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Research paper

Postoperative pain scores and analgesic requirements after thyroid surgery: Comparison of three intraoperative opioid regimens

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Purpose: This study was designed to compare the effect on postoperative pain, opioid consumption and the length of stay in postoperative care unit (PACU) after three different intraoperative analgesic regimens in thyroid surgery. Methods: Seventy five patients were enrolled into the study and assigned to one of three groups, fentanyl, sufentanil or remifentanil (n=25 for each group). Before the end of surgery, paracetamol 1 gr and nefopam 20 mg was also administered in all patients. Pain scores, opioid demand and the length of stay in PACU were assessed in a blind manner. Results: Post operative pain scores were significantly lower in the fentanyl and sufentanil groups compared to remifentanil group (55 ± 15, and 60 ± 10 versus 78± 12, P < 0.05). Patients in the remifentanil group stayed longer in the PACU 108± 37 min versus 78±31 and 73 ± 25 min, (P< 0.05). Conclusion: After remifentanil based analgesia, anticipation of postoperative pain with opioid analgesic appears mandatory even for surgery rated as being moderately painful, otherwise longer opioid titration due to higher pain scores might delay discharge time.

Key words: postoperative analgesia, morphine titration, thyroid surgery

1. INTRODUCTION

Post operative pain after thyroid surgery might be important especially in the early postoperative hours. Different techniques or medications including non-steroidal anti-inflammatory drugs (NSAID) in combination with propacetamol, oral morphine, buprenorphine, local anesthetics using either infiltration or combined superficial and deep cervical blockade have been assessed and/or suggested [1-4]. We hypothesized that the choice of opioid analgesic regimen might influence the immediate postoperative period especially the pain scores and the length of stay in the post anesthetic care unit (PACU). In this open randomized study, we compared postoperative pain management using three different intraoperative opioid analgesic regimens.

2. METHODS

After the approval of institutional review board of hospital Henri-Mondor and the informed consent obtained from each patient, seventy five adults ASA I-II scheduled for elective total thyroidectomy for multinodular goiter were enrolled into the study. All patients were euthyroid before surgery which was performed by the same surgeon. Patients were excluded if they had any analgesic medication or corticosteroid drug prior surgery. They were instructed the day before surgery about the study design and to express their pain in a 101 mm Visual Analogic Scale, [0 = no pain, 100 = maximum pain] (VAS). Premedication was hydroxyzine 50 mg 1 hour before surgery.

Patients were assigned according to a computerized list of random numbers into 3 groups. Group Fentanyl (n=25), group Sufentanil (n=25) and group Remifentanil (n=25). All patients had general anesthesia induced with propofol, 2.5-4 mg/kg. Tracheal intubation was performed without muscle relaxant, and anesthesia was maintained with isoflurane (end tidal 0.7-1%) and N2O/O2(50/50). Analgesia was started with a bolus fentanyl 2-3 µg/kg, sufentanil 0.2-0.3 µg/kg, or remifentanil 0.4-5 µg/kg and maintained with boluses of fentanyl 0.5-1µg/kg, sufentanil 0.08-0.15 µg/kg, until the end of the dissection of the first thyroid lobe while the infusion of remifentanil 0.05-0.25 µg/kg/min was maintained until the last surgical stitch.

If surgery had to be prolonged because of cancer or other surgical complication, the patient was excluded from the study and additional patients were enrolled.

After the dissection of the first thyroid lobe, all patients received 1g of paracetamol and 20 mg nefopam IV as part of multimodal prevention of postoperative pain. Except for the remifentanil group, no other analgesic was injected until extubation. Patients were extubated in the operating room.

In the operating room

The following parameters were recorded: Duration of anesthesia, duration of surgery, intraoperative anesthetics requirements and time to extubation defined as the delay between the end of surgery and extubation.

In the PACU

Clinical monitoring consisted of continuous EKG, pulse oximetry non invasive intermittent blood pressure measurements, respiratory frequency, pulse oximetry and temperature measurement with an infrared tympanic thermometer. The PACU staff and nurses were not aware of the analgesic assignment.

The following regimen of morphine titration was established in the PACU. Upon extubation patients were asked to rate pain in a (0-100mm) VAS, when the VAS score was greater than 40 mm intravenous morphine was titrated every 5 min in 2 mg increments and pain was assessed every 5 min until relief (VAS< 40). The following parameters were recorded: time of extubation, first VAS pain scores, the necessity, the amount of morphine titration to reach a VAS of < 40, the incidence of nausea and

vomiting and sedation score (0=awake, 1=mild, 2=sleepy but awakable, and 3 = very sleepy) and the length of stay in the PACU. The latter was decided by a physician unaware of the randomisation and based by stable vital signs for at least 30 min, VAS pain score of less than 40, lack of surgical complication, absence of opioid related side effects (nausea and vomiting) and a core temperature above 36° C.

In the surgical ward

Paracetamol injections were repeated systematically every 6 hours, while nefopam was repeated every 8 hours with a pain score evaluation by a nurse every 4 hours. If the VAS score was higher than 40, subcutaneous morphine 5-10 mg was injected.

Maximum postoperative pain scores, the necessity of morphine injection, the incidence of opioid related side effects (nausea and vomiting, and sedation) were noted for the first 24 postoperative hours.

