Morphine Patient Controlled Analgesia for Postoperative Analgesia in Patients Who Have Transplanted Cadaver Donor Kidneys

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Introduction. Patients who have chronic renal disease present challenges to anesthesiologists because of the sequelae of the underlying disease. Postoperative pain is usually mild to moderate after renal transplantation and is a concern because of underlying co-morbidities and variable responses of the graft. Effective postoperative pain management contributes to a a successful outcome after renal transplantation.

Methods. A retrospective study, based on the collected data from clinical process and registration of the acute pain unit.

Results. During 2007 and 2008, 124 patients were transplanted with cadaver donor kidneys. The final sample included 55 patients, namely 67% males and 33% females, whose ages range between 15 and 75 years (average, 47.23 years). Their American Society of Anesthesiologists physical status classification was 4 in 71% and 3 in 29%.

Analgesia during surgery used a fentanyl, paracetamol and morphine protocol (n = 47) or fentanyl, paracetamol, morphine, and local anesthetic infiltration (n = 8). The postoperative pain was quantified using a numerical rating scale (0–4) with mean value of 1.07 on day 1, a mean value of 1 on day 2, and a mean value of 0.67 on day 3. Postoperative analgesia with morphine patient-controlled analgesia was used for every patient, combined with paracetamol in 89% of cases. The average number of bolus demands was 60 with 26.4 effective boluses, the mean total administered dose was 26.6 mg. The major side effects were constipation (18%), pruritus (14%), nausea (13%), and vomiting (1.8%).

The following relations were significance: age and score of pain, pruritus and total dose of morphine, preoperative analgesia, and pain score on day 2.

Conclusions. Our results suggest that analgesia with morphine patient-controlled analgesia was an effective method to achieve control of postoperative pain in this population with few side effects.

AFTER improvements in perioperative care and postoperative immunosuppression, renal transplantation has become the best therapeutic option for end-stage renal failure. It not only improves quality of life but also prolongs life.[1] The 5-year survival rate is approximately 70%, whereas it is only 30% for a similar group of patients undergoing dialysis.[2]

Cases for patients who have end-stage renal failure are complex and present challenges to anesthesiologists because of the sequelae and co-morbidities. Because age is no longer a barrier for transplantation, one must consider associated morbidities.[3] The perioperative care of these patients must be performed by multidisciplinary staff in an appropriate experienced ward. Failure to provide appropriate care for these patients has implications for graft survival and may increase morbidity.[4]

After renal transplantation postoperative pain is usually mild to moderate. Postoperative pain is a concern because of underlying co-morbidities and variable responses of the graft. Effective postoperative pain management contributes to successful outcomes. Improperly controlled pain may lead to agitation, tachycardia, hypertension, and an increased risk of respiratory complications. There are two options for analgesia: systemic or epidural. Systemic analgesia may cause concern

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Table 1. Sample's CRF Etiologies Distribution

Etiology	Number of Patients
Unknown	20
Segmental and local glomerulosclerosis	7
IgA nephropathy	4
Diabetic nephropathy	4
Chronic glomerulonephritis	4
Obstructive uropathy	2
Hypertension	2
LES	1
Genitourinary malformation	1
ADPRD	1
hereditary nephropathy	1
Mesangioproliferative glomerulonephritis	1
HSP	1
Acute pieelonephritis	1
Lithiasic chronic pielonephritis	1
Reflux	1
Nephrotic syndrome	1
Fibrillar glomerulonephritis	1
Glomerulosclerosis and tubulointersticial nephritis	1

LES, systemic eritematous lupus; ADPRD, autossomal dominant poliquistic renal disease; HSP, Henoch-Schonlein purpura.

with impaired graft function; whereas epidural analgesia is a risky technique in patients who were on dialysis previously, because of the platelet dysfunction and residual heparin associated with the dialysis itself.[4–6]

