Prise en charge de la douleur : essais d'un protocole thérapeutique.

Management of pain: trial of a therapeutic protocol

Jemea B[1,2], metogo J., Bengono Bengon R. S[1] , S.V. Nga Nomo[3] ,Ada Ebo E,[3] Ndambwe A.[1], Atems[1] , Iroume C[1,2], Esiene A[1], Ngo Nonga B[1, 2] Ze Minkande J.

1. *Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1,*
2. *YaoundeUniversity Hospital Center, Cameroon*
3. *Département de chirurgie et spécialités, Institut universitaire de Technologie Médicale Yaoundé*

Auteur correspondant : Jemea Bonaventure, CHU Yaoundé, Tel 00237677867113, Email : Jemea@hotmail.fr
FMSB -.University of Yaounde1, PO Box 1364, Yaoundé,Cameroon.

Résumé

Introduction: L'objectif de notre étude a été de comparer trois protocoles antalgiques à savoir P1 : paracétamol-diclofénac ; P2 : paracétamol-tramadol et P3 paracétamol-tramadol-diclofénac. Pour y parvenir nous avons procédé à une étude prospective et comparative sur une période de 7 mois à compter de Décembre 2017. Le recrutement qui était consécutif concernait tous les patients opérés et soumis à un des protocoles des services de chirurgie digestive et traumatologie de l'Hôpital Central de Yaoundé (HCY) et des services de chirurgie générale, du Centre Hospitalier et Universitaire de Yaoundé (CHUY) et le Centre des Urgences (CURY).

Résultats: La population totale a été constituée de 105 patients opérés à raison de 35 patients par groupe Il s'agissait en majorité de sujets de sexe masculin (sexe ratio de 1,5) âgés en moyenne de 35,4 ans avec des extrêmes allant de 18 à 60 ans. La tranche d'âge la plus représenté était de 26 à 35 ans (37,1% des patients). La majorité de nos patients étaient classés ASA 1 (88,57% soit 93 opérés). la chirurgie digestive et traumatologique étaient les plus représentées (avec respectivement 47,6% soit 50 cas et 42,8% soit 45 cas) ; l'anesthésie générale était la plus pratiquée avec 72,4% (76 malades). La douleur a été évaluée à l'aide de l'échelle visuelle analogique à la 6ème heure, 12ème heure, 24ème heure et à la 48ème heure postopératoire. A H48, nous n'avons pas retrouvé de différence significative quel que soit l'intensité de la douleur ; concernant le groupe paracétamol-diclofénac et paracétamol-tramadol-diclofénac L'incidence des effets secondaires était de 14,28%, les nausées ont représenté la plainte principale suivies des vomissements et des douleurs épigastriques. Aucun des patients dans les deux groupes n'a reçu la morphine.

Conclusion: A l'issu de cette étude, nous avons retenu que l'adjonction d'un anti-inflammatoire non stéroïdien dans l'analgésie postopératoire permet un meilleur contrôle de la douleur tout en diminuant les effets secondaires dus au tramadol et permet une bonne épargne des morphiniques.

Mots clés : étude comparative, protocoles analgésiques, période postopératoire

Summary

Introduction: The objective of our research was to compare three protocols for the management of postoperatiove pain. P1 : paracétamol-diclofénac ; P2 : paracétamol-tramadol et P3 paracétamol-tramadol-diclofénac. To acheive this objective, we carried out a prospective and comparative study. during a period of 7 months, starting from December 2017, The consecutive recruitment involved all patients operated upon and who received one of the study protocols from the digestive surgery and traumatology units in three reference hospitals in Yaounde: the Yaounde Central Hospital (YCH), the general surgery unit of the Yaounde University Teaching Hospital (YUTH) and the Yaounde Emergency Centre (YEC).

