1ST CONGRESS OF PHARMACY
KONGRESI I PARË I FARMACISË

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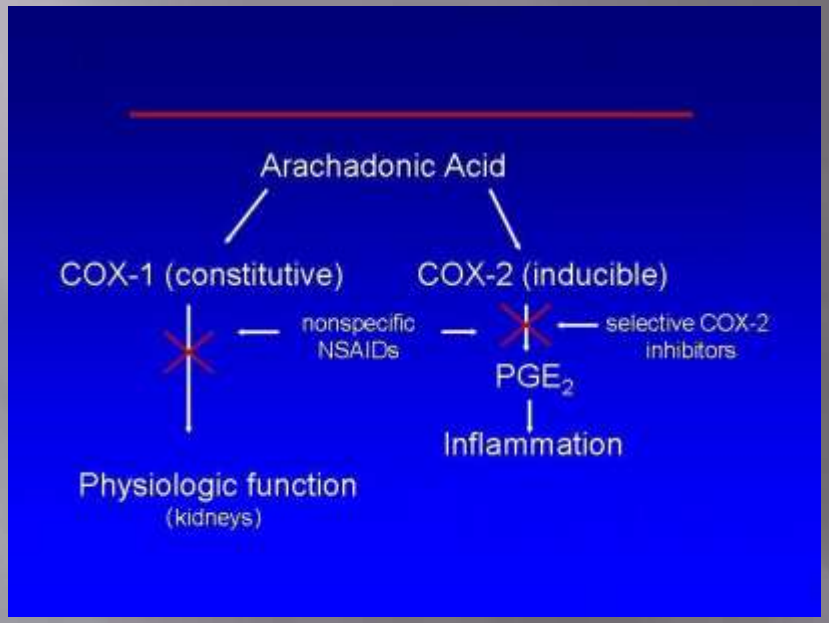
(NSAIDs) are the most commonly used analgesics that are recommended for the treatment of patients with migraine (a common headache disorder) associated with migraine attacks

- Ketoprofen is one of the most prescribed NSAIDs in the world for the treatment of headaches.
- Piroxicam is another NSAID that has been approved in recent years, with mechanisms of action by cyclooxygenase inhibition.

- Theoretically, this approach may lead to various adverse effects on the kidneys

- NSAIDs - COX inhibition - prevents neurogen inflammation in the trigeminovascular system and reduces pain.



- Continued vasoconstrictive activity of leukotrienes, angiotensin II, vasopressin, endothelin and catecholamines results in reduction of - (GFR) - kidney hypoperfusion may result - with - Acute Renal Injury - Acute kidney injury (AKI).
- Epidemiological study – nephrotoxicity (NSAID)-18-27%

Tab. 1. COX isoform selectivity assessed in the ëhole blood assays *in vitro* by cyclooxygenase inhibitors ((Reprinted ëith permission of Elsevier Ltd., [60])

Inhibitor	COX-1/COX-2 IC	
Aspirin	0.01	
S-Indobufen	0.043	Selective COX-1 inhibitors
Valeryl Salicilate	< 0.24	
Ibuprofen	0.50	
Naproxen	0.56	
S-Ketoprofen	0.61	
Flurbiprofen	1.00	
Sodium Salicylate	1.03	Non-selective COX inhibitors 20% nefrotoxicitet
6-MNA	1.49	
Indomethacin	1.90	AKI(Whelton et al., 2000).
Piroxicam	3.12	
Meloxicam	11.16	
Nimesulide	17.69	Relatively selective COX-2 inhibitor
Diclofenac	18.90	
SC-58125	143.30	
NS-398	168.00	Highly selective COX-2 inhibitor reduced AKI
Rofecoxib	410.00	

Paracetamol-hromboxane B2 and prosptaglandin-conjugated lipopolysaccharide, (Burkhard Hinz, 2007)

There is relatively little evidence of nephrotoxicity in pacient treated long period with different types of NSAIDs (Ketoprofen and Piroxicam) based on COX inhibition.

