RESEARCH ARTICLE

The Effect of Remifentanil– Propofol Compared with Fentanyl– Propofol on Urine Output in Patients Undergoing Lumbar Posterior Spinal Fusion

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Background: Remifentanil is a narcotic drug used in anaesthesia for establishment of hemodynamic stability. The purpose of this study was to compare the effects of remifentanil and fentanyl on urine excretion.

Methods: In a randomized clinical trial, 60 patients, who were candidates for elective surgery for lumbar posterior spinal fusion, were divided randomly into two groups of 30 as remifentanil – propofol (R) and fentanyl- propofol (F). Maintenance of anaesthesia drugs in group R included 100 mcg/kg/min propofol and 0.5- 0.25 mcg/kg/min remifentanil. It included 100 mcg/kg/min propofol and 5- 0.5 mcg/kg/min fentanyl in group F. Vital signs and urine output were recorded every half an hour.

Results: The mean age of patients was 49.5± 12.7 years. Urine output in group R showed significantly greater reduction than in group F (p< 0.001). Increase of urine output was seen in both groups over the time.

Conclusion: Urine output in patients undergoing lumbar posterior spinal fusion who received remifentanil was less compared to the fentanyl group.

Keywords: remifentanil; propofol; fentanyl; urine output; lumbar posterior spinal fusion

Anaesthesia and surgery affect normal kidney function through changes in glomerular filtration rate (GFR) [1]. Generally anaesthesia interventions using inhaled anaesthetics or intravenous drugs or local block decrease blood pressure and urine output [2-4]. Response to stress of major surgery near to operation time especially those who practice neurosurgery procedures may lead to a greater reduction of urine output through increasing levels of anti-diuretic [5-6]. Overall opioids cause antidiuretic effects and reduced secretion of electrolytes with stimulation of μ receptors. However, they cause results in diuresis and little changes in electrolyte secretion with simulation of kappa receptor [7]. E-2078, dynorphins sustainable analog, causes diuresis in rats through the stimulation of kappa receptor [8].

Remifentanil and fentanyl are among synthetic opioid analgesic drugs [9]. Remifentanil is an analogue of fentanyl. 4- piperidyl anilide has unique structure because of the ester bond. Ester structure makes this drug prone to hydrolysis by non-specific esterases in the blood and tissues [10]. Remifentanil is the first extremely short trace anaesthesia drug which is used for general anaesthesia. This drug suppresses hemodynamic, autonomic and somatic responses to painful stimulation reliably. It also provides the most predictable and the most rapid awakening after aesthesia, thus it is used for hemodynamic stability in patients under anaesthesia [11-14]. In some studies, effect of remifentanil has been reported as increased urine output. However, some others indirectly showed reduction in kidney function after surgery [4,15-18]. We investigated effects of remifentanil compared with fentanyl on urine output in patients undergoing elective surgery of lumbar posterior spinal fusion.

Methods

This study is a double blind randomized clinical trial. The study population included patients undergoing elective surgery for lumbar posterior spinal fusion, under general anesthesia, using intravenous method. In order to calculate sample size, according to pilot study (10 cases), mean urine output in patients receiving fentanyl was about 20 ml with 4 ml standard deviation (SD) at every half an hour. Our assumption was that remifentanil reduces urine output about 5 ml at every half an hour. Thus, sample size was calculated as 27 patients for showing this difference based on α = 0.05

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and 90 percent power. Considering probability of 10 percent of drop out, the study was conducted in two groups of 30 patients.

Samples were selected using convenient sampling among patients referring to Rasoul Akran Hospital and Firoozgar Hospital in Iran University of Medical Sciences in Tehran, during 2012 – 2013 who consented for participation and had inclusion criteria. Inclusion criteria included ASA I-II, age range 18 – 75 years, surgery duration ≥ 3 hours. Exclusion criteria included kidney disorders, blood urea and creatinine levels higher than normal (BUN > 20 and Cr > 1.5), dehydrated patient before the surgery, uncontrolled hypertension and diabetes, severe cardiovascular diseases, addiction to drugs, continuous blood pressure drop during surgery (systolic pressure less than 80), uncontrollable intraoperative bleeding (50% or more of a patient's blood volume) [19], use of positive end-expiratory pressure (PEEP) in anesthesia machine, disregarding fluid reception level during anesthesia, use of drugs and substances affecting renal function before and during surgery (such as aminoglycosides, magnesium sulfate, radiographic contrast agents, some heart drugs and blood pressure reductive drugs, etc.). Patients were randomly assigned in two groups of 30 based on computer randomized list.

