Urol Res (1984) 12:183–186

Urological Research

Testicular Blood Flow in Experimental Torsion and Epididymo-Orchitis Measured by ^{133}Xe Clearance Technique in Rabbits

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Accepted: December 13, 1983

Summary. Testicular blood flow was measured by intratesticular injection of ^{133}Xe both under control conditions and in experimental 720 degree intravaginal torsion (10 rabbits) and in epididymo-orchitis (5 rabbits). The results were statistically compared with each other. The blood flow was 35.8 ± 13.7 ml/100 g/min to the right testis and 35.4 ± 12.7 ml/100 g/min to the left testis under control conditions. The blood flow decreased to 16% and 8% of the control values 1 h and 8 h after torsion respectively. In epididymo-orchitis testicular blood flow stayed within normal limits. There was a significant difference in blood flow between the torsion and epididymo-orchitis groups ($p < 0.001$). Further investigation in man will demonstrate whether the ^{133}Xe clearance method can be used in the differential diagnosis of these two pathologies.

Key words. ^{133}Xe clearance, Testicular blood flow, Testicular torsion, Epididymo-orchitis.

Introduction

Although testicular torsion and epididymo-orchitis present similar symptoms at physical examination, the treatment and prognosis of these two pathologies are quite different. In torsion, in order to prevent the loss of the testis, immediate surgical intervention is necessary. Epididymo-orchitis, however, is treated medically. There is a need for a method that would be useful in the differential diagnosis of these two pathologies.

In our search for a fast and reliable diagnostic method for testicular torsion we used ^{133}Xe clearance to determine the testicular blood flow in rabbits under normal conditions and in experimental torsion and epididymo-orchitis. Although there are other methods to measure this parameter, ^{133}Xe clearance is the most widely used method, because it is simple, rapid and quantitative [12]. It does not change the physiological conditions and can be repeated at short intervals of time. Using either ^{133}Xe or ^{85}Kr clearance testicular blood flow was measured in various experimental animals and in man under normal conditions [2, 7, 8, 12, 15, 19]. There are no reports in the literature on the quantitative measurement of testicular blood flow in torsion and epididymo-orchitis.

Materials and Methods

Measurement of Partition Coefficients of ^{133}Xe

To calculate the blood flow to testes from the measured tissue clearance rates it is necessary to know the testis/blood partition coefficients of ^{133}Xe. Testis/blood partition coefficients are computed from the measured water/gas, erythrocyte/gas, plasma/gas and testis homogenate/gas partition coefficients of ^{133}Xe.

After ^{133}Xe clearance studies outlined below, heparinized blood samples were taken from rabbits. The animals were sacrificed and the testes were removed and homogenized. All the parameters mentioned above were determined according to the methods published previously [4]. ^{133}Xe (10 mCi/10 ml saline) was obtained from Amersham, England.

Animal Experiments

A total of 15 male rabbits (age: 1 year) was used. 10 of them were anesthesized by intraperitoneal injection of Nembutal (25 mg/kg). 25–50 μCi ^{133}Xe in 0.2 ml saline was injected directly into the testis tissue using tuberculin syringes and very fine needles. The clearance of the radioactive ^{133}Xe from the tissue was monitored by Renaltron IV System (Nuclear Chicago, Model 2524). The lower level discriminator was adjusted to 75 keV, the time constant to 1 s and the chart speed to 120 in/h. The detector of the instrument was placed over the testes immediately after the injection and the counting rate was continuously recorded for 5 min. The clearance of ^{133}Xe was studied both from the right and left testes separately.

After recording the clearance curves intravaginal torsion was performed on the right testis in 5 and on the left testis in the other 5 rabbits. Under sterile conditions through a scrotal incision the testis and the cord were explored. The testis was turned around its predicle through 720 degree and fixed to the scrotal wall with a 3/0 atraumatic chronic suture. To facilitate subsequent injections the scrotal incisions were not completely closed.

