

*Full Length Research Paper*

# Effect of renal colic analgesia on oxidative stress parameters

Muhammet Gokhan Turtay<sup>1\*</sup>, Hakan Oguzturk<sup>1</sup>, Cemil Colak<sup>2</sup>, Alaadin Polat<sup>3</sup> and Cemal Tasdemir<sup>4</sup>

<sup>1</sup>Department of Emergency Medicine, Faculty of Medicine, Inonu University, Malatya, Turkey.

<sup>2</sup>Department of Statistics, Faculty of Medicine, Inonu University, Malatya, Turkey.

<sup>3</sup>Department of Physiology, Faculty of Medicine, Inonu University, Malatya, Turkey.

<sup>4</sup>Department of Urology, Faculty of Medicine, Inonu University, Malatya, Turkey.

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Our aim in this study is to investigate serum oxidative stress parameters before and after fentanyl analgesia in renal colic which is a severe pain condition and to reveal if there is correlation between fentanyl analgesia and serum oxidative stress parameters in renal colic pain. Thirty two male patients, aged 18 – 65, (mean age 40.7±14.9) who applied to our hospital with the complaint of flank pain and were diagnosed with renal colic were accepted to study. Blood samples were taken from the patients who were diagnosed with renal colic as a result of physical examination and tests (urine analysis, plain radiography, ultrasonography, computed tomography) Pain management of the patients was carried out. Fentanyl (50 - 150 µg), an opioid analgesic, was used in all patients. When patients stated that the pain was definitely gone through, the blood samples were taken again. Blood samples were taken from each participant twice, before and after the analgesic. Malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) levels were measured from the blood taken. Statistical analysis of the levels which were obtained from before and after the fentanyl treatment was carried out. There were increases in CAT (P < 0.001), SOD (P =0.002), MDA (P < 0.001), and GPx (P = 0.28) activities in response after analgesic administration in the patients. In our study, the treatment of renal colic pain with fentanyl, an opioid analgesic, led to significant increases in the levels of SOD and CAT, which are antioxidant enzymes.

**Key words:** Renal colic, oxidative stress, analgesic.

## INTRODUCTION

It is known that oxidative stress and lipid peroxidation caused by reactive oxygen species (ROS) take part in the pathogenesis of most diseases. Harmful effects of ROS are tried to be balanced by antioxidant mechanisms. Malondialdehyde (MDA), a product of lipid peroxidation, has a correlation with the extensity of lipid peroxidation and is used to evaluate the levels of oxidative stress (Cochrane, 1991; Esterbauer, 1993). Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) are known as antioxidant enzymes

trying to balance oxidative stress. These enzymes have been used in the evaluation of oxidative stress (Vaculin et al., 2010; Oguzturk et al., 2010).

Renal colic, characterized by the sudden onset of severe pain in the flank and radiating inferior and groin, has an annual incidence of around 16 per 10, 000 people and a lifetime incidence 2 - 5% (Holdgate and Pollock, 2004). For most of the patients, the management of symptoms in an ambulatory setting is enough to promote spontaneous stone passage or relief of symptoms until elective definitive therapy (Preminger et al., 2007). For relieving the severe pain of renal colic, fentanyl, an opioid analgesic, may also be preferred in addition to pain killers such as paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids (Bektas et al., 2009; Eken et

\*Corresponding author. E-mail: [mgturtay@hotmail.com](mailto:mgturtay@hotmail.com). Tel: +90-422-341 0660 Ext: 3025. Fax: +90-422-341 0729.

**Table 1.** Descriptive statistics of the variables (n = 32, Mean ± SD).

Variable	Time relative to medication		P*
	Before	After	
CAT (K/mL)	0.26±0.07	0.33±0.09	<0.001
SOD (U/mL)	45.06±8.42	48.19±7.80	0.002
MDA (nmol/mL)	20.37±5.34	26.82±6.83	<0.001
GPx (U/mL)	0.14±0.04	0.15±0.04	0.28

\*: Paired t test.

al., 2009). The correlation between oxidative stress and formation of stone diseases in urinary system is well known (Huang et al., 2002; Tugcu et al., 2007). In another study on rats, it was shown that green tea had preventive effects on calcium oxalate urolithiasis because of its antioxidant effects (Itoh et al., 2005).

According to our knowledge in literature, there is no sufficient data mentioning the correlation of fentanyl with oxidative stress parameters in the renal colic pain. Our aim in this study is to investigate serum oxidative stress parameters before and after fentanyl analgesia in renal colic which is a severe pain condition and to reveal whether there is correlation between fentanyl analgesia and serum oxidative stress parameters in renal colic pain.

## MATERIALS AND METHODS

### Patients

The study was conducted between September 2009 and April 2010. Thirty two male patients, aged 18 – 65, (mean age 40.7±14.9) who applied to our hospital with the complaint of flank pain and were diagnosed with renal colic were accepted to study. First of all medical history of the patients was taken and recorded on computer assisted system. Patients having conditions that might affect oxidative stress parameters such as chronic medicine usage, having taken any medication for the complaint of pain, smokers and alcohol addicts, diabetes mellitus, cardiovascular disease, chronic obstructive pulmonary disease and thyroid disorder were excluded from the research. Blood samples were taken from the patients who were diagnosed with renal colic as a result of physical examination and tests (urine analysis, plain radiography, ultrasonography, computed tomography) and also pain management of the patients was carried out. Fentanyl (50 - 150 µg) was used in all patients. When patients stated that the pain was definitely recovered, blood samples were taken again. Blood samples were taken from each participant twice, before and after the analgesic. MDA, SOD, CAT, and GPx levels were measured in the blood. Statistical analysis of the levels which were obtained from before and after the fentanyl treatment was carried out.