Before induction of anesthesia, 1-2 mg midazolam and 3μg / kg fentanyl was given to both groups. Then, 1.5 – 2 mg / kg propofol as titer and 0.5 mg / kg atracurium was injected for induction. Before changing position, arterial line of patients was obtained and catheter was placed in both groups and urine output in the bag was recorded. Maintenance drugs included 100 μg / kg / min propofol infusion and 0.5 – 0.25 μg / kg / min remifentanil (for R group), fentanyl 0.5 – 5 μg / kg / min (for F group) and 10 mg atracurium every 20-30 minutes as bolus. Needed fluid level was calculated during the surgery. Following recording characteristics of patients, vital signs of patients, voided urine volume and fluid intake was calculated and recorded every 30 minutes. If voided urine volume reduced to less than 0.5 ml / kg / h, after 2.5 hours, firstly the urinary route to the bag was checked, and if there was no problem in the route, 2-3 mg lasix was injected intravenously and all cases responded to it. Changes in mean arterial pressure (MAP) were registered.

Collected data were entered into SPSS software. Frequency and frequency percentage were used for qualitative variables and mean and SD was calculated for quantitative variables. Qualitative data were analyzed using chi-square tests. Quantitative data were analyzed using t-test. For comparison of urine output level in recorded times in both groups, repeated measure ANOVA was used. In statistical analysis, p-value< 0.05 is considered as significant. Helsinki ethical principles were observed in this study. The study was approved by the ethics committee of Iran University of Medical Sciences and it was registered at IRCT Center with IRCT201111298083N2 code.

Results

Overall 67 patients were examined. One patient due to renal disorder, one patient due to addiction, two patients due to uncontrolled hypertension and one patient due to continuous drop in blood pressure during surgery were excluded and two patients were also excluded due to lack of consent to participate in the study. Finally, data were analyzed for 60 patients in two groups of 30 (Figure 1).

29 (48.3%) of patients were female. The mean age of patients was 49.5 ± 12.7 years between 19 to 74 years old. (Table 1) gives demographic information of patients in both groups. No significant statistical difference was observed between two groups which may denote suitable randomization of patients in both groups.

Received fluid volume (IV) in groups R and F was 3050 ± 420 ml and 3043 ± 351 ml respectively. No statistically significant difference was found (P = 0.9). Number of operated level of spinal column in group R was respectively 2 level in 9 (30%) patients, 3 level in 13 (43.4%), 4 level in 7 (23.3%), 5 level in 1 (3.3%) and in group F was 2 level in 5 (16.7%) patients, 3 level in 11 (36.6%), 4 level in 9 (30%), 5 level in 5 (16.7%). No statistically significant difference was found (P = 0.2). Overall, mean urine output in R group was lower than F group and this difference was statistically significant (p< 0.001) (Figure 2). Mean urine output of patients in terms of measured times in both groups is given in (Table 2). The difference was not significant in both groups after 3 hours. Change in MAP in groups R and F was 82 ± 5.8 and 83 ± 6.7 respectively. No statistically significant difference was found (P = 0.3).

Table 1- Demographic data in both groups

Variable	Remifentanil (n = 30)	Fentanyl (n = 30)	P-value
Age (year)	49.1 ± 14.3	50 ± 11	0.8
Gender (female/male)	17/13	12/18	0.2
Weight (kg)	79.2 ± 14	81.3 ± 11.4	0.5
ASA (I / II)	19/11	21/9	0.6

Table 2- The urine output means in remifentanil and fentanyl groups

Time (hr)	Urine output means(ml)		P value
	Remifentanil (n = 30)	Fentanyl (n = 30)	
Before intervention	19.8 ± 3.5	20.3 ± 2.8	0.5
First half hour	14.6 ± 16.4	26.3 ± 17.4	0.009*
Second half hour	19.5 ± 14.7	63 ± 50	<0.001*
Third half hour	27.8 ± 24.2	72.7 ± 69.6	0.002*
Fourth half hour	34 ± 33.5	92.7 ± 75.9	<0.001*
Fifth half hour	35.3 ± 38.4	109 ± 81	<0.001*
Sixth half hour	49 ± 47.4	140.2 ± 87.7	<0.001*
After 3 hours	778.3 ± 584.4	542.9 ± 43.7	0.09

Figure 1- Flow diagram of patients in the trial. (n= number of patient)