One hour after torsion ^{133}Xe clearance curves were obtained after injection of the same amount of ^{133}Xe, first from the normal testis and then from the testis with torsion. 8 h after torsion the experimental testis was covered with a 1 cm thick lead plate to prevent the interference of remaining radioactivity and a clearance curve was obtained from the normal testis after injection of ^{133}Xe. A clearance curve was recorded from the experimental testis without injection of a new sample of ^{133}Xe because there was sufficient radioactivity remaining from the injection at 1 h, due to decreased blood flow to this testis. It was necessary to record the clearance for a longer period of time (~0.5 h) in testes with torsion.

In the epididymo-orchits group of rabbits 36 h before the blood flow measurements *E. coli* (> 100,000 colonies) in 1 ml suspension was injected subcutaneously into the spermatic cord. ^{133}Xe was injected first to the normal testis and a clearance curve was recorded for 5 min and then the procedure was repeated for the experimental testis.

At the end of the experiments heparinized blood samples were withdrawn from the rabbits. Testes were removed and reserved for histopathological examination and for subsequent studies to determine the ^{133}Xe partition coefficients.

Calculation of Blood Flow

The following formula was used to calculate the blood flow to testis [3, 6]:

$$TBF\ (ml/100\ g/min) = 100\ \lambda k \qquad (1)$$

where TBF is the testicular blood flow expressed in milliliters per 100 g tissue per min. Here, λ is the partition coefficient of ^{133}Xe between testis and whole blood and is calculated in the following way:

$$\lambda = \frac{\lambda_{T/gas}}{\lambda_{E/gas} \cdot (H) + \lambda_{P1/gas} \cdot (1 - H)} \qquad (2)$$

The partition coefficients such as $\lambda_{T/gas}$ (T: testis), $\lambda_{E/gas}$ (E: erythrocytes) and $\lambda_{P1/gas}$ (P1: plasma) were experimentally determined and substituted in this formula to calculate λ at different hematocrit (H) values, expressed as a percentage.

To determine k (the clearance rate constant) each clearance curve was plotted on semilogarithmic graph paper and the best-fitting straight line (by eye) was drawn through the points. The halftime of ^{133}Xe clearance ($T_{1/2}$) in minutes was obtained from the linear plot and k was computed from the halftime using the relation $k = 0.693/T_{1/2}$. We obtained mono-exponential clearance curves giving only one $T_{1/2}$.

Calculated clearance rate constants (k) and ^{133}Xe testis/blood partition coefficients (λ) were substituted in Formula (1) to calculate the blood flow to the testis.

Histopathological Studies

Testis specimens were taken both from normal and experimental testes and were preserved in bovine solution for subsequent histological studies. They were stained with hematoxylin and eosin stain for paraffin section. Each preparation was examined under a light microscope (Carl Zeiss).

Statistical Analysis

The results were evaluated by a computer. The means and standard deviations in each group were calculated and the statistical significance between groups was checked according to the Student's t-test.

Results

In the rabbit the partition coefficients of ^{133}Xe for plasma/gas, erythrocyte/gas and testis/gas were 92.0 ± 4.0, 192.0 ± 4.2 and 158.6 ± 6.1, respectively.

The results of blood flow to the testis before and after torsion are summarized in Table 1 and in epididymo-orchitis in Table 2. The mean blood flow was 35.8 ± 13.7 ml/100 g/min in the right testis and 35.4 ± 12.7 ml/100 g/min in the left testis. There was no significant difference between the right and left testes ($p > 0.80$) (Table 3). One hour after torsion the blood flow to the normal testis was 30.4 ± 9.0, and 5.3 ± 1.7 ml/100 g/min to the testis with torsion. The difference was significant ($p < 0.001$). Eight hours after torsion the mean blood flow was 33.9 ± 8.8 in the normal testes and 2.7 ± 0.6 ml/100 g/min in the testes with torsion. The difference was again statistically significant ($p < 0.001$). There was no significant difference in blood flow in the normal testis at 1 h and 8 h compared to the beginning value ($p > 0.50$).

In epididymo-orchitis the mean blood flow was 37.4 ± 10.8 in the normal testis and 41.3 ± 12.1 ml/100 g/min in the pathological testis. Although this was higher in the experimental testis compared to the normal value, the difference was statistically insignificant ($p > 0.50$). This might be attributed to the insufficient number of observations. There was a significant difference between orchitis and torsion at 1 h and 8 h ($p < 0.001$).