Results: We obtained 105 patients operated upon, with 35 patients per group. The majority were male (sex ratio 1.5) with an average age of 35.4 years, and ranging between 18 to 60 years. The most represented age group was 26-35 years (37.1% of patients). The majority of our patients were classified as ASA 1 (88.57%, that is 93 of the operated). With respective to the type of surgery, digestive and trauma surgery were the most represented (with 47.6% or 50 cases and 42.8% or 45 cases respectively). General anesthesia was the most practiced with a percentage of 72.4% (76 patients). Pain was assessed using the Visual Analogue Scale at the 6th hour, 12th hour, 24th hour and 48th hour postoperatively. We did not find a significant difference regardless intensity of the pain. Concerning the group paracetamol-diclofénac and paracetamol-tramadol-diclofénac. The incidence of side effects was 14,28%, nausea and vomitting were the main complaint. In the three groups no patient received morphine.

Conclusion: At the end of this study, the addition of a non-steroidal anti-inflammatory drug in postoperative analgesia provides better pain relief while reducing the side effects of tramadol, and allows a good saving of morphinics

Key words: comparative study, analgesia protocol, post operative period

Introduction: Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage (1). Several studies have highlighted the inadequacy of postoperative pain relief, 15 to 50% of those operated upon experience severe postoperative pain despite the treatments offered to them (2), with the emergence of resilient chronic pain which constitutes a risk factor for iatrogenic opioid dependence according to information from the World Health Organization on opioid overdose in 2014. Furthermore, with the increase in the non-medical use of drugs by adolescents and young adults worldwide, this non-medical use of prescription drugs is becoming a major threat to public health. Indeed, opioids cause the greatest harm and account for 76% of drug-related deaths, according to the latest world drug report in 2018, published by the United Nations Office on Drugs and Crime (UNODC). According to the same report, 87% of the global total in 2016 of pharmaceutical opioid seizures, mainly tramadol, was found in North, West and Central Africa. Tramadol is therefore becoming a growing concern, thus the aim of this study being to improve the management of post-operative pain by reducing the risk of opioid dependence.

Methodology: This is a prospective and comparative study of three analgesic protocols, namely P1: paracetamol-diclofenac; P2: paracetamol-tramadol and P3 paracetamol-tramadol-diclofenac. This study was out during a period of 7 months, starting from December 2017, in three reference hospitals in Yaounde: the Yaounde Central Hospital (YCH), the Yaounde University Teaching Hospital (YUTH) and the Yaounde Emergency Centre (YEC). The consecutive recruitment involved all patients operated upon and who received one of the study protocols from the digestive surgery and traumatology units of the YCH, the general surgery unit of the YUTH and the YEC, aged 18 years and above. Inclusion criteria were, the immediate postoperative period, patients with no known allergy to paracetamol, diclofenac or Tramadol; and exclusion criteria involved candidates with severe drug adverse reactions. In each hospital, the protocols were assigned one after the other starting with P1. Dosages were identical in all 3 groups:

- paracetamol 1g/6h in slow direct intravenous administration
- Diclofenac 75mg/12h intramuscularly
- Tramadol 100mg/8h subcutaneously

Pain was assessed using the Visual Analogue Scale at the 6th hour, 12th hour, 24th hour and 48th hour postoperatively, with 0 and 100mm marks corresponding to no pain and unimaginable excruciating pain respectively. We thus classified the pain from 0 - 39mm as mild pain, 40 - 69mm as moderate pain and from 70mm upwards as severe pain. The patient's general assessment of his pain management was evaluated as well as the tolerance of the medication. The data was collected in the pre-operative phase with the pre-anesthetic consultation, in the intraoperative phase and in the postoperative phase with the evaluation of pain and adverse effects. The results were expressed as an average +/- standard deviation and in frequency. Chi-square and Fischer tests were used to compare the variables.

Results

We obtained 105 patients operated upon, with 35 patients per group. The majority were male (sex ratio 1.5) with an average age of 35.4 years, and ranging between 18 to 60 years. The most represented age group was 26-35 years (37.1% of patients). The majority of our patients were classified as ASA 1 (88.57%, that is 93 of the operated) and the rest as ASA 2; general anesthesia was the most practiced with a percentage of 72.4% (76 patients). With respective to the type of surgery, digestive and trauma surgery were the most represented (with 47.6 % or 50 cases and 42.8 % or 45 cases respectively). The 10 remaining cases were cases of thoracic surgery and gynecology.