In our hospital, all patients undergo general anesthesia and systemic analgesia for postoperative pain control. They receive patient-controlled analgesia (PCA) with morphine and paracetamol (1 g three times daily). Intravenous opioids provide the mainstay of analgesia in Europe, with the majority of medical centers favoring the use of morphine by PCA. A minority of medical centers use fentanyl despite its preferable pharmacokinetic profile with fast onset and offset times. Fentanyl has a lesser tendency to cause accumulation of active metabolites that cause side effects.[7] There is no strong evidence to support the use of one opioid over another in patients with renal impairment. In addition,

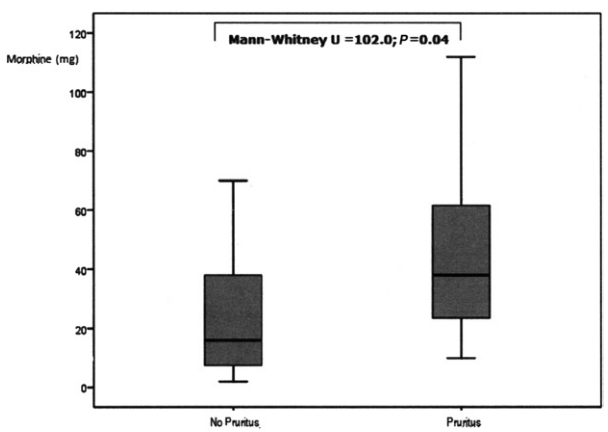

Fig 1. Pruritus and total dose of morphine (mg).

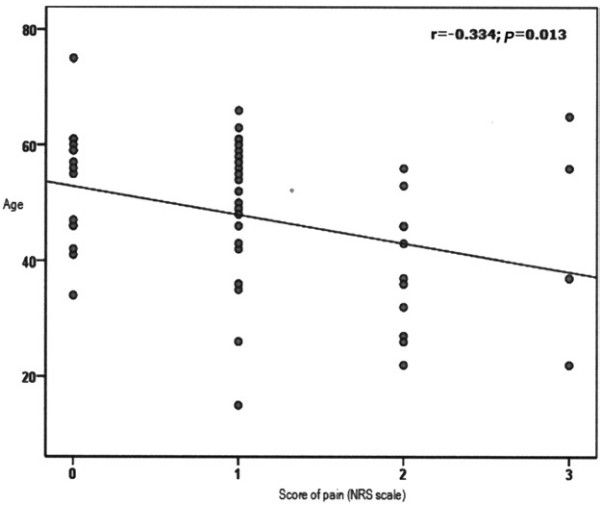

Fig 2. Age and outcome of pain.

despite the possibility of significant accumulation of potent metabolites, which may act in a negative-feedback loop to limit PCA, most medical centers use morphine with no apparent problems in this regard. A functioning graft contributes to effective analgesia.[8]

This study was to analyzes our analgesia protocol, reporting side effects and comparing them with the several patient characteristics.

METHODS

We performed a retrospective study, collecting data from clinical registers of the acute pain unit. We included data related to patient characteristics perioperatively and postoperatively after cadaver donor procedures in our hospital during 2007 and 2008. To characterize patients we used age, gender, American Society of Anesthesiologists physical status classification, co-morbidities, renal failure etiology, and previous renal transplantation. In the perioperative period we registered perioperatory analgesia. In the postoperative period we collected data on the level of pain, the use of PCA, the side effects, and graft function.

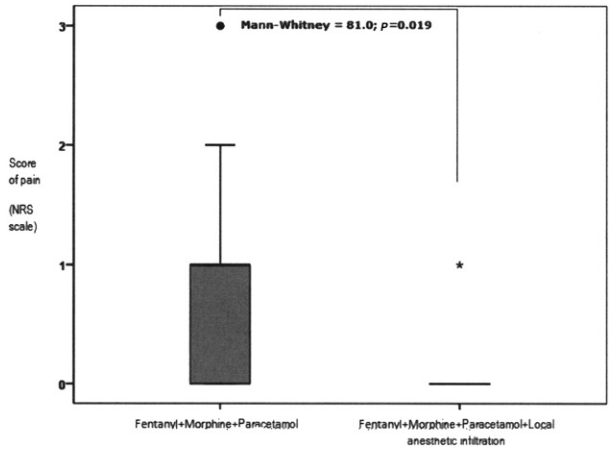

Fig 3. Perioperative analgesia and score of pain in day 2.

