International Journal of Current Science Research
www.drbgrpublications.in

Volume: 4; Issue: 11; November-2018; pp 1668-1686. ISSN: 2454-5422

Does use of intraoperative diclofenac sodium increase postoperative bleeding after prosthetic breast reconstruction ?

*Mohammed. Ben Aziz[1], Ha-Nam. Truong [1], Frederic. Urbain[2], Maher. Khalife[1]

[1]Department of Anesthesiology, Jules Bordet Institute 1000 Brussels, Belgium.

[2]Department of Plastic and Reconstructive Surgery, Jules Bordet Institute, 1000 Brussels, Belgium.

*Corresponding Author E-mail: mohammed.benaziz@bordet.be

Abstract

Background: Prosthetic breast reconstruction is the most commonly performed procedure in women following mastectomy. This painful procedure can be associated with some short- and long-term complications with prolonged hospital stay.

We evaluated the influence of diclofenac on intraoperative and postoperative complications as well as length of hospital stay.

Methods: A retrospective study comparing two groups of patients for intraoperative and postoperative complications undergoing Prosthetic breast reconstruction after prophylactic or curative mastectomy according to the type of intraoperative analgesia received.

Group diclofenac included 59 patients undergoing the procedure under general anesthesia with intraoperative diclofenac and group no diclofenac had 75 patients undergoing the same procedure under general anesthesia without intraoperative diclofenac.

Results: The two groups were comparable in terms of demographic Characteristics, preoperative radiotherapy and chemotherapy and the primary location of the tumor.

Intraoperative variables were not statistically different between the two groups except for intraoperative piritramide ($P = 0.03$).

Postoperative piritramide consumption was more frequently observed in group no diclofenac compared to group diclofenac (P =0.02) while there were no statistically significant difference for local complications and postoperative blood loss.

Length of hospital stay was higher in the group diclofenac (p=0.005)

Conclusion: Intraoperative administration of diclofenac seems to be safe on postoperative bleeding after Prosthetic breast reconstruction.

These findings should be confirmed in large prospective studies using specific guidelines. The relatively low number of serious complications denotes an adequate preoperative screening and stresses the importance of adequate maintenance of parameters throughout the perioperative process.

Clinical relevance: This study suggests that using intraoperative diclofenac may be safe on postoperative bleeding and blood transfusion and may reduce postoperative pain.

Keywords: diclofenac, general anesthesia, implant breast reconstruction, postoperative bleeding.

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

Introduction

Among women, breast cancer is the most commonly diagnosed cancer after non melanoma skin cancer, and it is the second leading cause of cancer deaths after lung cancer. In 2017, an estimated 255, 180 new cases of breast cancer (including 2,470 cases in men) will be diagnosed, and 41,070 deaths (including 460 deaths in men) will occur in United States (American Cancer Society, 2017).

Since the 1940s, the incidence of breast cancer has gradually increased in Western countries at a rate of approximately 1% per year (Boyle and Ferlay, 2005).

Novel approaches in oncological breast surgery and new technologies in the global management of women diagnosed with breast cancer will allow patients to access the best, individually tailored treatment (Cordeiro, 2008). Nevertheless, an estimated 28% to 60% of women affected by breast cancer will undergo a mastectomy (McGuire *et al.*, 2009).

One important modality of breast cancer therapy is surgical treatment, which has become increasingly less mutilating over the last century.

William Halsted introduced radical mastectomy including resection of the breast and its underlying pectoralis major muscle in order to cure all stages of breast cancer at the end of the nineteenth century (Sakorafas and Safioleas, 2010). Approximately 40 years later, Patey described a less radical modified type of mastectomy with preservation of the pectoralis major muscle yielding comparable local control and overall survival compared to Halsted (Patey, 1967).

Breast reconstruction can be performed at the same time that the oncological procedure is carried out to remove the breast cancer (immediate reconstruction), or it can be delayed until all adjuvant treatments have been completed (postoperative chemotherapy or radiotherapy) (Champaneria *et al*., 2012). Both immediate and delayed reconstruction can be performed using autologous tissue (i.e. tissue used for surgical reconstruction that comes from the patient's own body, such as the musculocutaneous pedicle or free flaps) or using implants.

Moreover, breast implant positioning after a mastectomy represents a minimally invasive procedure compared with autologous tissue breast reconstruction, and carries no risk of distant donor site-related morbidity (Jewell, 2012).