The aim of the study is to follow renal function in patients with cefalea-migraine treated long period with different types of NSAIDs.

- Determination of parameters with nephrological protocols in urine and serum: urea (serum), creatinine (serum / urine) and serum electrolyte status.
- Monitoring the activity of specific bioindicators as sensitive biomarkers for the identification of early nephrotoxicity: β2M and microalbuminuria.

Materials

-We used venous urine and blood from cephalic-migraine -
from Clinical Center-Neurology-Tetovo
-10 patients treated with Ketoprofen with a total dose of up to 100 mg per day, up to 10 years

-10 patients with Piroxicam 20 mg > 5 to 10 years, after of therapy, patients in comparison with the control group of examinees.
-with headaches> 15 days a month
Any history of kidney disease was exclusion criteria to enter the study

with an average age of 42,047 ± 7.41 years, with a range of 35-65 years

-control group of patients with an average age of 35-60 years.

METHODS AND INSTRUMENTS

Biochemical parameters	samples	methods	instruments
urea	serum	enzymatic assay	Dimension Rxl
creatinin	Serum/ urin	colorimetry method (Jaffe)	Dimension Rxl
elektrolite	serum	Jon selektiv elektrod (ISE)	Dimension EXL 200

Specific biomarkers methods and apparatus

Specific biomarcers	Mostra	Metoda	Apparatus
b2 M	urine	nephelometry	N B2M
Microalbuminurija	urine	Photoelectric colorimetry	Combina 13

Results and discussion

Group	(Creatinin (serum) mmol/L)			p-level
	mean ± SD	min-max	median (IQR)	
Control group :	66.21 ± 11.7	46 – 86	65.5(56–80)	
Piroxicam	68.33 ± 10.9	53 – 83		[a]p=0.56 ns
Ketoprofen	62.42 ± 12.8	47 – 83		[a]p=0.302 ns

Group	(Urea (serum) mmol/L)			p-level
	mean ± SD	min-max	median (IQR)	
Control group:	4.58 ± 0.9	2.5 – 6.6	4.45(4.1–5.1)	
Piroxicam	4.52 ± 1.1	3.1 – 6.5		[a]p=0.84 ns
Ketoprofen	5.70 ± 1.5	3.5 – 8		[a]p=0.0005 sig

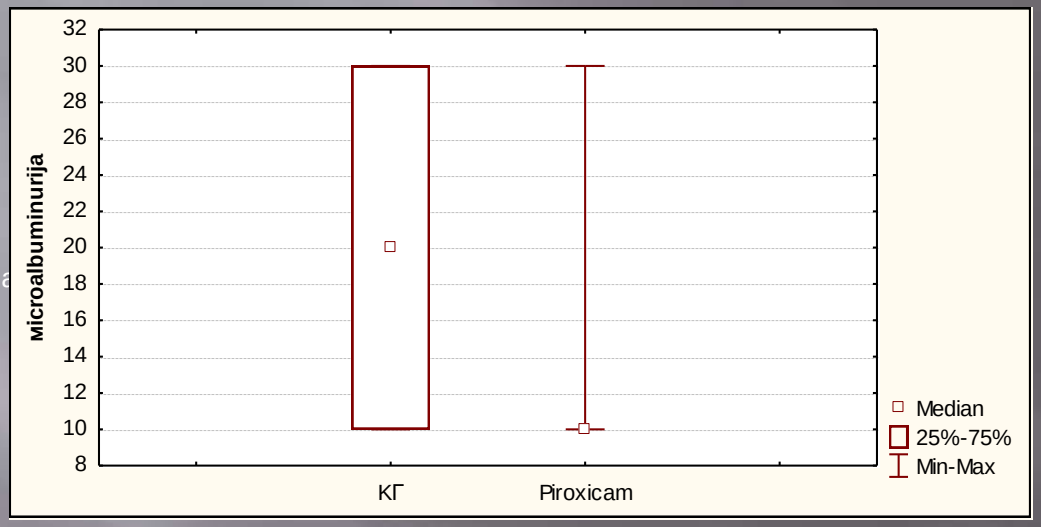
Group :	(Natrium (serum) mmol/L)			p-level
	mean ± SD	min-max	median (IQR)	
Control group :	139.02 ± 1.98	135 – 144	139.5(138–140)	
Piroxicam	139.5 ± 1.8	136 – 142		[a]p=0.44 ns
Ketoprofen	139.17 ± 1.7		139.5(137.5–140.5)	[b]p=0.88 ns