At the 6th hour postoperatively, the incidence of severe pain in all the operated patients was 69.52% (73 patients); there was no correlation between the treatment administered and the intensity of the pain, the difference between the groups was non-significant ($p = 0.175$). Figure one gives all the details of this results.

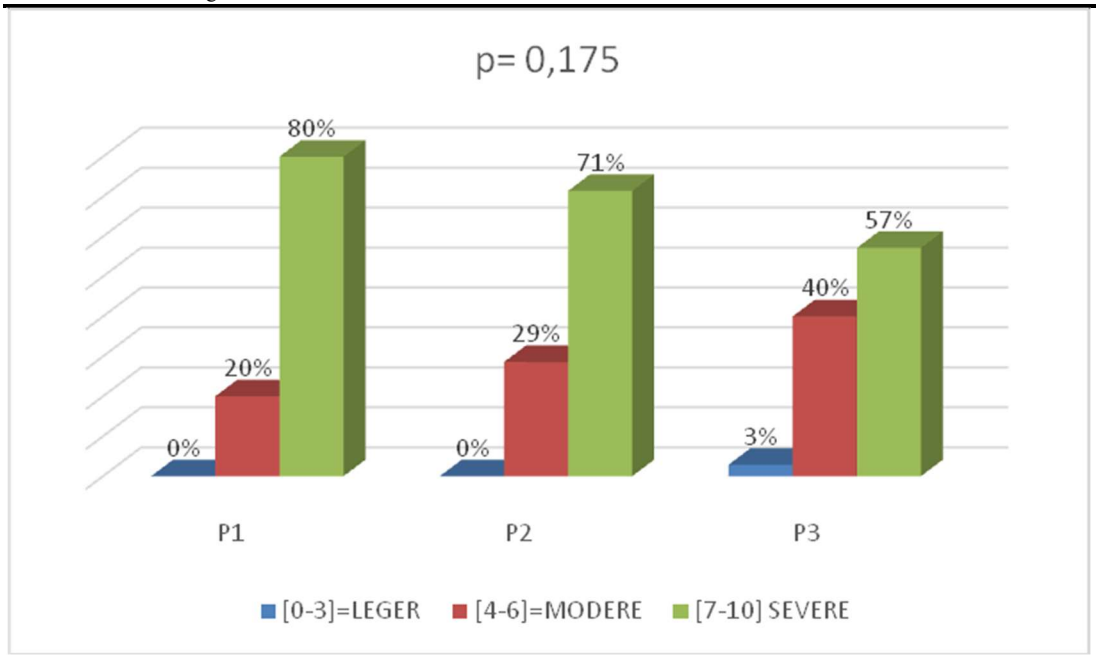

Figure 1: *Distribution of patients according to the intensity of pain at the 6th hour*

By the 12th hour, the incidence of severe postoperative pain had dropped to 33.6% (*figure 2)* but we still did not notice a significant difference at this stage (p= 0.07).