Our research protocol which mentioned-above was approved by The Inonu University Local Research Ethics Committee Malatya, Turkey and numbered with 2009/98.

### Blood analysis

SOD activity was determined according to the method of Sun, Oberley and Li (Sun et al., 1988). The principle of SOD activity assay is based on the inhibition of Nitroblue Tetrazolium Chloride

(NBT) reduction. SOD activity is inversely proportional to the absorbency value of formazone at 560 nm. Results were expressed as U/mL. CAT activity was measured at spectrophotometer by using Aebi's method (Aebi, 1974). CAT activities were expressed as K/mL. GPx activity was measured according to the method of Paglia and Valentine (Paglia and Valentine, 1967). GPx enzyme activities were expressed as U/mL. MDA was measured according to Uchiyama and Mihara's study (Uchiyama and Mihara, 1978). The method is based on the coupling of MDA with thiobarbituric acid at +95°C. All the measurements (standards and samples) were carried out at the upper n-butanol phase. The results were expressed as nmol/mL.

### Statistical analysis

A sample size of 32 achieves greater than 90% power to detect the difference between the null hypothesis mean and the alternative hypothesis mean with a significance level (alpha) of 0.05 using paired t-test (Hintze, 2008). Normal distribution for all variables was verified by the Shapiro-Wilk test. The values were given as mean ± standard deviation (SD). CAT, GSH, SOD, and GPx levels were compared using paired t-test. Statistical analysis was performed with SPSS 15.0 for Windows (SPSS, Chicago, Illinois, USA) and PASS 2008. P ≤ 0.05 was considered statistically significant.

## RESULTS

There were increases in CAT (P < 0.001), SOD (P = 0.002), MDA (P < 0.001), and GPx (P = 0.28) levels in response after analgesic administration in the patients (Table 1).

The levels of CAT, SOD, and MDA were significantly increased (p < 0.05). However, after fentanyl treatment amelioration of GPx values did not reach to significant degree.

## DISCUSSION

In this study it was shown that the treatment of renal colic pain with an opioid analgesic, fentanyl, increased the antioxidant enzymes levels. One of the pain mechanisms in renal colic is the inflammation at the level of calculus (Davenport et al., 2005). Acute and chronic inflammation may lead to formation of free oxygen radicals (Chapple, 1997; Wang et al., 2004; Dozor, 2010). Intense pain of renal colic in a person also causes emotional stress, and it is known that emotional stress may lead to oxidative

stress (Cernak et al., 2000; Gozen et al., 2005; Szuster-Ciesielska et al., 2008; Bouayed et al., 2009). While NSAIDs act directly on the release of prostaglandin, which is the real cause of the pain, opioids just relieve the pain of the patient and do not act directly on the real cause of the pain (Holdgate and Pollock, 2004). According to our results fentanyl, used in the current study, decreased the pain and emotional stress of the patient with renal colic due to its sedative and analgesic effects and consequently caused an increase in the levels of SOD and CAT that are strongly antioxidant enzymes; whereas MDA level increased due to inflammation that is the main cause of pain.

Excessive radical production and/or decreased antioxidants may lead to a condition called oxidative stress (Oguzturk et al., 2010). Free radical production leads to lipid peroxidation and MDA formation which is end product of lipid peroxidation by especially effecting lipids in the cell membrane (Gozen et al., 2005). MDA is a molecule which is active chemically, and it may have some harmful effects on especially proteins by easily diffusing into surrounding cells and tissues (Yilmaz et al., 2007). Antioxidant defense mechanisms are developed in order to prevent the harmful effects of free oxygen radicals in the body. SOD, CAT and GPx are known as antioxidant enzymes. These antioxidant enzymes protect body against oxidative stress (Ji and Leichtweis, 1997). Oxidative stress implicates various diseases including cancer, diabetes, male infertility, autoimmune diseases, atherosclerosis and cardiovascular disorders (Bouayed et al., 2009).

When patients apply to emergency services with suspicion of renal colic, medical history is taken and their physical examination is carried out after tests are requested for diagnosis and differential diagnosis of renal colic. The tests are urine analysis, plain radiography, ultrasonography, computed tomography, intravenous urography. However, there may be some delays in the analgesic treatment and treatment of the underlying cause of renal pain while the tests are carried out. A significant amount of time may be wasted for diagnosis, analgesic application and the treatment of main cause. In our study, the treatment of renal colic pain with fentanyl led to an increase in the SOD and CAT levels whereas increasing of MDA production continued probably because of ongoing inflammation. When the earlier the underlying cause is treated and the earlier renal colic pain is treated, the fewer patients may expose to the harmful effects of oxidative stress which appears in the pathogenesis of most diseases.

## Conclusion

In the current study, the treatment of renal colic pain with fentanyl, an opioid analgesic, led to significant increases in the levels of SOD and CAT, which are known as

powerful antioxidant enzymes.

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