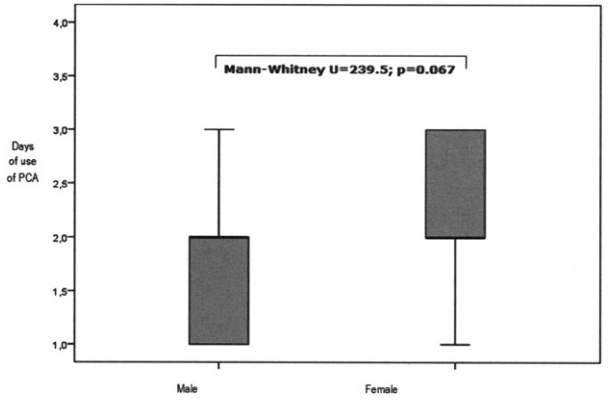

Fig 4. Gender and days of use of PCA.

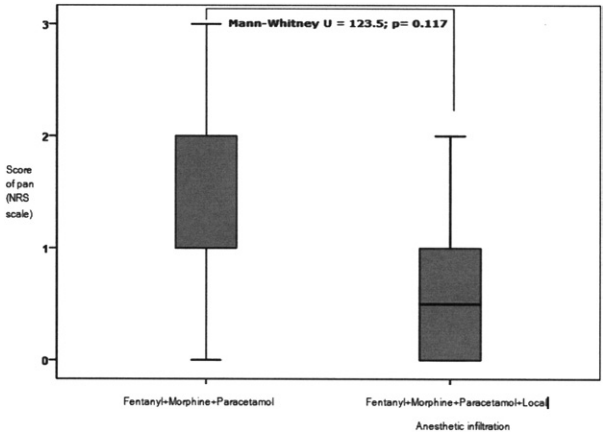

Fig 5. Perioperative analgesia and score of pain in day 1.

The Statistical Package for Social Sciences (SPSS, version 15.0 for Windows, Inc. Chicago, IL, USA) was used to evaluate Kolmogorov-Smirnov test statistics for sample normality distribution. For comparisons between groups, we used the Student *t*-test whenever the parameters presented a gaussian distribution, and the Mann-Whitney test for a non-gaussian distribution. Spearman's rank correlation coefficient was used to evaluate relationships between data sets. Significance was accepted at $P < 0.05$.

RESULTS

Sample Data

During 2007 and 2008, 124 patients were transplanted with cadaver kidneys in our hospital. Due to the lack of data our final sample included 55 patients including 67% males and 33% females with an age range of 15 to 75 years (average, 47.23). Their ASA physical status was 4 in 71% and 3 in 29%.

Some patients did not initiate dialysis, therefore, the duration of dialysis varied between 0 and 384 months (average, 52.25). Six patients had undergone a previous renal transplantation; only 35 maintained a urinary output.

Co-morbidities in the sample were: hypertension (n = 35), cardiac dysfunction (n = 11), metabolic disorders (n = 7), anemia (n = 4), respiratory pathology (n = 4), obesity (n = 2), use of antiaggregants (n = 7), and hypocoagulation (n = 2). The etiology of renal failure was unspecified/unknown in the majority of cases (n = 20). Segmental and focal glomerulosclerosis was the second most frequent cause. Table 1 shows the distribution of etiologies.

Perioperative Period

Perioperative analgesia was performed with a fentanyl + paracetamol + morphine protocol (n = 47) or a fentanyl + paracetamol + morphine + local anesthetic infiltration (n = 8).

Postoperative Period

Postoperative pain was quantified using a numerical rating scale (0–4); zero indicated a non–pain state and 4 indicated the worst imaginable pain: the mean pair rating was 1.07 on day 1, 1.0 on day 2, and 0.67 on the day 3.