An estimated one-half to two thirds of women who undergo a mastectomy will proceed to have an alloplastic reconstruction (Le GM, O'Malley, Glaser *et al*., 2005). However the use of submuscular implants causes substantial post-operative pain, probably due to fasciomuscular stretch. In an earlier study, we investigated pain intensity in women undergoing breast surgery and found that immediate breast reconstruction was associated with intense post-operative pain in the primary recovery period (Legeby *et al*., 2002).

It has been shown that breast reconstruction with mastectomy causes more pain than mastectomy alone (Caffo *et al*., 2003). On return to normal function or during accelerated mobilization after procedures generating high pain intensity, opioids alone are insufficient (Kehlet *et al*., 1996). Surgery induces an acute inflammatory response that may exacerbate some mechanisms of pain.

Retrospective analyses suggest that intraoperative use of non-steroidal anti-inflammatory drugs (NSAIDs) may be associated with a better outcome after mastectomy and lung cancer surgery (Forget *et al*., 2010; Azab *et al*., 2013).

We conducted a retrospective review following concerns involving a suspected increase in the post-operative bleeding when diclofenac was administered perioperatively in patients undergoing prosthetic breast reconstruction.

The present study sought to assess the postoperative period when an NSAID (diclofenac) was added to the standard perioperative analgesia regimen.

As NSAIDs affect bleeding time by suppressing thromboxane synthesis (Spowart *et al*., 1988; Bean-Lijewski and Hunt, 1996; Niemi *et al*., 1997), we also measured blood loss during and after the surgical procedure.

Materials and Methods

After the approval of the Ethics Medical Committee, we reviewed the medical records and the anesthesiology charts of 134 patients who underwent Prosthetic breast reconstruction after mastectomy, from January 2007 to June 2014 by the same experienced surgeon, at Jules Bordet Institute.

The following patient characteristics were reviewed: age, gender, weight, height, body mass index (BMI), American Society of Anesthesiologists (ASA) score, past medical history, cardiovascular risk factors including diabetes and smoking, chronic medication use including anticoagulants and non-steroidal anti-inflammatory drugs (NSAID), and alcohol use. Data from the preoperative chemotherapy or radiotherapy as well as the tumor characteristics and their definitive histopathological examinations were noted. Intraoperative data were also collected regarding preoperative information. We gathered manuscript anesthesiology peroperative reports or INNOVIAN peroperative recorder reports (Anesthesia information management system to create a complete, continuous, paperless record of patient's anesthetic care) depending on the availability, operative and anesthesia time, type of anesthesia with the products used and their dosages, type and quantity of fluid resuscitation, hemodynamic data, intraoperative blood loss and number of patient transfused.

Postoperative data were also gathered in post anesthesia care unit (PACU) postsurgical files: we noted postoperative blood loss, morphine and piritramid consumption, respiratory complications, cardiac complications and infectious complications. Two groups were constituted based on the type of intraoperative analgesia received with or without intraoperative diclofenac.

All these characteristics are presented in Table 1, Table 2 and Table 3, according to the type of intraoperative analgesia used.

General endotracheal anesthesia was given intravenously according to the standards used in our institute. Hemodynamic monitoring included cardiac monitoring by electrocardiogram (ECG), noninvasive blood pressure (NIBP), oximeter, capnography (ETCO2: end-expiratory carbon dioxide concentration) and bispectral index (indicating the level of sedation and guiding the administration of anesthetics agents to maintain adequate hypnotic level). The patient's body temperature was kept constant by a heating blanket.

Surgical technique

A skin-saving incision technique was used when no previous surgical procedure had been done. The pectoralis fascia was left intact in order to obtain muscular cover for the expander prosthesis. Lymph node dissection in the axilla was performed as a level I—II procedure where lymph nodes and fat were excised separately and not en bloc, so as to reduce nerve injury. The gel- and saline-filled expander prosthesis was inserted in a submuscular pocket and the filling valve used for post-operative saline expansion was placed in a subcutaneous pocket along the mid-axillary line.

For postoperative analgesia both groups of patients received intraoperative paracetamol with or without 75 mg of diclofenac combined with intraoperative opioids (piritramide).

Paracetamol 1000 mg was given intravenously to all patients 1 h before end of surgery and post-operatively every 8 h. According to our institution policy, no patients were given low-molecular-weight heparin before surgery.