Histopathological studies showed hemorrhage and edema in the epididymis, cord and peritesticular tissue in

Table 1. The mean testicular blood flow (ml/100 g/min) in normal testes and in torsion

No. of observations	Before torsion		Torsion			
	Right testis	Left testis	1 h		8 h	
			Normal	Torsion	Normal	Torsion
10	35.8 ± 13.7	35.4 ± 12.7	30.4 ± 9.0	5.3 ± 1.7	33.9 ± 8.8	2.7 ± 0.6

Table 2. The mean testicular blood flow (ml/100 g/min) in normal testis and in epididymo-orchitis

No. of observations	Normal Testis	Epididymo-orchitis
5	37.4 ± 10.8	41.3 ± 12.1

Table 3. Comparison of results of testicular blood flow in control and experimental groups

Groups compared		p
1	2	
Control (right testis)	Control (left testis)	> 0.800
Control (0 h)	Control (1 h)	> 0.500
Control (0 h)	Control (8 h)	> 0.500
Control (1 h)	Torsion (1 h)	< 0.001
Control (8 h)	Torsion (8 h)	< 0.001
Torsion (1 h)	Torsion (8 h)	< 0.001
Control	Epididymo-orchitis	> 0.500
Epididymo-orchitis	Torsion (1 h)	< 0.001
Epididymo-orchitis	Torsion (8 h)	< 0.001

acute testis torsion. There was considerable edema in the interstitium of the testis and hemorrhagic areas below the capsule. The veins were filled with fresh thrombi. No irreversible changes such as degeneration in the germinal epithelium, necrosis or gangrene in the testis were observed.

In the epididymo-orchitis group a considerable amount of edema in the epididymis, cord and peritesticular tissue, and polymorphonuclear leucocyte infiltration was observed. In the interstitium of the testis there was widespread edema but no leucocyte infiltration. Spermatogenic activity was normal in all the preparations.

Discussion

Our results for testicular blood flow under normal conditions are in agreement with those reported in the literature [2, 8, 19]. No statistically significant difference was observed in the blood flow to the right and left testes ($p > 0.800$) in our study. Brown and Waites [2] had similar findings in rats and rabbits. However, Fritjofsson et al. [5] in man and Jensen and Waites [7] in the rhesus monkey obtained higher blood flows in the right testis compared to the left.

In the literature there is no report on the quantitative measurement of testicular blood flow in torsion or in epididymo-orchitis. We have observed decreased blood flow in rabbits with 720° torsion compared to the control value ($p < 0.001$). The blood flow decreased further at 8 h compared to the value obtained at 1 h ($p < 0.001$). We did not observe zero flow rate in any of the rabbits studied; there was always a slope in the clearance curves. These results are in agreement with our histopathological studies on tissue specimens. No irreversible changes, necrosis or gangrene were observed even 8 h after torsion. The time factor and the degree of torsion are very important in rescuing the testis in torsion, the time of onset of irreversible changes varying inversely with the degree of torsion [16]. Bartsch et al. [1] investigated histopathological changes in 42 subjects with testicular torsion and reported necrosis only after 12 h of torsion.

Although there are other methods such as Doppler Ultrasound [9] and ^{99m}Tc scrotum scintigraphy [10] to differentiate the two pathologies, testicular torsion and epididymo-orchitis, both of these methods have shortcomings. In comparative studies, ^{99m}Tc scrotal scintigraphy gave more reliable results than ultrasound [11, 14, 17]; however, there are reports of false-negative testicular torsion using this method [13, 17, 18].

The ^{133}Xe clearance method measures directly and quantitatively the amount of blood flow to the testis. In this study there was no significant difference in blood flow to the normal testis at 1 h and 8 h ($p > 0.500$) after torsion was applied to the other testis. This means that surgical trauma or injections in one testis do not effect the blood flow to the other testis. The blood flow to the testis with torsion decreased to 16% at 1 h and 8% at 8 h compared to the initial value. In orchitis the blood flow stayed within normal limits and the difference between the torsion and orchitis groups was statistically significant ($p < 0.001$). Our results obtained in rabbits are encouraging. We propose that the ^{133}Xe clearance technique should be further investigated in man to demonstrate whether it can be used in the differential diagnosis of testicular torsion.

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