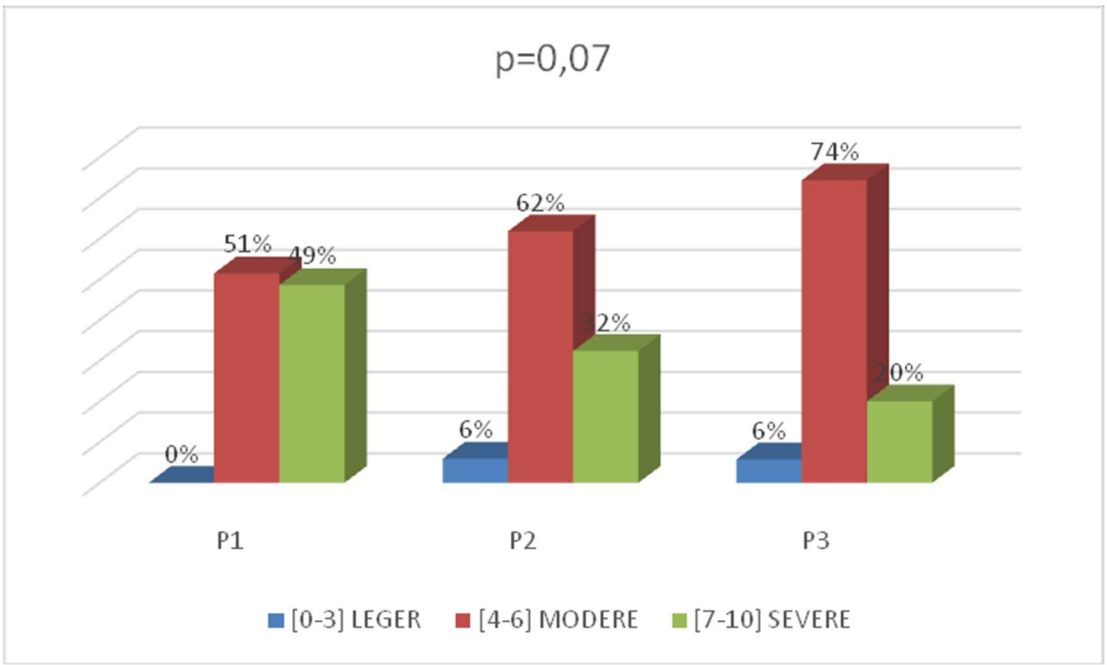

Figure 2: *Distribution of patients according to the intensity of pain at the 12th hour*

After 24 hours of treatment, the intensity of the pain depended on the treatment of the patients, the overall difference between the groups was significant (p= 0.029).

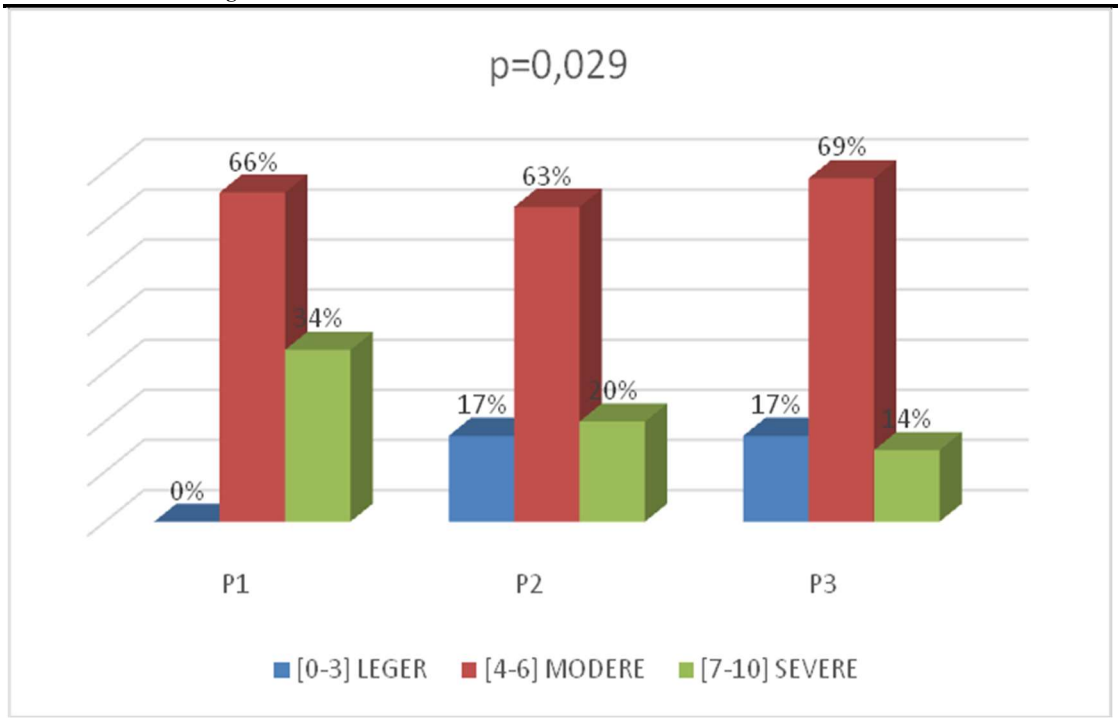

Figure 3: *Distribution of patients according to the intensity of pain at the 24 hours*

At the 48th hour, only 23 patients had severe pain (21.9%) the difference was statistically significant (p=0.042).

