last 10 years aimed to establish the best choice of anesthesia for IH repair among general, regional and local anesthesia. Each of these techniques has advantages and disadvantages, but most of the authors prefer local anesthesia (13, 14, 16, 17). General anesthesia is generally reserved for long stay admissions, and it does not represent the best choice for Day Surgery treatment. The use of central-type loco-regional anesthesia (subarachnoid or epidural anesthesia) has been

considered in many scientific reviews (13-15); this technique, with an excellent control of intra-operative pain, results in high compliance for the patient and for the surgeon, but it requires a longer stay and it would not allow an early patient mobilization; moreover, it is associated with post-operative urinary retention (approximately 30% of cases) (13). This could delay the discharge, because voiding is considered in many studies one of the parameters for deciding discharge in the Post-Anesthetic Discharge Scoring System (PADSS) (21, 22). Regional anesthesia, using short-acting anaesthetics, added to spinal opioids, can reduce the postoperative side effects and can be reserved to selected patients (1).

According to the European Guidelines (1) and to the international literature (13-20), the first approach should be local anesthesia, which yields a satisfactory pain control, high satisfaction for the surgeon and the patient, a low percentage of intra- and post-operative complications, a faster discharge and an early mobilization. However, the main limitation of local anesthesia is that it could provide insufficient analgesia in some special conditions (e.g., obesity and/or large hernias); in these cases, the use of a large amount of local anesthetic drug could increase the toxicity risk and could hide surgical planes. In addition, some anxious patients live dramatically the relationship with the operating theatre and the surgical experience. Therefore, we propose an analgesia-sedation that allows a better patient compliance to the surgical treatment (23-28).

The continuous infusion of remifentanil at a mean of $0.052\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ was satisfactory and in no case we needed to convert to general anesthesia due to pain.

Comparing the two groups, analgesia-sedation with remifentanil (group R) versus analgo-sedation with fentanyl (group F), different mean values on the VNS (verbal numeric scale, Table 2) were observed. The intra-procedural mean value of VNS in the group R was 1.83 ± 0.86 vs 2.61 ± 0.92 in group F (p value < 0.0001); the mean value of VNS at the discharge in the group R was 1.22 ± 1.01 vs 2.82 ± 1.10 in group F (p value < 0.0001).

Concerning the assessment of effect of drugs on hemodynamics, the results obtained confirm the validity of remifentanil in maintaining hemodynamic stability; as the mean values of the systolic blood pressure (SBP) and diastolic blood pressure (DBP) in group R were respectively 122.53 ± 13.43 mmHg and 74.67 ± 11.12 mmHg; the mean value of Mean Arterial Pressure (MAP) was 90.62 ± 11.88 mmHg. These results were essentially superposable, with on-

ly minimal differences, to the mean values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) recorded in group F, which were respectively 123.96 ± 15.77 mmHg and 78.41 ± 12.55 mmHg; the mean value of Mean Arterial Pressure was 93.59 ± 13.62 mmHg (p value < 0.0001).

In relation to the oxygenation, the peripheral oxygen saturation (SpO_2) level was maintained within the normal range ($>92\%$) in both group; in group R the mean value of SpO_2 was $98.97 \pm 0.46\%$, in group F was $98.69\pm 0.74\%$, with minimal differences (p value < 0.0001). Also in this case, remifentanil proves to be as safe as fentanyl in keeping this respiratory parameter stable.

Even if the t-test proves that the mean values comparisons are highly statistically significant, we retain that the differences between blood pressure and peripheral oxygen saturation mean values are too little to allow to confirm that a drug is superior to the other. On the contrary, the comparison between the VNS, both intra-procedural and at discharge, shows that remifentanil allows a better pain control than fentanyl. However, the most important characteristic of remifentanil is that it is rapidly metabolized by the hydrolysis of the ester linkage by nonspecific blood and tissue esterases (9, 25), so the recovery from its effects occurs rapidly (from 5 to 10 minutes), even after continuous infusion. This feature makes remifentanil particularly appropriate to provide analgesia in some Day Surgery interventions, allowing faster patient recovery and discharge.

The dilution adopted in this study was $10\mu\text{g}\cdot\text{ml}^{-1}$, that appears to be safer than the five times higher concentration usually used in surgical anesthesia, e.g. Total Intravenous Anesthesia/Target-Controlled Infusion (TIVA/TCI) (25, 30). Moreover, there are many cases of postoperative nausea and vomiting (PONV) during and after the use of morphino-mimetics drugs (29-32). In this study, cases of PONV didn't occur, but episodes of PDNV were reported. This aspect is very important, since PONV represents one of the most frequent complications in DS (together with pain and bleeding) and it cannot allow a fast discharge. PDNV refers to episodes of nausea and vomiting which arise after the discharge, and this phenomenon might be due to the short half life of Ondansetron (about 3 hours) administered during the surgical procedure. Dexamethasone was administered to all the patients in whom PDNV occurred, since it could affect recovery and other postoperative therapies. Remifentanil seems to be a very useful and manageable drug in anesthetic practice, but at the same time it is neces-

sary that it be used by trained professionals, who know the benefits and the possible adverse effects of this drug (33-37). It is an excellent drug for pain control during intra-operative procedures for IH repairs in Day Surgery, it ensures optimal hemodynamic stability and the preservation of the respiratory function and its efficacy and safety were highlighted by the patients satisfaction (35). Furthermore, surgeons could perform the most painful tissue handling during the intervention (e.g. spermatic cord traction or prosthesis fixation) without patient resistance in case of evoked pain.

In conclusion, this last two-year experience shows that remifentanyl, due to its pharmacokinetic and pharmacodynamic properties and few adverse effects that makes it extremely easy to handle, determined a small, but positive revolution in the anesthesiological management of IH repair.

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