Statistical analysis

Statistical analysis were performed using chi square tests or Fisher exact test for categorical variables and using non parametric wilcoxon tests for continuous variables.

Variables were presented in term of median and interquartile range (IQR). In order to compare the two groups, were tested continuous variables for normality (Shapiro-Wilk).

All of the tests were two-sided and performed with a 5% alpha risk.

Results

Demographics and preoperative characteristics of all included patients (n=134) are reported in Table 1. The two groups did not differ on those characteristics.

In regard with intraoperative variables, statistical analysis showed a significant principal effect of group on intraoperative piritramide (p = 0.03), the intraoperative diclofenac group was associated with neither intraoperative blood loss nor the occurrence of intraoperative transfusion (Table 2).

No difference was observed regarding duration of surgery, anesthesia time and intraoperative quantity of colloids given (all p's>0.05).

As for postoperative complications (table 3), t-test analysis revealed that intraoperative diclofenac group had significantly length of hospital stay (p=0.005).

Fisher Exact tests revealed that intraoperative diclofenac group significantly differed from the other group in terms of postoperative piritramide consumption (p = 0.002) Table 3 - Fig 1.

As for postoperative complications, Fisher Exact tests revealed that diclofenac group had significantly more tramadol consumption in post anesthesia care unit (PACU) (p=0.02) Table 3- Fig 3, these patients who had not received piritramide postoperatively and who clearly expressed moderate pain controlled perfectly by tramadol.

There were no other statistically significant differences between groups regarding Post Anesthesia care unit blood loss, Total blood loss during hospitalization and postoperative Breast hematoma as observed in Table.3 - Fig. 2.

The crude comparisons of the difference in the amount of per- and post-operative bleeding between the two groups were analyzed using Wilcoxon tests.

Discussion

Implant reconstruction following mastectomy has increased at a steady rate since 1998 and is now utilized more frequently than autologous reconstruction. This trend can be attributed to the increased understanding of indications and patient selection for implant reconstruction:

Common and long-term complications, type of prostheses, timing options for reconstruction and the adjuvant use of radiotherapy. Nowadays, it is of importance that every woman having

a high risk constellation (family history), being diagnosed with a genetic mutation and/or being affected with breast cancer gets the possibility to be presented to a multidisciplinary board of a certified breast center prior to surgery in order to be informed about all treatment modalities, including the various modalities of breast reconstruction.

Postoperative pain is the most common symptom after implant breast reconstruction, and is associated with delay in postoperative recovery and prolonged hospitalization (Counihan and Favuzza, 2009). Nonsteroidal anti-inflammatory drugs (NSAIDs) are a key component of contemporary perioperative analgesia and work along with opioids to establish the multimodal perioperative analgesia treatment. It has been shown that NSAIDs can reduce the dosage of opioids by 30% (Marret *et al*., 2005) for postoperative analgesia.

Our study shows that intraoperative diclofenac, successfully decreased the postoperative piritramide consumption associated with implant breast reconstruction Fig 1.

Improved pain relief with NSAID has been reported previously. Rømsing concluded in a review that the analgesic effect with concurrent use of paracetamol and an NSAID was superior to paracetamol alone (Rømsing *et al*., 2002), and Legeby found improved pain relief after addition of Diclofenac to paracetamol and opioids for the first 20 post-operative hours after implant breast reconstruction (Legeby *et al*., 2005).

Few earlier studies have addressed postoperative pain and pain relief after mastectomy and implant breast reconstruction. Legeby found that mastectomy with implant breast reconstruction generated intense postoperative pain which was often difficult to relieve adequately with opioids alone (Legeby *et al*., 2002).

The addition of an NSAID to paracetamol provides additional analgesic efficacy and significant reductions in opioid use ranging from 33% to 46% compared with paracetamol alone (Hyllested *et al*., 2002).

Another interesting finding in our study was bleeding after diclofenac administration, the crude comparisons of the difference in the amount of per- and post-operative bleeding between the two groups were analyzed using Wilcoxon tests and reveled no statistically significant differences between groups regarding Post Anesthesia care unit blood loss, Total blood loss during hospitalization and postoperative Breast hematoma.

Intraoperative NSAIDs are controversial due to their effect on platelet aggregation, and there is a reluctance among surgeons to use NSAIDs because of the hypothetical risk of haematoma and possible re-operation. This fear may be overestimated. Therefore, although diclofenac does affect platelets, it may not produce an' abnormal haemostatic state in previously normal individuals. However, it was shown that certain members of the population are more sensitive to the haemostatic effects of aspirin than others (Mielk, *et al*., 1969).