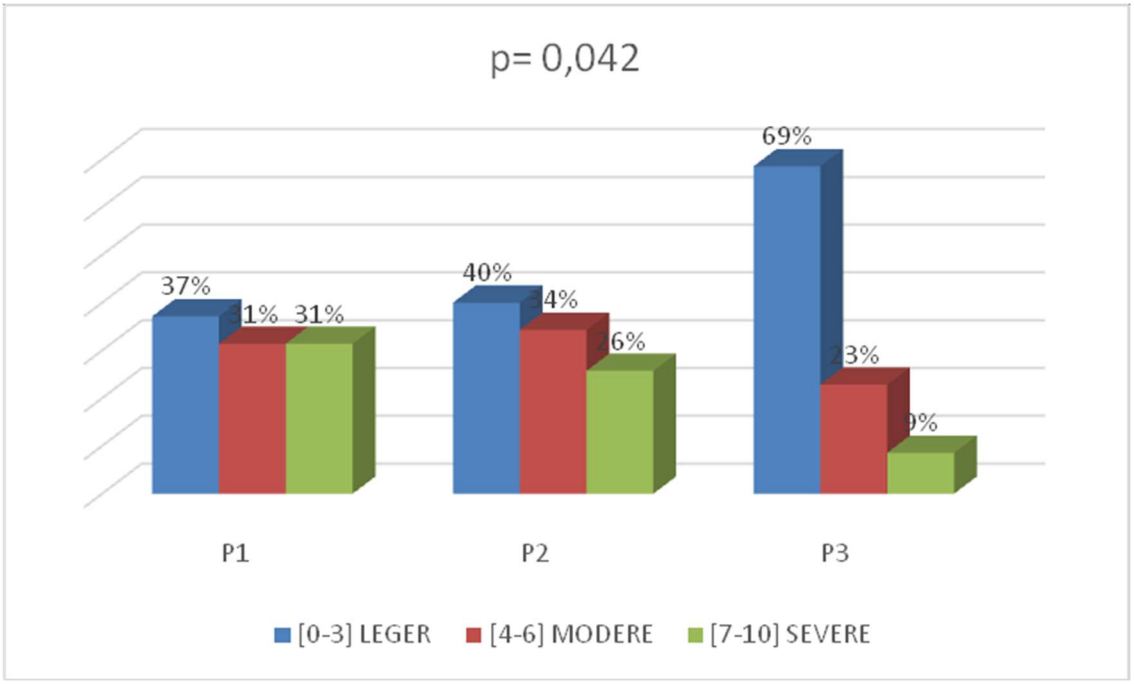

Figure 4: *Distribution of patients according to the intensity of pain after the 48 hours*

Table II: *Comparison between protocol 1 and protocol 3 according to the intensity of pain at the 48th hour (VAS)*

Variables		*Protocol P1*	*Protocol P3*	*OR*	*Min CI*	*Max CI*	*P-value*
Visual Pain	***Mild***	*13*	*24*	***3,6923***	*1,1367*	*9,9335*	***0,016***
at H48	*Moderate*	*11*	*8*	*0,6465*	*0,2231*	*1,8731*	*0,5916*
	Severe	*11*	*3*	***0,2045***	*0,0514*	*0,8147*	***0,034***

Table II*: Comparison between protocol 1 and protocol 3 according to the intensity of pain at the 48th hour (VAS)*

Variables		*Protocol P1*	*Protocol P3*	*OR*	*Min CI*	*Max CI*	*P-value*
Visual Pain	***Mild***	*13*	*24*	***3,6923***	*1,1367*	*9,9335*	***0,016***
at H48	*Moderate*	*11*	*8*	*0,6465*	*0,2231*	*1,8731*	*0,5916*
	Severe	*11*	*3*	***0,2045***	*0,0514*	*0,8147*	***0,034***

More specifically, when comparing the paracetamol-diclofenac and paracetamol-tramadol groups, we did not find any significant difference whatever the intensity of the pain; for the paracetamol-diclofenac and paracetamol- tramadol-diclofenac group, the difference was significant for mild pain (p=0.016) and for severe pain (p=0.034); moreover, between the paracetamol-tramadol and paracetamol-tramadol-diclofenac group, the difference was significant for mild pain (p=0.0301) and severe pain (p=0.055).

