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Renal Tubular Damage After Renal Stone Treatment

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Summary. 50 patients were studied with respect to renal tubular damage related to open operative, percutaneous and extracorporeal shock wave treatment of renal stones. Preoperative and postoperative urinary N-acetyl-glucosaminidase (NAG) levels were measured as a marker of renal damage. There was no significant evidence of renal tubular damage in patients who underwent a conventional or percutaneous nephrolithotomy; urinary NAG excretion was significantly increased after ischaemic surgery. After extracorporeal shock wave lithotripsy (ESWL) serum NAG levels increased, probably because a damage of the white blood cells in cutaneous and renal circulation, but a slight increase of urinary NAG excretion could suggest a mild renal tubular damage especially in case of more than 2,000 shocks.

Key words: Renal stones – Renal surgery – Percutaneous nephrolithotomy – Extracorporeal shock wave lithotripsy – Urinary enzymes

Introduction

The primary aims of stone management are a complete stone removal and a correction of urinary tract anomalies with minimal parenchymal damage.

Renal lesions after conventional open surgery are related to anesthesia, surgical trauma or intraoperative ischaemia.

The complete surgical removal of a staghorn stone may requiere multiple parenchymal incisions and intraoperative renal ischaemia.

Several different methods have been suggested to protect renal function against warm ischaemia (surface cooling and hypothermic perfusion, provision of metabolites preoperatively and inhibition of renal enzymatic systems). The preservation of renal integrity during prolonged ischaemia by hypothermia is well documented [7, 10].

The percutaneous nephrolithotomy (PCN) has added great advantages to stone treatment because of the minimal damage to the abdominal wall and to the renal collecting systems. The disadvantage of PCN may be loss of renal function due to the percutaneous track and to stone disintegration procedures.

Finally the experience of several centers demonstrates that about 95% of all renal stones can be treated by extracorporeal shock wav lithotripsy (ESWL) alone or by combination therapy of ESWL and PCN.

Few data [3] are available about long term effects of shock waves on renal parenchyma, nevertheless with the help of different imaging procedures (IVP, sonography, CT, NMR) it was shown that there are alterations related to the number of shock waves applied [4].

These lesions of the renal parenchyma [1, 4, 6] might be due to transitory intrarenal edema and to both intra and perirenal haemorrhage.

We evaluated urinary N-acetyl-glucosaminidase (NAG) excretion after stone treatment.

The activity of glycosidases, such as NAG, increases in the ischaemic renal cortex. In fact these enzymes are localized in cortical tubular cell lysosomes.

The cells of the proximal tubule are the first to become necrotic following ischaemic or vascular lesions; afterwards tubular necrosis causes a great rise in lysosomal enzyme activity.

The increased urinary excretion of NAG is correlated with necrosis of cells from the proximal tubule.

Damage to the brush border of tubular cells is accompained by an increase in different enzymes, such as alanine aminopeptidase (AAP), but when slight renal ischeamia occurs it produces an insignificant increment in urinary enzyme activity.

On the other hand decreased tubular reabsorption of filtered protein due to tubular dysfunction may cause an excessive urinary excretion of low molecular weight enzymes, such as lysozyme. Nevertheless this pattern is not specific because similar ones may be found with renal tubular damage secondary to infection, nephrotoxic drugs or anesthesia.

Table 1. Urinary NAG to creatinine ratio before and anfter nephrolithotomy (N), ischaemic nephrolithotomy (IN), percutaneous nephrolithotomy (PCN), extracorporeal shock wave lithotripsy (ESWL)

Treatment	Patients (n)	Preoperative (U/g)	Postoperative (U/g)
N	7	7.2 ± 7.0	16.7 ± 15.7
IN	8	6.9 ± 5.5	51.7 ± 48.3[a]
PCN	11	0.7 ± 1.1	2.8 ± 3.0
ESWL	24	5.7 ± 6.6	9.8 ± 8.9

[a] $P < 0.05$

Table 2. Serum enzymes before and after ESWL

	Preoperative	Postoperative
GOT (U/l)	15.6 ± 9.2	20.8 ± 12.9
GPT (U/l)	17.8 ± 10.8	25.5 ± 21.3
LDH (U/l)	176.6 ± 50.1	263.2 ± 98.7[c]
CK (U/l)	43.2 ± 18.9	134.3 ± 164.2[a]
NAG (U/l)	22.5 ± 9.2	42.7 ± 33.7[b]