The effect of diclofenac on surgical blood loss is unclear, Previous studies have found that pre-operative administration of lower doses of diclofenac do not increase blood loss after gynaecological laparotomy (Rorarius *et al.*, 1989) or transurethral prostatectomy (Bricker *et al*., 1987).

Two meta-analyses (Marret 2003; Moiniche 2003) reviewed the use of NSAIDs and the risk of bleeding after tonsillectomy in both adult and paediatric patients. Marret *et al*., 2003 concluded that NSAIDs increased the risk of re-operation for haemostasis after tonsillectomy but Moiniche *et al.*, 2003 concluded that NSAIDs should be used cautiously until further data were available.

Cardwell *et al.,* 2005 concluded that there is currently no evidence that using NSAIDs caused any statistically significant increase in bleeding requiring further clinical intervention.

A Cochrane systematic review (Standing *et al*., 2009) considered diclofenac for acute pain in children (perioperative pain, migraine, renal colic and soft tissue injury and fractures). This paper included two studies from our review (Öztekin 2002; Thiagarajan 1993) and included outcomes of bleeding requiring surgical intervention and nausea or vomiting, or both. The authors concluded that diclofenac did not appear to increase the incidence of perioperative bleeding (Mantel-Haenzel RR 1.25, 95% CI 0.31 to 4.97). They also conclude that there is a reduction in nausea and vomiting (Mantel-Haenzel RR 0.58, 95% CI 0.47 to 0.73).

In addition it may be prudent to avoid the use of diclofenac or another NSAID in the presence of other defects of haemostasis or coagulation. Indeed, the administration of a NSAID could reveal a subclinical haemostatic problem.

Limitation

This study has many methodological limitations, especially its retrospective design, with its inherent selection bias.

NSAIDs were administered depending on the preference of the anesthesiologist in charge of the patient.

Therefore, some information were missing in the consulted files, limiting the available variables. Our results need replications from prospective randomized trials in order to confirm the tendencies observed with those samples.

Conclusions

Intraoperative administration of diclofenac seems to be safe on postoperative bleeding after Prosthetic breast reconstruction. The addition of NSAID to paracetamol before the end of surgical procedure reduced opioid consumption on post anesthesia care unit and improved pain relief.

Further studies are required assessing the impact of NSAIDs on bleeding on this surgery. Future studies should be sufficiently powered to consider the relatively uncommon risk of bleeding. They should be sufficiently blinded and avoid the bias introduced by opioid rescue analgesics, different surgical techniques and surgeries in breast reconstruction.

Conflict of interest: All the authors have no conflict of interest for this study.

Acknowledgement: This project is funded by the Department of Anesthesia, Critical Care and Pain Medicine, Jules Bordet Institute. Brussels

The contribution each author made to the manuscript:

Literature search, figures, study and writing scientific articles for publication:

Dr Ben Aziz Mohammed: corresponding author

Data collections: via computerized medical record; ORIBASE and INNOVIAN peroperative recorder reports (Anesthesia information management system to create a complete, continuous, paperless record of patient's anesthetic care):

- Dr Truong Ha-Nam

Data analysis, statistical research and data interpretation:

- Dr Truong Ha-Nam.

Linguistic revision and design of the text:

- Dr Khalife Maher & Dr Urbain Frederic

Bibliography

American Cancer Society: Cancer Facts and Figures 2017. Atlanta, Ga: American Cancer Society, 2017

Boyle P, Ferlay J. Cancer incidence and mortality in Europe, 2004. *Annals of Oncology* 2005;**16**(3):481–8

Cordeiro PG. Breast reconstruction after surgery for breast cancer. *New England Journal of Medicine* 2008; **359**(15):1590–601.

McGuire KP, Santillan AA, Kaur P, Meade T, Parbhoo J, Mathias M, et al. Are mastectomies on the rise? A 13-years trend analysis of the selection of mastectomy versus breast conservation therapy in 5865 patients. *Annals of Surgical Oncology* 2009; **16**(10):2682–90.

Sakorafas GH, Safioleas M. Breast cancer surgery: an historical narrative. Part II. 18th and 19th centuries. *Eur J Cancer Care (Engl)* (2010) **19**(1):6–29. doi:10.1111/j.1365-2354.2008.01060.