Table I*: Comparison between protocol 1 and protocol 2 according to the intensity of pain at the 48th hour (VAS)*

Variables		*Protocol P1*	*Protocol P2*	*OR*	*Min CI*	*Max CI*	*P-value*
Visual	*Mild*	*13*	*14*	*1,1282*	*0,4307*	*2,9555*	*1*
Pain at	*Moderate*	*11*	*12*	*1,1383*	*0,4195*	*3,0889*	*1*
H48	*Severe*	*11*	*9*	*0,7552*	*0,2666*	*2,1391*	*0,792*

The incidence of side effects was 14.28%, nausea being the main complaint followed by vomiting and epigastric pain. Patients in the paracetamol-tramadol group accounted for the largest proportion of patients with nausea, a percentage of 66.67% after 48 hours of treatment. With regards to the vomiting, 80% of the patients belonged to the paracetamol-tramadol group and none of the patients in the paracetamol-diclofenac group presented vomiting. The incidence of nausea and vomiting correlated with treatment, giving values of p=0.012 and p=0.034 respectively (table IV). In the two groups no patient received morphine

Table IV*: Distribution of Side effects among the groups*

SIDE EFFECTS	*P1*	*P2*	*P3*	*P-value*
Nausea	*11,11*	*66,67*	*22,22*	***0,012***
Emesis	*0*	*80,00*	*20,00*	***0,034***
Epigastric Pain	*60,00*	*20,00*	*20,00*	
Vertigo	*0*	*67*	*33*	
Drowsiness	*0*	*50*	*50*	
Dry Mucosa	*0*	*100*	*0*	
Headache	*0*	*67*	*33*	
Diaphoresis	*33*	*33*	*33*	

Discussion

This prospective study on postoperative pain was confined to the early postoperative period. Postoperative pain is considered to be a form of acute pain due to surgical trauma, with an inflammatory reaction and the initiation of an associated afferent neuronal barrier **[3]**. We used the Visual Analogue Scale (VAS) because it is the most efficient psychometric tool to quantify the intensity of a painful sensation **[2]**. Our sample size was 105 patients, which differs from that of Atangana et al who recruited 174 patients operated upon in 10 months, which could be explained by the fact that our study took place over a shorter period of time (3 months). We found in our population 60% men against 40% women, this result seems to be close to that of a study carried out in Ethiopia on the evaluation of postoperative pain, where

the male sex represented 64.3% of the population (4). In the general population, the type of anesthesia most commonly used was general anesthesia (72%) and we found a low anesthetic risk in more than half of our patients, 88.57%; these results are in agreement with a previous study conducted by Atangana et al in Yaoundé **[2]**. We did not establish any link between the type of anesthesia and DPO as more than half of the patients were under general anesthesia. At the 6th hour, we counted 69.52% (EVA) of patients with severe pain, i.e. more than half of the population; these rates are close to those of two previous studies in Nigeria where 79.6% and 68% of patients respectively experienced moderate to severe pain in the immediate post-operative period **[5]**, but are different from the 46% rate of severe pain for Soyanwo in Congo **[6]**. This high rate could be explained by the fact that in the postoperative period, the time delay to administer the drugs varied as a function of the availability of the drugs. In this study, there was no significant difference according to age (p= 0.661) in the groups, which eliminates the possibility of confusion or influence of this factor in the results.

