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ULTRASTRUCTURAL CHANGES ON SPERM AFTER EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY IN PATIENTS WITH DISTAL URETERAL STONE

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□ *Theoretically, ESWL can cause several side effects on the male reproductive system. We determined here the long-term effects of ESWL on sperm with transmission electron microscopy (TEM) in patients with distal ureteral stone. Fifteen men with stones in the distal ureter applied to our clinic formed the group of study. The other 15 men with renal or upper ureter stones formed the group of control. The ESWL sessions, including maximum 19 kW energy level and 3000 shock waves, were performed with Siemens Lithostar (electromagnetic; Siemens Medical Systems, Erlangen, Germany) lithotriptor. We examined the semen samples from all patients on the day before and 90 days after ESWL. The semen samples were examined with transmission electron microscopy (TEM) to detect ultrastructural changes on the day before and 90 days after ESWL. All the statistical analyses were realized with SPSS 10.0 (SPSS Inc., Chicago, USA) statistical package program. When the control and study groups were compared for initial and day 90 sperm concentration and motility, a significant decrease was found in the study group. Although there was no important anomaly in the control group, we determined some damage on sperm structure in 5 patients (33.3%) who are in the study group 3 months after ESWL. It can reduce sperm concentration and motility permanently. It can also cause severe ultrastructural defects on sperm after a long term period in patients with lower ureteral stone. Therefore, we suggest other treatment modalities for young men with distal ureteral stones to prevent the development of male infertility.*

Keywords ESWL, infertility, sperm, stone, TEM, ureter

Most patients with distal ureteral stone that do not pass spontaneously can be treated by some treatment modalities such as extracorporeal shock wave

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lithotripsy (ESWL), ureteroscopy (with pneumatic, laser, ultrasound, electrohydraulic lithotripsy or basket extraction) and open or laparoscopic surgery. Selection of the treatment is related to stone size, location, composition, and patient or physician preference. Generally, ESWL is the first choice in patients with ureteral calculi because it is reasonably effective and less invasive. However, ESWL may cause several side effects on the male reproductive system [1, 8, 10]. It has a lot of known destructions in different organs.

The distal part of ureter lies anatomically close to the seminal vesicle. Testes are also near the effect area of ESWL. Theoretically, it is possible that ESWL can affect these organs in the patients with distal ureteral stone. However, there are few studies of possible effects of ESWL on semen quality and testes with contradictory results [1]. Here, we determined the long-term effects of ESWL on sperm with transmission electron microscopy (TEM) in the patients with distal ureteral stone.

MATERIAL AND METHODS

Fifteen men with stones in the distal ureter admitted to our clinic were included in the study group. The mean age for the study group was 24.53 $\pm$ 3.89 years. Fifteen men with renal or upper ureter stones were included in the control group. The mean age for the control group was 23.93 $\pm$ 3.45 years.

Patients with an infertility history and abnormal semen parameters before the session of ESWL were not included in the study. All patients were treated with one ESWL session; maximum 19 kW energy level and 3,000 shock waves. The ESWL sessions were performed using a Siemens Lithostar (electromagnetic; Siemens Medical Systems, Erlangen, Germany) lithotriptor. The semen samples from all patients were examined on the day before and 90 days after ESWL, and the sperm concentration and motility were noted.

The semen samples were examined with a transmission electron microscopy (TEM) to determine sperm morphology on the day before and 90 days after ESWL. Samples were fixed for 24 hours with 2.5% glutheraldehyde then post fixed in OsO4 for 1 hour. After dehydration in alcohol with increasing grade, specimen were treated with propylene and then embedded in Araldite CY212. Semi-thin sections were stained with methylene-blue and examined under the light microscope, and then 60–90 nm thick ultra-thin sections were stained with uranyl acetate and lead citrate. They were examined and photographed in JEOL JEM 1200 EX electron microscope.

Statistical analyses were done using SPSS 10.0 (SPSS Inc., Chicago, IL). Repeated measurements were compared by using Friedman test, and the

differences were compared by Mann-Whitney U test. P values ≤ 0.05 were considered statistically significant.

RESULTS

There was no statistically significant difference between the age of the control and study groups ($t=0.447$, $P=0.658$). In the control group, there was no statistically significant difference between the sperm concentration and motility parameters on the day before and 90 days after the ESWL session ($\chi^2=4.429$; $P=0.109$).

The differences between the measurements were tested by the variant analysis in the study group and we found statistically significant differences for the parameters of sperm concentration and motility between the day before and 90 days after ESWL session ($\chi^2=26.143$; $P \leq 0.001$).