Patey DH. A review of 146 cases of carcinoma of the breast operated on between 1930 and 1943. *Br J Cancer* (1967) **21**(2):260–9. doi:10.1038/bjc.1967.28.

Champaneria MC, Wong WW, Hill ME, Gupta SC. The evolution of breast reconstruction: a historical perspective. *World Journal of Surgery* 2012; **36**(4):730–42.

Jewell ML. Silicone gel breast implants at 50: the state of the science. *Aesthetic Surgery* 2012; **32**(8):1031–4.

Le GM, O'Malley CD, Glaser SL, et al. Breast implants following mastectomy in women with early-stage breast cancer: prevalence and impact on survival. Breast Cancer Res 2005; 7:R184-93.

Legeby M, Segerdahl M, Sandelin K, Wickman M,O¨ stman K, Olofsson Ch. Immediate reconstruction in breast cancer surgery requires intensive post-operative pain treatment but the effects of axillary dissection may be more predictive of chronic pain. Breast 2002; 11: 156—62.

O. Caffo, M. Amichetti, A. Ferro, et al. Pain and quality of life after surgery for breast cancer .Breast Cancer Res Treat, 80 (2003), pp. 39-48

Kehlet H, Rung GW, Callesen T. Postoperative opioid analgesia: Time for a reconsideration? J Clin Anesth 1996; 8: 441—5.

Forget P,Vandenhende J, Berliere M, et al. Do intraoperative analgesics influence breast cancer recurrence after mastectomy? A retrospective analysis. Anesth Analg 2010; 110: 1630–5

Azab B, Chainani V, Shah N, McGinn JT. Neutrophil–lymphocyte ratio as a predictor of major adverse cardiac events amongdiabetic population: a 4-year follow-up study. Angiology 2013;64: 456–65

Spowart K, Greer IA, McLaren M, Lloyd J, Bullingham RE, Forbes CD. Haemostatic effects of ketorolac with and without concomitant heparin in normal volunteers. Thromb Haemost 1988; 60: 382—6.

Bean-Lijewski JD, Hunt RD. Effect of ketorolac on bleeding time and postoperative pain in children: a double-blind, placebo-controlled comparison with meperidine. J Clin Anesth 1996; 8: 25—30.

Niemi TT, Taxell C, Rosenberg PH. Comparison of the effect of intravenous ketoprofen, ketorolac and diclofenac on platelet function in volonteers. Acta Anaesthesiol Scand 1997; 41: 1353—8.

T.C. Counihan, J. Favuzza Fast track colorectal surgery Clin Colon Rectal Surg, 22 (2009), pp. 60-72

E. Marret, O. Kurdi, P. Zufferey, F. Bonnet Effects of non-steroidal anti-inflammatory drugs on patient-controlled analgesia morphine side effects: meta-analysis of randomized controlled trials Anesthesiology, 102 (2005), pp. 1249-1260

Rømsing J, Møiniche S, Dahl JB. Rectal and parenteral paracetamol, and paracetamol in combination with NSAIDs, for postoperative analgesia. Br J Anaesth 2002; 88: 215—26.

M. Legeby, K. Sandelin, M. Wickman , and C. Olofsson. Analgesic efficacy of diclofenac in combination with morphine and paracetamol after mastectomy and immediate breast reconstruction. Acta Anaesthesiol Scand 2005; 49: 1360—1366

Legeby M, Segerdahl M, Sandelin K, Wickman M,O¨ stman K, Olofsson Ch. Immediate reconstruction in breast cancer surgery requires intensive post-operative pain treatment but the effects of axillary dissection may be more predictive of chronic pain. Breast 2002; 11: 156-62.

Hyllested M, Jones S, Pedersen JL, Kehlet H. Comparative effect of paracetamol, NSAIDs or their combination in postoperative pain management: a qualitative review. Br J Anaesth 2002; 88: 199-214.

Mielk CH, Kaneshiro MM, Maher IA, The standardized Normal Ivy bleeding time and its prolongation by aspirin. Blood 1969;34 : 204-15

Rorarius MGF, Baer GA, Metsa-Ketela T, Miralles J Pammaki E, Vapaatalo H. Effects of peri-operatively administered diclofenac and indomethacin on blood loss, bleeding time and plasma prostanoids in man. European Journal of Anaesthesiology 1989; 6 33542

Bricker SRW, Savage ME, Hanninc CD. Peri-operative blood loss and non-steroidal anti-inflammatory drugs: an investigation using diclofenac in patients undergoing transurethral resection of the prostate. European Journal of Anaesthesiology 1987; 4 429-34.