[a] $P < 0.05$
[b] $P < 0.01$
[c] $P < 0.001$

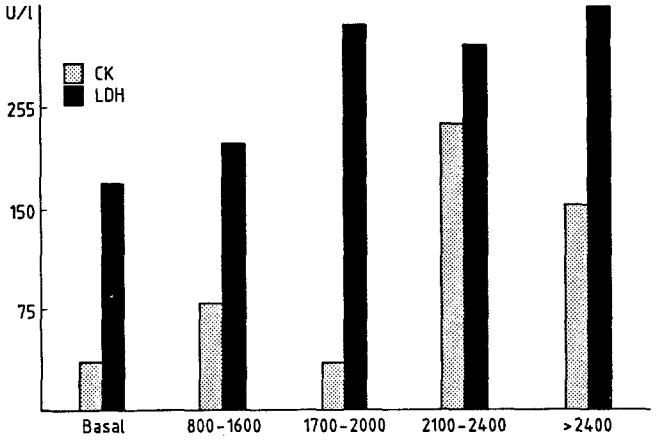

Fig. 1. Shock wave count and values of serum CK and LDH after ESWL

In conclusion the study of urinary NAG excretion would appear to be the most valuable to detect early damage of renal tubular cells.

Materials and Methods

We studied 50 patients with renal stones. The patients were divided into the following groups who underwent different stone treatments:

- group I (7 patients): conventional open surgery (pyelonephrolithotomy);

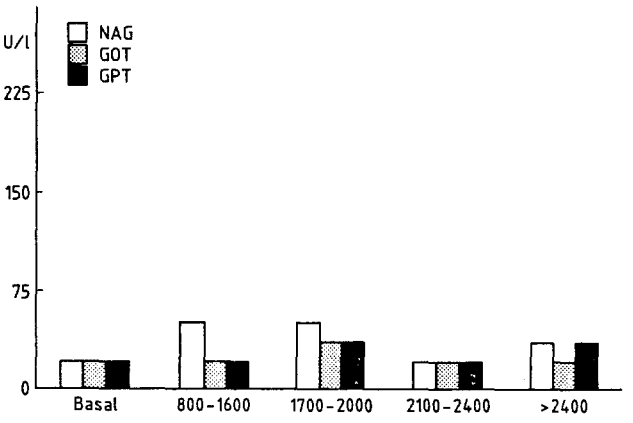

Fig. 2. Shock wave count and values of serum NAG, GOT and GPT after ESWL

- group II (8 patients): ischaemic pyelonephrolithotomy with hypothermia by surface or endovenous perfusion cooling (average time of renal ischaemia was 44', range 33'–60');
- group III (11 patients): percutaneous nephrolithotomy (PCN);
- group IV (24 patients): extracorporeal shock wave lithotripsy (Dornier HM1) (average count of shock wave was 2,000, range 800–2,600, voltage 18–26 kV).

Blood and urinary samples were obtained on the preoperative day and 24 hours after the procedure.

After conventional and percutaneous surgery the urinary samples of the operated kidney were collected from nephrostomy drains.

Serum and urinary creatinine and NAG were determined by colorimetric methods. Urinary NAG to creatinine ratio was calculated.

Serum enzymes (CK, LDH, GOT, GPT) were measured before and after ESWL to test associated damage to liver, red cells or voluntary muscles of abdominal wall. Statistical evaluation was performed using Student's test.

Results

After conventional nephrolithotomy urinary NAG had a mild increase, while after percutaneous nephrolithotomy it remained unchanged.

After ischaemic surgery striking changes in urinary NAG excretion were observed. Although a small number of patients was studied, the difference between the preoperative urinary NAG mean value and the postoperative one was statistically significant ($P < 0.05$). Normal values were recovered within 15 days.

After extracorporeal shock wave lithotripsy urinary NAG excretion had a slight, but not significant increase (Table 1); serum NAG, CPK and LDH levels significantly increased, no significant variations of other serum enzymes were observed (Table 2).

The postoperative values of serum and urinary enzymes were related to the shock wave count (Figs. 1–3).

CK and LDH increased with shock wave count as shown in Fig. 1.

Urinary NAG increased if a shock wave count of more than 2,000 was administered.

