

Impact of parecoxib on hospital discharge: retrospective analysis of Brazilian health insurance

Impacto de parecoxibe na desospitalização: análise retrospectiva da saúde suplementar no Brasil

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ABSTRACT

BACKGROUND AND OBJECTIVES: Adequate postoperative pain and renal colic control is critical for patients' recovery and to decrease hospitalization costs and the use of resources. So, this study aimed at evaluating hospitalization time of patients treated with parecoxib sodium versus other non-steroid anti-inflammatory drugs to manage postoperative pain of appendectomy or fractures and renal colic.

METHODS: This is a retrospective data analysis of Brazilian private hospitals medical bills, including patients treated with non-steroid anti-inflammatory drugs to decrease post-appendectomy pain (n=1618), post orthopedic fracture pain (n=2858 and renal colic (n=6555), between January and June 2014. Mean hospitalization time was evaluated according to each group of drugs. Mean difference among groups was calculated by the Kruskal-Wallis method.

RESULTS: Mean hospitalization time for patients submitted to appendectomy was 1.95 days with parecoxib versus 2.20 with other non-steroid anti-inflammatory drugs (p= 0.006). For patients submitted to orthopedic fracture surgery, mean time was 1.75 days with parecoxib versus 1.93 days with other anti-inflammatory drugs (p=0.008). Parecoxib has also significantly decreased hospitalization time for renal colic as compared to other drugs (25.2h versus 32.9h; p<0.001).

CONCLUSION: Parecoxib sodium has provided shorter hospitalization time with possible decrease in use of resources and costs and should be considered a choice for such painful conditions.

Keywords: Cyclooxygenase-2 inhibitors, Hospitalization, Parecoxib, Postoperative period, Renal colic.

RESUMO

JUSTIFICATIVA E OBJETIVOS: O controle adequado da dor pós-operatória e cólica renal é fundamental para a recuperação do paciente e redução de custos relacionados à hospitalização e utilização de recursos. Assim, o objetivo deste estudo foi avaliar o tempo de hospitalização entre pacientes tratados com parecoxibe sódico *versus* outros fármacos anti-inflamatórios não esteroides, no manuseio da dor pós-operatória associada à apendicectomia ou fraturas e cólica renal.

MÉTODOS: Uma análise retrospectiva de dados de contas médicas de hospitais privados no Brasil foi realizada, incluindo pacientes tratados com anti-inflamatório não esteroide para redução da dor pós-apendicectomia (n=1.618), dor pós-fratura ortopédica (n=2.858) e cólica renal (n=6.555), entre janeiro e junho de 2014. O período médio de internação foi avaliado de acordo com cada grupo de fármacos. A diferença média entre os grupos foi avaliada utilizando o método de Kruskal-Wallis.

RESULTADOS: O tempo médio de permanência hospitalar para pacientes submetidos à apendicectomia foi de 1,95 dias com parecoxibe *versus* 2,20 com outros anti-inflamatórios não esteroides (p = 0,006). Para pacientes submetidos a cirurgias de fraturas ortopédicas, o tempo médio foi de 1,75 dias com parecoxibe *versus* 1,93 dias para outros anti-inflamatórios (p=0,008). Parecoxibe também apresentou redução significativa no tempo de internação hospitalar para cólica renal em comparação com outros fármacos (25,2h *versus* 32,9h; p<0,001).

CONCLUSÃO: Parecoxibe sódico demonstrou menor tempo de permanência hospitalar com possível redução na utilização de recursos e custos, devendo ser considerado como uma escolha para estas condições dolorosas.

Descritores: Cólica renal, Dor, Inibidores de ciclo-oxigenase 2, Hospitalização, Parecoxibe, Período pós-operatório.

INTRODUCTION

Postoperative pain (POP) is the unpleasant consequence of tissue injury and inflammatory responses, incurred as result of diseases, traumas and/or surgeries. When tissue is injured, cells release inflammatory substances, among them prostaglandins, which cause hypersensitivity and pain^{1,2}.

After surgical procedures, including appendectomy and orthopedic surgeries, pain is an expected outcome. Approximately 80% of patients have acute postoperative (PO) pain

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which, if not adequately controlled, affects both the use of medical resources and patients' ability to return to normal activities after hospital discharge^{3,4}. Pain management in this period is critical, because it allows controlling pain-induced clinical changes, leading to less use of resources and shorter hospitalization time^{5,6}.