Marret E, Flahault A, Samama C-M, Bonnet F. Effects of postoperative, nonsteroidal, antiinflammatory drugs on bleeding risk after tonsillectomy. Anesthesiology 2003; 98:1497-502.

Moiniche S, Romsing J, Dahl JB, Tramer MR. Nonsteroidal anti-inflammatory drugs and the risk of operative site bleeding after tonsillectomy: a quantitative systematic review. Anesthesia and Analgesia 2003;96:68-77

Cardwell ME, Siviter G, Smith AF. Non-steroidal anti-inflammatory drugs and perioperative bleeding in paediatric tonsillectomy. Cochrane Database of Systematic Reviews 2005, Issue 2. [DOI: 10.1002/14651858.CD003591.pub2]

Standing JF, Savage I, Pritchard D, Waddington M. Diclofenac for acute pain in children. Cochrane Database of Systematic Reviews. 2009/10/13 2009, issue 4:CD005538. [19821348]

Oztekin S, Hepaguslar H, Kar AA, Ozzeybek D, Artikaslan O, Elar Z. Preemptive diclofenac reduces morphine use after remifentanil-based anaesthesia for tonsillectomy. Paediatric Anaesthesia 2002; 12(8):694-9. [MEDLINE: 12472706]

Thiagarajan J, Bates, Hitchcock M, Morgan-Hughes J. Blood loss following tonsillectomy in children. A blind comparison of diclofenac and papaveretum. Anaesthesia 1993; 47:132-5. [MEDLINE: 08460760]

Table 1. Preoperative characteristics, stratified by intraoperative diclofenac use or not.

	No Diclofenac (N = 75)		Diclofenac (N = 59)		P-value
Age					
Mean ± std	51.8 ± 10.5		50.3 ± 11.1		0.42
Median (min-max)	51 (27 to 81)		49 (24 to 73)		(t-test)
BMI					
Mean ± std	22.9 ± 3.7		23.2 ± 4.2		0.67
Median (min-max)	21.9 (17.3 to 35.7)		23.1 (17.3 to 42.7)		(t-test)
ASA score					
I	27	36%	26	44%	0.53
II	47	63%	33	56%	(Fisher Exact)
III	1	1%	-	-	
Smoking					
Yes	12	16%	11	19%	(chi-square)
Alcohol intake	13	17%	11	19%	0,96 (Mantel Haenszel chi-square)
Diabetes mellitus	0	0	2	3%	0.19 (Fisher Exact)
HTA	15	20%	9	15%	0.51 (Fisher Exact)
COPD	1	1%	3	5%	0,32 (Fisher Exact)
CAD					
No	75	100%	59	100%	-
Preoperative antiagregant	2	3%	3	5%	0,65 (Fisher Exact)
Preoperative anticoagulant No	75	100%	59	100%	-

Preoperative NSAIDS	1	1%	1	2%	1 (Fisher Exact)
Preoperative lung disease	0	0	1	2%	0,44 (Fisher Exact)
Preoperative chemotherapy	5	7%	3	5%	1 (Fisher Exact test)
Preoperative radiotherapy	16	21%	15	25%	0,58 (chi-square)
Primary cancer :					
Breast	75	100%	59	100%	-
Metastases	3	4%	1	2%	0,63 (Fisher Exact)

Table 2. Intraoperative characteristics, stratified by intraoperative diclofenac use or not.