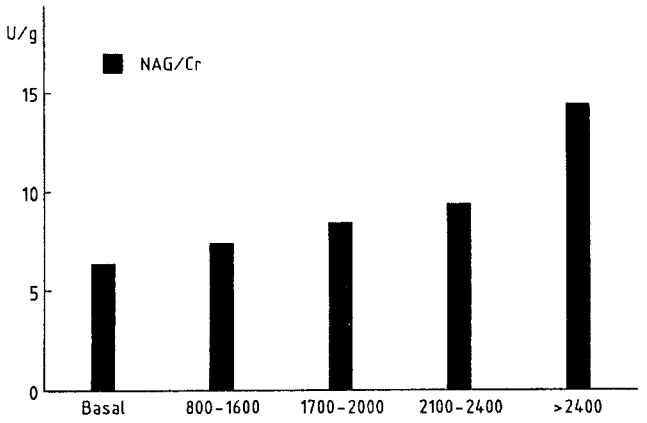

Fig. 3. Shock wave count and values of urinary NAG to creatinine ratio after ESWL

Discussion

Serum creatinine variations cannot detect postoperative alterations of renal function, since the functional loss of the operated kidney is compensated by the controlateral kidney.

A good marker of tubular damage is the urinary excretion of enzymes. Renal tubular cells contain several enzymes with a molecular weight of more than 70,000, which are therefore excluded from significant filtration in the glomeruli.

Renal tissue is the main source of urinary excretion of NAG and other enzymes that under pathological conditions (tubular necrosis) are released in remarkable amounts in the urine.

In an experimental rat model it was shown that urinary NAG excretion is a very reliable marker of renal tubular damage [8].

Conventional open surgery produces a transitory reduction in tubular renal function, but tubular necrosis is diagnosed only after prolonged renal ischaemia. The degree of tubular impairment depends on several factors: surgical trauma, time of ischaemia, anesthesia, drug-induced nephrotoxicity and urinary tract infection.

On the contrary after percutaneous nephrolithotomy there was no evidence of any tubular damage.

Ruiz Marcellan and Ibarz Servio [9] demonstrated a marked increase in serum NAG and LDH after shock wave application suggesting the presence of renal microdamage.

The serum NAG and LDH elevation after ESWL is not diagnostic of renal damage because these enzymes are present in other cells in addition to renal tubular cells.

In fact most of the enzymes in plasma are the result of blood cell metabolism. The enzymes present in the red cells mainly carry out the process of extracting energy from glucose for oxygen transport. In particular, lactate dehydrogenase (LDH) catalyzes the reversible reduction of pyruvate to lactate.

Blood cells, in cutaneous and renal circulation, may lyse when exposed to shock waves resulting in increased levels of serum enzymes.

Chaussy [2] reported that the red blood cells were broken by shock wave exposure in vitro, but no significant hemolysis was observed in animals. On the contrary Kishimoto et al. [5] could demonstrate significant increases in plasma-free hemoglobin, LDH and GOT after ESWL which were considered as the results of hemolysis (5–10 g of blood/treatment).

Myolysis and hemolysis are potential sources of creatinine phosphokinase (CK) and glutamic oxaloacetic transaminase (GOT) elevation in the serum.

The neutrophil granules contain a wide assay of enzymes, most of which catalyse catabolic reactions, but they also include NAG and other glycosidases. An increase of serum NAG could be related to the liberation of enzymes from leucocitary lysosomes, which occurs when white cells are exposed to shock waves in renal circulation. After ESWL a significant increase in serum NAG might have been due to the damage of the white blood cells rather than the renal tubular ones. Moreover under cisplatinum chemotherapy (a heavy metal antitumor agent whose major acute toxicities include renal tubular necrosis but not hemolysis) serum NAG didn't increase whereas urinary NAG significantly increased (unpublished data).

However after ESWL urinary NAG excretion slightly increased possibly due to early tubular damage.

Urinary NAG excretion is a more specific indicator of renal tubular damage because a very small amount of the enzyme is filtered; the renal cortex is the main source of urinary NAG excretion.

Therefore the number of shock waves employed and their intensity has to be planned to minimize any potential damage to renal tubular function especially in case of more than 2,000 shocks, although a wide clinical experience shows the safety of ESWL.

The use of the new generation lithotripters, where lower pressures to the interposed tissues are created, may produce a lower risk of renal damage; however the second generation machines are not yet suitable to treat large stones, which need the highest numbers of shocks and therefore cause the highest pressures.

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