Acute pain is also a risk factor for chronic pain³. After surgery, the risk for developing chronic pain varies from 10 to 50% depending on the surgery. So, an effective therapy to manage acute postoperative pain may not only improve pain in the short term but also bring long term results for patients⁴.

Thirty-eight percent of patients with significant pain during the first 24 PO hours of laparoscopic appendectomy or fractures often have acute pain⁷.

Renal colic is a frequent urologic urgency presenting with severe pain. Immediate strategy for its relief is the administration of parenteral analgesic which has the advantage of early analgesia and easy titration as compared to muscular, oral or rectal routes. Adequate renal colic management prevents the need for short-term recurrent analgesia, thus decreasing hospitalization time^{8,9}.

Anti-inflammatory and opioids are the most prescribed and indicated drugs to treat PO pain and renal colic¹⁰. However, opioids have potential risk for severe adverse events (AE) and should be used with caution¹¹. According to literature data, more common gastrointestinal AE related to opioids are nausea, vomiting and constipation, while central nervous system effects include excessive sleepiness, dizziness and adverse effects on cognitive function, psychomotor coordination, balance and alertness. So, it is estimated that more than half the hospitalized patients need other adjuvant treatments to handle these events after opioid administration, in addition to longer hospitalization time and higher hospitalization-related costs⁴.

In light of this scenario, non-steroid anti-inflammatory drugs (NSAIDs) are to be highlighted as important tools to treat PO pain, due to their analgesic efficacy. NSAIDs inhibit, selectively or not, both cyclooxygenase enzyme forms (COX-1 AND COX-2). Non-selective NSAIDs inhibit both COX-1 and COX-2. Those associated to COX-1 may have significant adverse effects, such as gastrointestinal tract bleeding, renal function changes and higher risk for PO bleeding. COX-2 selective inhibitors have more favorable safety profile since they spare COX-1 enzyme and do not have clinically significant effect on platelet aggregation or gastrointestinal function^{5,6}. In addition, evidences have shown decreased PO opioid consumption in patients using selective COX-2 inhibitor NSAIDs, with consequent shorter hospitalization time and lower costs related to pain management and hospital stay^{12,13}.

For surgical patients intolerant to oral drugs or for those where they are contraindicated, there is the need for effective intravenous (IV) analgesia without AE associated

to non-selective NSAIDs or opioids. However, currently available opioids for IV administration, such as ketorolac, are associated to events such as erosions, ulcers and gastrointestinal bleeding, platelet aggregation changes and acute renal failure due to COX-1 inhibition¹⁴.

Parecoxib sodium is a drug with anti-inflammatory and analgesic properties, indicated for PO and acute renal colic prevention and management. It is a valdecoxib pro-drug and the first COX-2 selective inhibitor NSAIDs available for IV administration^{15,16}. After single dose (40mg) it relieves pain twice as faster as compared to placebo¹⁷. Parenteral administration allows its use in case of postoperative nausea and vomiting¹⁸, it is an option for acute pain management and does not have the AE profile associated to non-selective COX inhibitors¹⁹. Parecoxib sodium has also economic advantages as compared to non-selective NSAIDs, such as ketoprofen, ketorolac and tenoxicam, because it is associated to decreased AE and opioid, antacids and antiemetic consumption²⁰, in addition to decreased use of manpower and inputs generated when administered more than once a day²¹.

This study aimed at evaluating hospitalization time (less than or equal to five days) between groups of patients treated with parecoxib sodium as compared to other non-selective IV NSAIDs (ketoprofen, ketorolac and tenoxicam) to manage POP associated to appendectomy or orthopedic surgeries and acute renal colic.

METHODS

This was a retrospective analysis of medical bills of beneficiaries of health plans by means of a database (Orizon) of health insurance companies information processes. By means of this database, information on 110 health insurance companies were accessed, representing more than 18 million beneficiaries throughout Brazil.

Medical bills data of patients treated with anti-inflammatory drugs to decrease POP (n=1618), orthopedic fractures POP (n=2858) and renal colic (n=6555) were included from January to June 2014, describing hospital stay equal to or less than 5 days. For renal colic, hospital stay data were stratified in less than 24h, more than 24h and general (in hours).