	No Diclofenac (N = 75)		Diclofenac (N = 59)		P-value
Duration Anesthesia (min)					
N	75		59		0.23
Mean ± std	135 ± 43		148 ± 57		(Wilcoxon)
Median (min-max)	121 (48 to 274)		135 (79 to 365)		
Duration surgery (min)					
Mean ± std	106 ± 40		114 ± 57		0,91 (Wilcoxon)
Median (min-max)	99 (10 to 212)		135 (39 to 327)		
Crystalloids : PLasmalyte					
N	75		59		0.66
Mean ± std	1320 ± 518		1280 ± 485		(Wilcoxon)
Voluven					
	11		16		0,12 (wilcoxon)
300 ml	-		1 (6%)		
500 ml	10 (91%)		15 (94%)		
1000 ml	1 (9%)		-		
Intraoperative blood loss (ml)					
Mean ± std	22 ± 34		21 ± 38		0,76 (Wilcoxon)
Median (min-max)	10 (0 to 180)		10 (10 to 250)		
Transfusion No	74	100%	59	100%	-
Intraoperative ultiva	62	86%	40	73%	0,06 (chi-square)
Intraoperative sufentanil	11	15%	16	29%	0,06 (chi-square)
Intraoperative piritramide	54	75%	32	57%	0,03 (chi-square)
Intraoperative corticosteroids	56	78%	40	71%	0,41 (chi-square)

Table 3. Postoperative characteristics, stratified by intraoperative diclofenac use or not.

	No Diclofenac (N = 75)		Diclofenac (N = 59)		P-value
Post Anesthesia care unit blood loss (ml)					
Mean ± std	51 ± 57		62 ± 67		0,31 (Wilcoxon)
Median (min-max)	40 (0 to 375)		45 (4 to 350)		
Total blood loss (ml)					
Mean ± std	660 ± 376		766 ± 529		0,48 (Wilcoxon)
Median (min-max)	595 (15 to 1830)		703 (55 to 2540)		
Length of hospital stay (days)					
Mean ± std	8.3 ± 3.7		10.4 ± 4.5		0,005 (t-test)
Median (min-max)	8 (3 to 21)		10 (2 to 22)		
Respiratory complications NO	75	100%	59	100%	-
Infected prothesis	5	7%	3	5%	1 (Fisher Exact)
Breast hematoma	2	3%	3	5%	0,65
Deep Vein Thrombosis	1	1,3%	0	0	
Piritramide PACU	66	90%	42	74%	0,02 (Fisher Exact)
Tramadol	2	3%	8	14%	0.02 (Fisher Exact)
postoperative nausea and vomiting	7	10%	6	11%	1 (Fisher Exact)

Fig. 1 .Patients Piritramide consumption in the post anesthesia care unit (PACU)