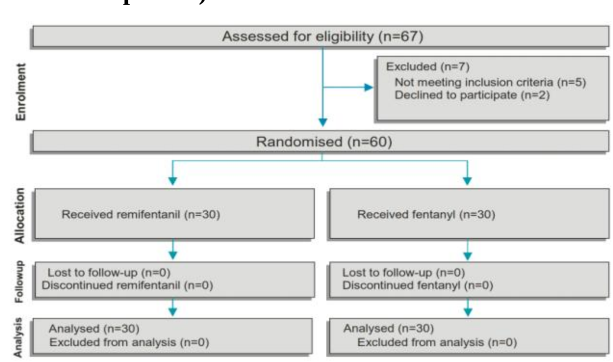
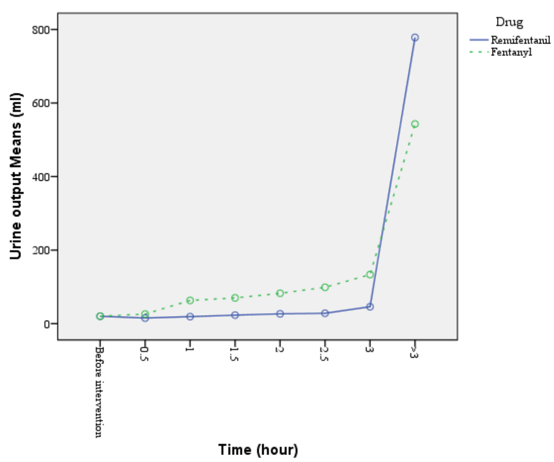


Figure 2- Comparison of mean urine output in terms of measured time in both groups



Discussion

Factors causing kidney damage near to surgery have been examined in many studies [20-24]. The effects of opioids on the lower urinary tract, including impairment of micturition, urinary retention appears after intrathecal drug therapy. All opioids change bladder sensation, but detrusor muscle contraction decreases just after fentanyl and buprenorphine prescription. After taking fentanyl, sufentanil, alfentanil and probably remifentanil in humans, plasma levels of antidiuretic hormone, renin and aldosterone, does not increase, and this suggests protecting renal function or little changes in this function [25].

Our study showed that urinary output in patients receiving remifentanil reduced more than the group who received fentanyl. Because of difficulties in measuring urine output prior to anesthesia (rejection of patients for catheterization), formula of least urine output (0.5 ml / kg / h) for a period of half an hour was used for better comparison. Urine output was increasing in both groups, while this increase was higher in fentanyl group than remifentanil and it was significantly different between measurement times and both groups in different times. It can be justified as follows: role of stress and reduced blood pressure at induction time can cause reduction of urine output. In fentanyl group, urine is more increased due to earlier release of stress, but this drug causes effect on kidneys, whether with effect on μ receptor or effect on anti-diuretic hormone, or they have lower urine output compared to fentanyl group due to inability to control stress hormones.

Malinovsky compared aerodynamic effects of intravenous morphine, buprenorphine, fentanyl and nalbuphine. This study that showed all opioids, can change bladder sensations, but fentanyl and buprenorphine just decreased detrusor muscle cramps [26]. Terashi showed that anesthesia using remifentanil in patients with chronic kidney diseases (CKD) under orthopedic surgery may have protective effect on kidney [27].

Ko et al. studied effect of remifentanil on kidney in patients under right hepatectomy surgery and found increase in urea and creatinine in patients with reduced GFR after surgery in the group receiving remifentanil [16]. Kawai studied effect of remifentanil on urine output in group with and without remifentanil in general anesthesia and found that mean urine output was higher in patients receiving remifentanil [4]. Yago studied remifentanil effect on urine output in patients under laparoscopy and found urine output in patient's receiving remifentanil was higher than common anesthesia [15]. Authors in two former studies believe that remifentanil caused reduction in stress hormones during anesthesia which increased urine output in patients. In both studies, mean total output was measured in both groups and their control group did not receive fentanyl as maintenance. In our study, increasing of urine output was observed in the remifentanil group, but it was lower compared to the fentanyl group. Perhaps fentanyl inhibits stress of hormones more. Severe continuous blood pressure drop was not observed in this study in both groups.

Conclusion

Urine output in patients undergoing lumbar posterior spinal fusion who received remifentanil was greater reduction compared to fentanyl group. It is suggested that in case there are facilities for more precise determination of possible effect of remifentanil on stress hormones during surgery and anesthesia, these hormones are measured. Also it is recommended that urine output of patients before initiation of anesthesia and entrance to surgery room is measured in similar future studies so that a normal status of urine output is obtained.

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