Eligibility criteria included patients in single-therapy with tenoxicam, ketoprofen or ketorolac for managing renal colic or for postoperative pain relief in patients submitted to appendectomy and fracture-related procedures. Renal colic data were located by means of the international code of diseases (ICD-10): N20, N21, N22, N23. For appendectomies and fractures, search was carried out by means of the Unified Supplementary Health Terminology (USHT) table codes. For appendectomy, codes 31.003.079 and 31.003.583 were considered and for fractures, procedures of the group related to musculoskeletal system and joints, sub-group of upper and lower limbs, spine and arthroscopy were considered (Table 1).

Table 1. Code of the Unified Supplementary Health Terminology of fracture procedures considered for the analysis

30.715.130	30.729.157	52.090.540
30.715.148	30.729.165	52.090.558
30.715.156	30.729.173	52.120.104
30.715.164	30.733.081	52.120.120
30.718.040	30.734.061	52.120.350
30.718.058	30.736.064	52.130.150
30.718.074	30.737.060	52.130.169
30.719.089	48.020.168	52.130.223
30.719.097	48.020.176	52.130.231
30.719.100	48.020.184	52.130.240
30.720.109	48.020.192	52.130.258
30.720.117	48.020.206	52.130.371
30.721.130	48.020.214	52.130.525
30.721.148	48.020.273	52.140.059
30.721.156	48.020.281	52.140.067
30.721.172	52.010.260	52.140.130
30.721.180	52.010.279	52.140.253
30.721.199	52.010.457	52.140.270
30.722.357	52.010.511	52.150.070
30.722.365	52.050.033	52.150.089
30.722.381	52.050.041	52.150.127
30.722.403	52.050.262	52.150.151
30.722.411	52.050.289	52.160.092
30.722.420	52.050.297	52.160.149
30.722.438	52.060.136	52.160.220
30.722.446	52.060.144	
30.722.527	52.060.160	
30.722.535	52.060.179	
30.725.119	52.060.209	
30.725.127	52.070.077	
30.725.135	52.070.093	
30.726.093	52.070.140	
30.726.107	52.070.166	
30.726.115	52.080.099	
30.726.123	52.080.102	
30.726.158	52.080.129	
30.727.111	52.080.170	
30.727.120	52.090.221	
30.727.138	52.090.272	
30.727.146	52.090.280	
30.728.118	52.090.299	
30.728.126	52.090.302	
30.729.149	52.090.310	

Treatment with parecoxib sodium was compared to three other therapeutic options (ketoprofen, ketorolac and tenoxicam) also used to manage renal colic and postoperative pain associated to appendectomy or fractures.

Statistical analysis

An exploratory analysis was carried out to evaluate quality of data and data where patients' identification was not defined were excluded. Hospitalization time (quantitative variable) was described by means of mean, median, maximum and minimum. And exploratory analysis was carried out by means of Shapiro-Wilk normality test to define whether the sample had normal distribution. In case of non-normal distribution, non-parametric Kruskal-Wallis test was used to determine equality among three or more groups, and post-hoc Nemenyi-Damico-Wolfe-Dunn test was used to test the difference among groups after Kruskal-Wallis. Significance level was 5%. Analyses were carried out with Statistical R, version 3.1.1 software.

RESULTS

The analysis of medical bills of health plan beneficiaries from January to June 2014 has shown that mean hospitalization time for managing post-appendectomy pain with parecoxib sodium was 1.95 days, as compared to 2.20 days with other NSAIDS (Table 2). Kruskal-Wallis test has shown significant difference between the parecoxib group and the group with other treatments (p=0.006), rejecting the hypothesis of equality between groups.

Table 2. Hospitalization time of patients with post-appendectomy pain treated with parecoxib as compared to other non-steroid anti-inflammatory drugs* (in days)

	Parecoxib	Others
Mena (SD)	1.95 (1.03)	2.20 (1.13)
Median	2	2
(Min-Max)	(1 - 5)	(0 - 5)
Kruskal-Wallis test	(p=0.006)	

*Other NSAIDS were ketoprofen, ketorolac and tenoxicam. NSAIDS = non-steroid anti-inflammatory drugs; SD = standard deviation; Min = minimum; Max = maximum.

The same analysis was carried out for the management of POP of orthopedic fractures, and mean hospitalization time with parecoxib sodium was 1.75 days as compared to 1.93 days with other NSAIDS (Table 3). Kruskal-Wallis test has shown significant difference between the group treated with parecoxib and the group with other treatments (p<0.008).