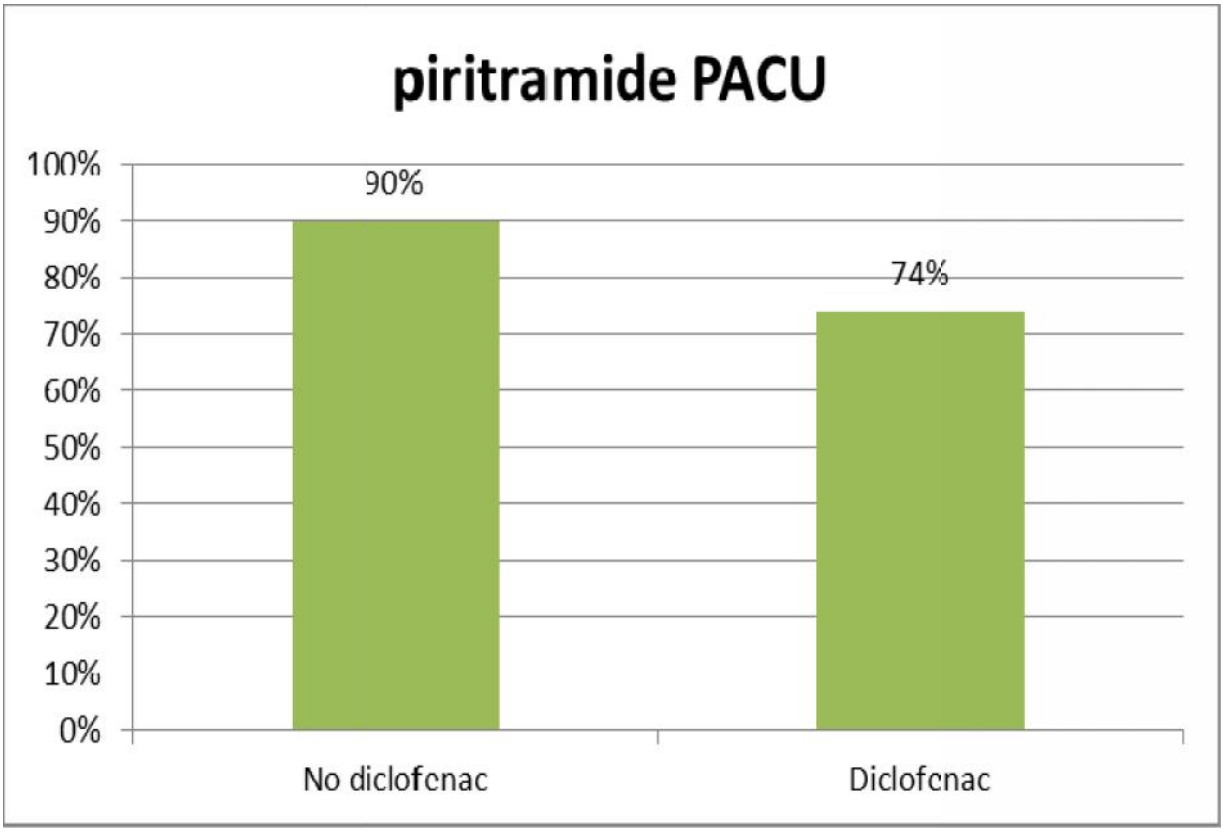

Fig. 2. Total Blood loss between the two groups

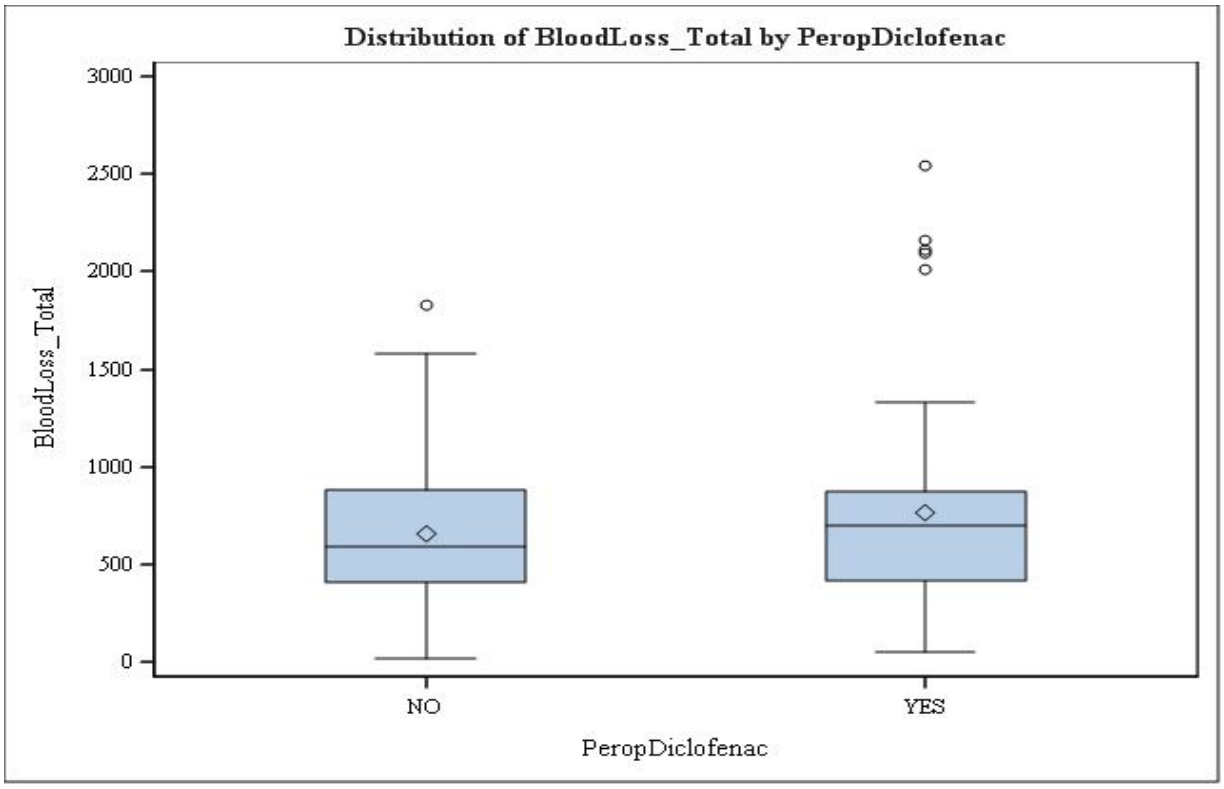

Fig. 3. Tradonal used in the post anesthesia care unit