Comparing the three protocols, we found no significant difference at the 6th hour (p=0.175) and at the 12th hour (p=0.07) according to the VAS, this result being in agreement with a study by Lepri et al in 2006 which found no statistically significant difference in the pain score during the first 18 hours of the postoperative period after subjecting patients to different treatments **[7]**. Group 3 consisting of paracetamol-tramadol-diclofenac provided effective pain relief with a high percentage of cases compared to the other protocols at each evaluation; this would be due to the combination of an opioid with a non-steroidal anti-inflammatory drug which is in line with the study by Adetunji et al in 2013 which showed that the combination of an opioid with an NSAID provided better pain relief **[8]** ; this finding is also consistent with the study by Kolawole and Fawole which suggested that the analgesic properties of tramadol would be enhanced when used in combination with other drugs in a setting of multimodal analgesia **[5]**. On Day 2 we found a statistically significant difference between the effects of the different protocols on pain (p=0.042). In fact, with protocol 3 patients were more than 3 times more likely to experience mild pain (OR=3.5; 95% CI=1.47-8.21; p=0.007), this result is similar to that of Chandawale in India which found a significant reduction (p=0.001) on day 3 of treatment when comparing tramadol-diclofenac with tramadol-paracetamol **[9]**. Whereas, there was no significant difference between paracetamol-diclofenac and paracetamol-tramadol protocols on day 2 of treatment, which could be explained by the fact that diclofenac could be as effective as tramadol in the management of postoperative pain, which would be an advantage considering the risk of dependency associated with tramadol, but no study to our knowledge shows this equivalence. The most common side effects were nausea followed by vomiting and epigastric pain, consistent with a study done in India **[9]**. We found a significant relationship between nausea and the medication administered (p=0.012) and between vomiting and the medication administered (p=0.034). This would show the link between adverse effects and the protocols, excluding other factors such as anesthesia. In addition, nausea and vomiting are among the main adverse events of tramadol and it was used in two protocols in our study increasing the risk of these events occurring.

Conclusion

The addition of a non-steroidal anti-inflammatory drug in postoperative analgesia provides better pain relief while reducing the side effects of tramadol, and allows a good saving of morphine.

Table III*: Comparison between protocol 2 and protocol 3 according to the intensity of pain at the 48th hour (VAS)*

Variables		*Protocol P2*	*Protocol P3*	*OR*	*Min CI*	*Max CI*	*P-value*
Visual Pain	***Mild***	*14*	*24*	***3,2727***	*1,2244*	*8,7478*	***0,0301***
at H48	*Moderate*	*12*	*8*	*0,5679*	*0,1981*	*1,6284*	*0,4278*
	Severe	*9*	*3*	***0,2708***	*0,0664*	*1,1042*	***0,055***

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal.

Financial support and sponsorship

Nil.

Conflicts of interest: *There are no conflicts of interest.*

References

1. **Adeniji AO, Atanda OOA**. Randomized comparison of effectiveness of unimodal opioid analgesia with multimodal analgesia in post-cesarean section pain management. J Pain Res. 2013; 6: 419-24.
2. **Atangana R, Bahebeck J, M NN, Eyenga VC, Hentchoya R, Manyacka P, et al.** Prise en charge de la douleur post-opératoire immédiate en salle de soins post interventionnels. Clin Mother Child Heal. 2006; 3 (1): 17-20.
3. **Chaturvedi S, Chaturvedi A**. postoperative pain management. Indian J Crit care Med. 2007; 11 (4): 204-11.
4. **Woldehaimanot TE, Eshetie TC, Kerie MW**. Postoperative Pain Management among Surgically Treated Patients in an Ethiopian Hospital. pubmed. 2014; 9 (7): 1-9.
5. **I.K.Kolawole, A.A.Fawole**. Postoperative pain management following caesarian section in university of llorin teaching hospital. african J online. 2003; 22 (4): 305-9.
6. **O.A.Soyanwo**. Postoperative pain control prescription pattern and patients experience. West african J Med. 1999;18: 207-10.
7. **Lepri A, Sia S, Catinelli S, Casali R, Novelli G**. Patient-controlled analgesia with tramadol versus tramadol plus ketorolac. Ed Minerva Medica. 2006;72 (1-2): 59-67.
8. **Adeniji AO, Atanda OOA**. Randomized comparison of effectiveness of unimodal opioid analgesia with multimodal analgesia in post-cesarean section pain management. J Pain Res. 2013; 6: 419-24.
9. **Chandawale AS, Sundar S, Kaliaperumal, Latchoumibady, Biswas S, Gabhane M, et al**. Efficacy and safety profile of combination of tramadol-diclofenac versus tramadol-paracetamol in patients with acute musculoskeletal conditions, postoperative pain, and acute flare of osteoarthritis and rheumatoid arthritis: a Phase III , 5-day open-label. J Pain Res. 2014;7:455-63.