Table 3. Hospitalization time of patients with postoperative pain of fractures treated with parecoxib as compared to other non-steroid anti-inflammatory drugs* (in days)

	Parecoxib	Others
Mena (SD)	1.75 (1.06)	1.93 (1.18)
Median	1	2
(Min-Max)	(1 - 5)	(1 - 5)
Kruskal-Wallis test	(p<0.008)	

*Other NSAIDS were ketoprofen, ketorolac and tenoxicam. NSAIDS = non-steroid anti-inflammatory drugs; SD = standard deviation; Min = minimum; Max = maximum.

Table 4. Hospitalization time of patients with renal colic treated with parecoxib as compared to other non-steroid anti-inflammatory drugs* (in hours)

	Less than 24h		More than 24h		General	
	Parecoxib	Others	Parecoxib	Others	Parecoxib	Others
Mena (DP)	12.7 (6.2)	14.9 (6.4)	41.6 (19.3)	45,5 (20,5)	25,2 (19,7)	32,9 (22,2)
Median	11	16.1	35.4	40,1	21,7	27,0
(Min-Max)	(0 - 24)	(0 - 24)	(24 - 116)	(24- 120)	(0 - 116)	(0 - 120)
Kruskal-Wallis test	(p<0.001)		(p<0.001)		(p<0.001)	

*Other NSAIDs were ketoprofen, ketorolac and tenoxicam. NSAIDs = non-steroid anti-inflammatory drugs; SD = standard deviation; Min = minimum; Max = maximum.

For managing acute renal colic, data analysis has shown that for hospitalization time below 24h there has been significant difference between the group treated with parecoxib as compared to the group of other treatments (12,7h vs. 14,7h, respectively; $p<0.001$; Table 4). There has been also significant difference for hospitalization time above 24h between parecoxib and other NSAIDs (41.6h vs. 45.5h, respectively, $p<0.001$; Table 4). Mean general hospitalization time was 25.2h for parecoxib as compared to 32.9h for other drugs ($p<0.001$; Table 4).

DISCUSSION

Data analysis has shown that parecoxib was significantly more efficient in decreasing hospitalization time of painful patients submitted to appendectomy, to fracture-related procedures and with renal colic, as compared to other drugs.

A randomized study carried out in the USA in 2004 has shown that IV parecoxib sodium in the preoperative period, followed by oral valdecoxib, in the PO of patients submitted to elective laparoscopy was also related to shorter hospitalization time, lower pain intensity and significant AE decrease, such as vomiting in the first 24h as compared to placebo¹². Similarly, compared to the use of opioids, a study carried out in the United Kingdom in 2007 has shown that parecoxib could decrease 1.36 days in hospitalization time of patients with postoperative pain¹³.

These findings may directly reflect on costs associated with pain management of patients submitted to surgical procedures or with acute renal colic. An economic analysis of data of Brazilian private hospitals published in 2014 has shown that treatment with parecoxib sodium has significantly decreased hospitalization costs, with a mean economic benefit of 297 reais per patient with POP and 1100 reais per patient with renal colic, proving that parecoxib may benefit not only patients' recovery but may also decrease hospitalization costs²¹.

In addition, parecoxib for pain control has also shown significant savings in adjuvant drugs consumption. Fujii and Mould-Quevedo²⁰ have carried out a study in five private Brazilian hospitals to evaluate costs related to the use of antacids, antiemetics and opioid and non-opioid analgesics for the PO of orthopedic surgical patients. Medical data were selected

based on the use of parecoxib, ketoprofen, ketorolac and tenoxicam. Only parecoxib has shown significant decrease in the use of adjuvant drugs, with estimated savings of 37.2 dollars per patient as compared to other NSAIDs^{22,23}.

A limitation of this study is its generalization. There are no reliable national records of surgical procedures performed or a list of renal colic cases, with consequent scarcity of data of the supplementary health system and other sponsors. So, this study has used just data of health insurance companies linked to the Orizon company. In addition to this limitation, other variables which could have influenced hospitalization time were not taken into consideration and sample size was not calculated according to the objective of the analysis; however, analyzed data were enough to have statistical power.

CONCLUSION

In our study, according to data of Brazilian Supplementary Health beneficiaries, it was possible to observe that parecoxib sodium to manage POP associated to appendectomy or surgical treatment of orthopedic fractures and acute renal colic could decrease hospitalization time as compared to non-selective NSAIDs (ketoprofen, ketorolac and tenoxicam).

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