

Experimental Varicocoele in the Rat – A New Experimental Model

II. Effect on Impregnating Ability

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Summary. In this paper the impregnating ability of rats in whom a varicocoele was induced according to principles described in a previous work was assessed. The animals, 20 adult male Wistar rats, were subdivided into 4 groups and treated as follows. In Group 1 a varicocoele was produced by partial ligation of the iliac vein proximal to the entry of the testicular vein. Group 2: same as Group 1 but incomplete ligation. In Group 3 an anterior transposition of the common iliac artery to the vein was carried out. In Group 4 a small side-to-side fistula between the common iliac artery and vein was created. The impregnating ability was evaluated by caging each operated animal with two fertile female rats. Only two animals, one belonging to Group 1 the other to Group 2, were unable to impregnate their partners.

Key words: Experimental varicocoele, Impregnating ability, Partial ligation, Iliac vein, Incomplete ligation, Anterior transposition, Side-to-Side fistula.

Introduction

There is not a well documented relationship between varicocoele and infertility. The high incidence of varicocoele has prompted some groups to search for a reliable experimental model which might explain the mechanism of varicocoele-related infertility [1, 10]. Numerous experimental models have been put forward in the rat. We have created a new model which mimics the haemodynamic situation present in a clinical varicocoele and avoids the criticism that there is no pressure gradient between the inferior vena cava and the left renal vein and inversion of blood flow in the testicular vein. In our animal model, in view of the peculiar anatomy of the Wistar rat, we tried to obtain various haemodynamic changes from the more conventional ones – partial or complete occlusion of the common iliac vein above the entry of the testicular vein – to our new procedure

which results in the so called “nut-cracker” phenomenon obtained by the anterior transposition of the left common iliac artery in front of the common iliac vein, and the creation of venous engorgement by a small side-to-side fistula between the common iliac artery and vein [3].

The histological results confirmed the data reported by other authors [1, 10] that no significant structural alterations of the testes were observed after simple ligation of the iliac vein. However, in animals in whom an arterial nutcracker was performed we were able to demonstrate alterations of the germinal epithelium in the left testis, whereas the contralateral testis remained unaffected. Minor histological changes were also recorded in the animals of the group with an arterio-venous fistula [3]. On the basis of these preliminary observations we decided to investigate the biological effects produced by such an artificially created varicocoele.

Material and Methods

20 albino mature Wistar rats of proven fertility were selected for the investigation. The animals were subdivided in four randomly assigned groups.

Group 1: (5 rats) In these animals a complete ligation of the common iliac vein above the entry of the testicular vein was performed, according to the procedure described in our previous work [3].

Group 2: (5 rats) In this group the same procedures were carried out, with the only difference that the common iliac vein was only partially ligated.

Group 3: (5 rats) These animals were submitted to the anterior transposition of the common iliac artery, as described elsewhere [3].

Group 4: (5 rats) In this latter group of rats a small side-to-side fistula between the common iliac artery and vein was carried out [3].

After the operation all the animals were allowed to recover for a period of 30 days and each was then caged with two fertile female rats either until a pregnancy occurred or for 30 days. If no pregnancy occurred, two new females were caged and left for

Table 1

Groups	No of Pregnancies in		Total No of Pregnancies
	1st Period	2nd Period	
Group 1	3	1	4
Group 2	2	2	4
Group 3	5	—	5
Group 4	5	—	5

another 30 days. At the end of the experimental period the animals were sacrificed, the testes removed and examined histologically as previously described [3].

Results

23 out of 25 animals were able to impregnate their partners within the observation period, only two animals, belonging respectively to Group 1 and Group 2, were not, even after the 2nd period (Table 1). The macroscopic appearance of the testes was normal in all cases and no differences were noted among the various groups. The histological patterns of the examined testes did not differ substantially from those already discussed in the first part of this work and did not vary even after 90 days. The major alterations were observed in the animals of Groups 1 and 2 while only minor alterations already described were found in the rats of Group 4 [3].

The right testes showed a completely normal histological appearance in every instance.

Discussion

These results of the impregnating ability of rats in whom an experimental varicocele was created by various methods do not provide an explanation of the mechanism by which clinical varicocele affects spermatogenesis. A review of the literature and the data reported in Part I of this work demonstrate that experimental varicocele obtained by producing an obstruction to the outflow of the testicular vein produces damage to the germinal epithelium only rarely [1, 10]. We have tried to reproduce the clinical situation more closely by attempting to get a reversed blood flow in the testicular vein, reproducing the "nut-cracker" phenomenon by means of an arterio-venous fistula. Furthermore an increased testicular inflow to the testis was produced in some animals.

The assessment of semen quality is being investigated in another study by a vasocystostomy and constitutes Part III of this work.

From re-examination of our own as well as other similar experimental papers we think we can affirm that, under experimental conditions, there is no significant correlation between the structural alterations of the testis caused by an artificially induced varicocele and its biological implications. In fact Al Juburi and associates [1] observed in the dog only minimal and sporadic histological alterations, while the sperm quality was significantly impaired [1]. However, in one of these studies the biological impact of an artificial varicocele was evaluated in terms of impregnating ability. Therefore, we thought it would be interesting to check such a parameter in a new experimental model that was proved to be capable of producing significant structural alterations of the germinal epithelium. However, in this case also we could not find any conclusive correlation between the degree of structural impairment and fertility. Only two animals out of 25, both belonging to the groups with no evidence of structural alterations, did not impregnate their partners. One explanation of this finding might be that the contralateral testis was always normal. This could suggest that in infertile men factors other than merely an augmentation of the venous pressure in the testicular vein and/or an increased temperature are responsible for the impairment of spermatogenesis. Some authors [4, 5] postulate that reflux of vasoactive substances from adrenal or renal tissue to the testicular vein is harmful in human varicoceles.

Experimentally this is difficult to prove since in dogs the adrenal vein does not drain into the left renal vein, but rather drains into the left phrenico-abdominal vein which terminates in the lateral surface of the inferior vena cava [1, 10]. Despite this anatomical difference Al Juburi et al. were able to find a decline in semen quality in dogs in whom an artificial varicocele was created, suggesting that other factors may be responsible for the testicular damage [1].

In our rat model, in which reflux from kidney or adrenal can be ruled out, the alteration in testicular vein haemodynamics resulting from our procedures can cause, in selected instances permanent structural alterations of the testis on the affected side, but cannot produce a reduction of the impregnating ability.

Our experimental model, chiefly in the animals of Group 3, mimics very closely the situation encountered in the type 2 clinical varicocele, according to the classification proposed by Coolsaet [6], where the cause of scrotal varicosities is obstruction of the left common iliac vein by the common iliac artery, causing the so-called "distal nut-cracker" phenomenon. Of interest is the observation of Hirsch et al. that the minor semen alterations in men with varicocele were observed in the group without reno-spermatic reflux [8].

Although clear-cut conclusions cannot be drawn, we think that animal models in varicocele investigations can be useful and deserve further study to better clarify the relationship between testicular damage and biological implications.

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