Statistical analysis

The sample size was calculated to obtain a difference in the immediate postoperative pain scores of 30 mm and a standard deviation of 15, with a power of 0.8, a *P* value of 0.05 was considered to be significant. Data were analyzed using Jandel Sigmastat statistical software (San Rafael, Ca, USA). ANOVA and Kruskall Wallis Rank sum test were used for comparison between groups depending on distribution.

3. RESULTS

Six patients were withdrawn from the study: 4 out of 6 for prolonged surgery for the presence of cancer, and 2 out of 6 for surgical hematoma and drainage. All other patients completed the study. Demographic characteristics and intraoperative anesthetics requirements are represented in Table 1 and 2.

Table 1. Patients characteristics

	Group Sufentanil (n=24)	Group Fentanyl (n=24)	Group Remifentanil (n=21)
Weight (kg)	70±16	68±18	71±18
Height (cm)	168±7	170±9	168±8
Age (yr)	44±12	48±14	47±13
(male /female)	9/15	7/17	7/14

Values are ± SD as appropriate.

Extubation delays were significantly lower in the remifentanil group, P<0.05, (Table 2).

The initial postoperative pain scores in the PACU were significantly lower in the sufentanil and fentanyl group compared to remifentanil group, (*P*<0.05). The necessity and total amount of morphine titration in the PACU were significantly less in the sufentanil and fentanyl group compared to the remifentanil group, (*P*<0.05) Table 2.

In the surgical ward, maximum pain scores and the incidence and the amount of morphine requirements were not different between groups.

No patient had heavy sedation in either of the groups.

The incidence of nausea and vomiting was not different between groups.

Table 2. Intraoperative anesthetic and surgical characteristics, Pain scores, length of stay in the PACU, opioid demand and opioid related side effects.

	Group Sufentanil (n=24)	Group Fentanyl (n=24)	Group Remifentanil (n=21)	significance
Sufentanil/Fentanyl/ Remifentanil (µg)	25±5/-/-	-/260±65/-	-/-/650±260	NA
Duration of surgery (min)	70± 22	80± 23	73±25	NS
Extubation delay (min)	10 ± 6	12 ± 5	4±3*	P<0.05
VAS (mm) After extubation	55±15	60 ±10	78±12*	P<0.05
Necessity of Titration	11/24	13/24	21/21*	P<0.05
Amount of morphine in PACU (mg)	4±3	5±3	10±4*	P<0.05
Length of stay in the PACU (min)	78±31	73±25	108±30*	P<0.05
Incidence of PONV (%)	46%	43%	52%	NS
Sedation ; (0/1/2/3)	12/12/0/0	10/14/0/0	12/9/0/0	NS
Maximum postoperative pain scores in the ward (First 24 hours)	50±20	55±23	50±25	NS
Additional morphine in the surgical ward (First 24 hours)	12%	13%	15%	NS

* Group remifentanil versus group fentanyl and sufentanil. (PACU = post anesthetic care unit, PONV = postoperative nausea and vomiting, VAS = visual analgesic scale)

4. DISCUSSION

This study shows that the combination of paracetamol and nefopam alone was not sufficient to adequately control postoperative pain after thyroid surgery especially after remifentanil based analgesia and suggest the use of an opioid based analgesia in the early postoperative period. However opioid were necessary only in 1/3 of patients after sufentanil and fentanyl based analgesia while almost always necessary in case of remifentanil based analgesia. The necessity of anticipation of postoperative pain in case of remifentanil analgesia is well documented [5-7]. Nevertheless it is not always clear whether this anticipation should use opioid analgesics or other agents [8-10]. In addition, we could detect a delay in discharge criteria in the remifentanil group most probably related to higher pain scores and longer necessity of titration. On the other hand delay to extubation was shorter in the remifentanil group, this might have some advantages especially when neurologic assessment is mandatory [11]. Thyroid surgery is rated as being moderately painful [12, 13], therefore we hypothesized that anticipation of postoperative pain with a combination of paracetamol and nefopam could adequately prevent postoperative pain and yield acceptable pain scores in all groups. However this was not the case as pain scores were significantly higher in the remifentanil groups. This difference might have several explanations, including the concept of hyperalgic activity after remifentanil based analgesia [14] but also the pharmacokinetic of fentanyl and sufentanil yielding a moderate degree of postoperative analgesia [15, 16]. Our study has some limitations including the fact the anesthetist in charge of the procedure was aware of the analgesic assignment, however since the outcome of the study was focused on immediate postoperative period we believe the results could not be affected. Postoperative pain

after thyroid surgery might have different explanations including the skin incision, pharyngolaryngeal morbidity after intubation and neck hyperextension [17, 18]. Multiple techniques and protocols have been suggested in order to decrease postoperative pain after this type of surgery, including local anesthetic using infiltration or cervical block and multimodal analgesia using (NSAID) [1, 2, 19]. We are aware that the latter drugs are also efficient in reducing morphine consumption in this type of surgery, however the addition of a third non opioid analgesic drug in addition to paracetamol and nefopam could have made the endpoint of the study more difficult to reach. Thyroid surgery is associated with high incidence of nausea and vomiting; however the incidence of these symptoms in our group of patients was comparable to other studies [20].

In summary, when compared to fentanyl and sufentanil, the use of remifentanil was associated with a significant increase in immediate postoperative pain and the length of stay in the PACU. This study highlights the importance of anticipating postoperative pain by opioid when remifentanil is used even though when the surgery is described as yielding low to moderate level of post operative pain.

Conflict of interest

The authors have declared that no conflict of interest exists.

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