Pain score evaluation was performed during the use of PCA with morphine a PCA with morphine was used for maximum of 3 days an (average, 1.91 days). Postoperative analgesia with morphine PCA was used on every patient and was associated with paracetamol in 89% of cases. The average number of demands was 60 with 26.4 effective boluses. The mean total dose administered was 26.6 mg. The major side effects reported were constipation (18%), pruritus (14%), nausea (13%), and vomiting (1.8%).

Relationships Between Sets of Data

Significance was observed for the following relations: pruritus and total dose of morphine, age and score of pain; perioperative analgesia, and score of pain on day 2 (Figs 1–3). A positive tendency was described for the following: gender and days of PCA use, and perioperative analgesia and pain score on day 1 (Figs 4 and 5). Evaluation of relationships between other sets of data (all the other patents characteristics and their relationship with use of PCA, score of pain, and side effects) showed no statistical significance.

Table 2 through 7 show the relationships between data sets.

Table 2. Test Statistics Comparison Based on Patient Gender

Test	Duration of Hemodialysis	Duration of Peritoneal Dialysis	Time Without Urinary Output	Number of Morphine Demands	Number of Morphine Boluses	Total Dose of Morphine	Number of Days of PCA Use
Mann-Whitney U	324.500	270.000	270.000	331.000	329.500	311.000	239.500
Wilcoxon W	495.500	973.000	441.000	502.000	1032.500	1014.000	942.500
Z	−.153	−2.266	−1.324	−.036	−.063	−.395	−1.835
Asymp sig. (2-tailed)	.879	.023	.186	.971	.950	.693	.067

DISCUSSION

Our results suggested that analgesia using PCA with morphine was effective to control postoperative pain in this population with few side effects. Female patients used the PCA for longer periods than male patients. Higher pain scores were reported among younger patients. It is also clear that the infiltration of the incision site with local anesthetic provided lower pain scores.

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Table 3. Test Statistics Comparison Based on Nausea

Test	Duration of Hemodialysis	Duration of Peritoneal Dialysis	Time Without Urinary Output	Number of Morphine Demands	Number of Morphine Bolus	Total Dose of Morphine	Number of Days of PCA Use	Age
Mann-Whitney U	20.000	24.500	11.500	8.000	20.000	20.000	24.500	17.500
Wilcoxon W	21.000	25.500	1496.500	1493.000	1505.000	1505.000	1509.500	1502.500
Z	−.441	−.316	−1.144	−1.197	−.441	−.441	−.172	−.599
Asymp. sig. (2-tailed)	.659	.752	.253	.231	.659	.659	.863	.549
Exact sig. [2×(1-tailed Sig.)]*	.764	.909	.436	.327	.764	.764	.909	.655

*Not corrected for ties.

Table 4. Test Statistics Comparison Based on Constipation

Test	Duration of Hemodialysis	Duration of Peritoneal Dialysis	Time Without Urinary Output	Number of Morphine Demands	Number of Morphine Bolus	Total Dose of Morphine	Number of Days of PCA Use	Age
Mann-Whitney U	98.000	200.000	200.000	178.500	195.500	199.500	203.500	111.000
Wilcoxon W	1133.000	255.000	1235.000	1213.500	1230.500	1234.500	258.500	1146.000
Z	−2.774	−1.094	−.639	−1.015	−.644	−.557	−.513	−2.491
Asymp. sig. (2-tailed)	.006	.274	.523	.310	.520	.578	.608	.013

Table 5. Test Statistic Comparison Based on Pruritis

Test	Duration of Hemodialysis	Duration of Peritoneal Dialysis	Time Without Urinary Output	Number of Morphine Demands	Number of Morphine Bolus	Total Dose of Morphine	Number of Days of PCA Use	Age
Mann-Whitney U	143.000	182.000	183.000	100.500	100.000	102.000	92.500	139.000
Wilcoxon W	179.000	1310.000	1311.000	1228.500	1228.000	1230.000	1220.500	175.000
Z	−1.075	−.287	−.140	−2.089	−2.102	−2.054	−2.494	−1.171
Asymp. sig. (2-tailed)	.282	.774	.889	.037	.036	.040	.013	.242
Exact sig. [2×(1-tailed Sig.)]*	.294	.898	.916	.035	.035	.040	.021	.252

*Not corrected for ties.