When the control and study groups were compared for initial and day 90 sperm concentration and motility, a significant decrease was found in the study group ($U=44{,}000$; $P=0.004$ and $U=12{,}000$; $P \leq 0.001$, respectively).

The lamina propria of the seminiferous tubules, Sertoli cells and Leydig cells and the ultrastructure of the spermatozoa in the control and study groups were normal on the day before ESWL session.

Although there was not any important anomaly in the control group, we determined some damage on sperm structure in 5 patients (33.3%) who are in the study group 3 months after ESWL. In these cases, the doublet microtubules were disorganized. There were severe edema at structures forming the tail and the mitochondria (Figure 1). Acrosome and the nucleus were in normal feature. There were vacuoles and projecting parts around the nucleus. Two heads were diffused in one of the cases. The structures of the neck were disorganized and the dense fibers were scattered (Figure 2).

DISCUSSION

ESWL has rapidly become a non-invasive method of treating kidney and ureteral stones since its introduction in the 1980s. Although ESWL has minimal complications, its potential male reproductive system effects are unknown. Also, there have been few studies of possible effects of ESWL on semen quality and gonads with contradictory results [1, 8–9, 10].

Although the general acceptance in the literature is that ESWL affects male fertility parameters in patients with lower ureteral stones, this effect seems to be temporary until the recovery period (about 90 days), we reported previously ESWL could affect the sperm parameters permanently in patients with lower ureteral stone [3]. In the present study, we aimed to determine the long-term ultrastructural effects of ESWL on sperm.

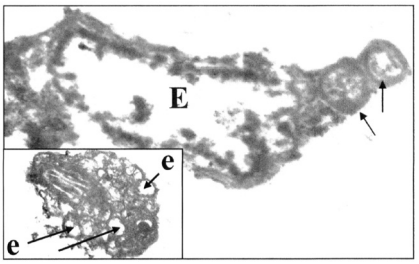

FIGURE 1 Transverse section of tail (original magnification ×30 K). Edema of the structures of the tail and mitochondria, disorganization of the doublet microtubules. E: Edema, e: Edema of the mitochondria. Arrow showing doublet microtubules.

We determined severe damages on sperm structure in 5 patients 3 months after ESWL. This means that ESWL can cause permanent damage on sperm. However, Basar et al. reported no ultrastructural changes on spermatozoa in rabbits after ESWL [2]. Some studies have examined the effects of disruption of the organogenesis of germ cells caused by the teratogenic potential of high-energy shock waves in a number of systems, such as in vitro effects of human spermatozoa [6]. Ohmori et al. showed that spermatozoa and testis were irreversibly damaged with an increasing number of shock waves [8]. We think the permanent damage of sperm occur due to testes, seminal vesicles and other parts of reproductive system close to the area of shock wave effect in males with less ureteral stones.

We do not have detailed clinical data on the effects, and further studies are required. It is already known that male infertility is a multifactorial equation. For this reason, ESWL may contribute to such a result.

Treatment of distal ureteral stones remains controversial [5]. Options include ureteroscopic extraction, ESWL, open or laparoscopic removal. Although ESWL can be tried as a first treatment option because of its

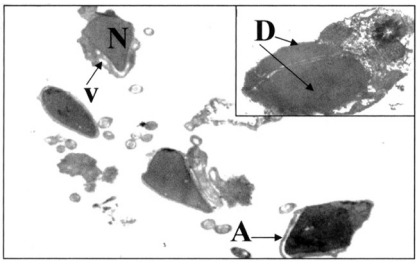

FIGURE 2 Section through the head (original magnification ×5000 K, small figure ×25 K). Vacuoles, projecting parts around the nucleus and a double head. N: nucleus, V: Vacuole, D: Double head, A: Acrosome.

noninvasive nature, its usefulness for lower ureteral stones is limited [5]. Other treatment modalities, such as ureteroscopy, open or laparoscopic surgery, are more efficacious than ESWL for the definitive treatment of distal ureteral stones [4, 7, 11]. Furthermore, we found that ESWL could affect the ultrastructural construction of sperms. Therefore, we suggest other treatment modalities for young men with distal ureteral stones to prevent the development of male infertility.

CONCLUSIONS

ESWL reduces sperm concentration and motility permanently in males with distal ureteral stone. It can also cause severe damage on sperm structure. Thus, ESWL should not be the first-line treatment in these patients, if their fertility is important.

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