Group	(Natrium (serum) mmol/L)			p-level
	mean ± SD	min-max	median (IQR)	
Control group :	139.02 ± 1.98	135 – 144	139.5(138–140)	
Piroxicam	139.5 ± 1.8	136 – 142		[a]p=0.44 ns
Ketoprofen	139.17 ± 1.7		139.5(137.5–140.5)	[b]p=0.88 ns

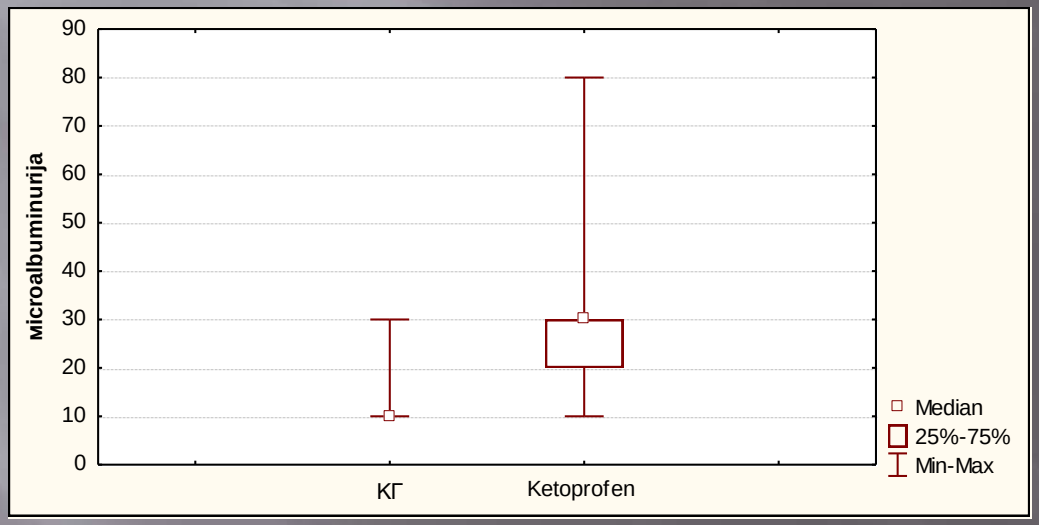
Group :	(Kalium (serum) mmol/L)			p-level
	mean ± SD	min-max	median (IQR)	
Control group :	4.27 ± 0.3	3.5 – 5.1	4.25(4.1–4.5)	
Piroxicam	4.33 ± 0.3	3.8 – 4,8		[a]p=0.57 ns
Ketoprofen	4.52 ± 0.5	3.6 – 5.1		[a]p=0.031 sig

[a](t – test) [b](Mann-Whitney test)

.Monitoring the values of spacial biomarkers



Piroxicam have been shown to be intermediate (between Aspirin and Indomethacin) in their relative capacity for the occurrence of acute renal disorders (Whelton et al., 2000; D.Uzeiri.Havziu, 2014).



Patricio A. et al.,(1988). We report here a case of irreversible renal failure after treatment for 10 days with Ketoprofen
- Although both species inhibit COX1, Piroxicam is the most renoprotective.

- From a clinical biochemical point of view, this fact suggests that non-selective COX inhibitors Ketoprofen significantly affect glomerular changes.
- High sensitivity of microalbuminuria (marker for the identification of early glomerular lesions) has been confirmed.
- We cannot confirm for nephrotoxicity so longer investigations based on histopathological data are needed.

Thank you