Table 6. Correlations for All Data

	Age	Duration of Hemodialysis	Time Without Urinary Output	Duration of Peritoneal Dialysis	Total Dose of Morphine	Number of Days of PCA Use	Number of Morphine Bolus	Number of Morphine Demands
Age								
Pearson Correlation	1	.112	−.019	−.435	−.154	−.200	−.170	.084
Sig. (2-tailed)		.417	.889	.001	.263	.143	.214	.541
N	55	55	55	55	55	55	55	55
Duration of hemodialysis								
Pearson Correlation	−.112	1	.134	−.147	.077	.055	.064	−.012
Sig. (2-tailed)	.417		.329	.285	.578	.691	.640	.929
N	55	55	55	55	55	55	55	55
Time Without Urinary Output								
Pearson Correlation	−.019	.134	1	−.149	−.082	−.134	−.074	−.046
Sig. (2-tailed)	.889	.329		.278	.550	.329	.594	.739
N	55	55	55	55	55	55	55	55
Duration of peritoneal dialysis								
Pearson Correlation	−.435	−.147	−.149	1	−.102	.067	−.098	−.104
Sig. (2-tailed)	.001	.285	.278		.461	.629	.477	.448
N	55	55	55	55	55	55	55	55
Total dose of morphine								
Pearson Correlation	−.154	.077	−.082	−.102	1	.545	.99	.727
Sig (2-tailed)	.263	.578	.550	.461		.000	.000	.000
N	55	55	55	55	55	55	55	55
Number of days of PCA use								
Pearson Correlation	−.200	.055	−.134	.067	.545	1	.538	.431
Sig. (2-tailed)	.143	.691	.329	.629	.000		.000	.001
N	55	55	55	55	55	55	55	55
Number of morphine bolus								
Pearson Correlation	−.170	.064	−.074	−.098	.996	.538	1	.727
Sig. (2-tailed)	.214	.640	.594	.477	.000	.000		.000
N	55	55	55	55	55	55	55	55
Number of morphine demands								
Pearson Correlation	.084	−.012	−046	−.104	.727	.431	.727	1
Sig. (2-tailed)	.541	.929	.739	.448	.000	.001	.000	
N	55	55	55	55	55	55	55	55

Table 7. Score of Pain in Day 1 Using Analysis of Variance

	Sum of Squares	df	Mean Square	F	Sig.
Age					
Between groups	1431.627	3	477.209	3.189	.031
Within groups	7631.901	51	149.645		
Total	9063.527	54			
Sex					
Between groups	1.208	3	.403	1.885	.144
Within groups	10.901	51	.214		
Total	12.109	54			
Duration of hemodialysis					
Between groups	58370.208	3	19456.736	3.763	.016
Within groups	263694.229	51	5170.475		
Total	322064.436	54			
Duration of peritoneal dialysis					
Between groups	5.539	3	1.846	.141	.935
Within groups	667.842	51	13.095		
Total	673.382	54			
Time without urinary output					
Between groups	1.298	3	.433	.836	.480
Within groups	26.411	51	.518		
Total	27.709	54			
Number of morphine demands					
Between groups	18233.968	3	6077.989	.958	.420
Within groups	323576.760	51	6344.642		
Total	341810.727	54			
Number of morphine bolus					
Between groups	3024.827	3	1008.276	1.946	.134
Within groups	26427.901	51	518.194		
Total	29452.727	54			
Total dose of morphine					
Between groups	3024.757	3	1008.252	1.993	.127
Within groups	25803.502	51	505.951		
Total	28828.258	54			
Number of days of PCA use					
Between groups	8.157	3	2.719	7.541	.000
Within groups	18.389	51	.361		
Total	26.545	54			