URINARY EXCRETION OF INTERSTITIAL CELL
STIMULATING HORMONE AND SPERM CONCENTRATION
IN 219 MALES

By
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ABSTRACT

219 male partners of barren marriages were examined with regard to urinary ICSH (LH) excretion and sperm concentration. The mean ICSH excretion in a group of patients with azoospermia was significantly higher as compared to a group of patients with more than 20 million sperms per ml. The individual excretion values were found to be widely distributed with a considerable overlapping between the groups. Only very few patients with low sperm counts had remarkably low ICSH excretion values. It appears as though only a very limited number of patients with impaired spermatogenesis would benefit from replacement therapy including gonadotrophins with ICSH activity; at least from a theoretical point of view.

In recent years human gonadotrophins have been introduced as a therapeutic agent in cases of male infertility (Gemzell & Kjessler 1964; MacLeod et al. 1964, 1966; Lunenfeld et al. 1965) because of a postulated relative insufficiency of the endogenous secretion of gonadotrophins in some infertile males. To elucidate the possible significance and mode of action of the different gonadotrophins with regard to the spermatogenic process the relation between sperm producing capacity and the secretion of the different gonadotrophic hormones had to be investigated. In 1931 it was shown by Hamburger (1931) that the excretion of total gonadotrophic hormones from the pituitary gland increased considerably in castrated human males. Since then much attention has been paid to the problem of the human male gonadal-hypophyseal feed-back mechanism (reviewed by Johnsen 1964, 1967). However, the question still remains unsettled. Present day knowledge on gonadotrophic hormone activities in the
human male is mainly based on bioassays measuring the so called «total» gonadotrophin excretion in the urine as expressed in Mouse Uterus Units (MUU). More detailed knowledge on FSH and ICSH in the human male under normal and pathological conditions is needed and can be obtained by immunoassay. The present study deals with the excretion of the interstitial cell stimulating hormone (ICSH or LH) in the urine and the relation to sperm concentration in 219 male partners of barren marriages.

SUBJECTS

The Uppsala University Sterility Clinic admits all types of sterile couples for investigation. Each male partner regardless of what is known about the reproductive performance of the corresponding female is analysed on several occasions. The present investigation includes 219 men who registered at the Clinic during a 20 months period 1966–67, without any further selection. Their ages ranged from 19 to 52 years with a mean of 31.6 years.

MATERIALS AND METHODS

Twenty-four hour urine samples were collected at the second visit and kept deep-frozen for a few days until analysed. ICSH in urine was determined by the radiimmunosorbent technique of Wide & Porath (1966) with the following modifications. Antibodies to HCG were coupled to CNBr-activated Sephadex (Wide et al. 1967). A highly purified HCG preparation (13 000 IU/mg AB Leo, Sweden) or a highly purified human pituitary ICSH (LH) preparation (Sc 26, Roos) was labelled with 125I. The results were expressed in microgram per 24 hours using the pituitary ICSH preparation as a provisional standard preparation. The biological and immunological activity of this pituitary ICSH preparation was 16 000 IU (2nd IRP) per mg (Roos 1968). Identical results were obtained with these labelled hormone preparations.

Serial analyses of seminal ejaculates were performed on 4 different occasions over a 12 week period according to the methods of Kjessler (1966). Two seminal samples were first collected each at intervals of one week, following a three day period of ejaculatory abstinence. Following a period of 10 weeks, which has been suggested to be the time necessary for a complete spermatogenetic regeneration cycle (Heller & Clermont 1964), 2 new sperm samples were collected again at intervals of one week. The results were compared in order to make sure that no transient exogenous factor would be involved in spermatogenesis and thus influence the results. The mean value of the different estimations was regarded as representative of the patients sperm production capacity.

RESULTS

The material was subdivided into three groups according to sperm concentration. Group A: patients with azoospermia (80 cases), group B: patients with severe oligospermia, up to 20 million sperms per ml (92 cases) and group C:
patients with more than 20 million sperms per ml (47 cases). The geometric mean of the ICSH excretion values was calculated for each group and the results are shown in Table 1. The individual excretion values were found to be widely distributed with a considerable overlapping between the groups. A statistical comparison between the mean values of the three groups was made (Table 1). A highly significant difference was found between group A, with azoospermia (mean value 2.41 µg/24 h), and group C, with more than 20 million sperms per ml (mean value 1.34 µg/h). The distribution of the ICSH excretion values in the total material including all 219 males is shown in Fig. 1 and the same distribution within each of the three subgroups A, B and C is shown in Figs. 2–4. A unimodal distribution was clearly revealed with regard to the total number of patients as well as to those within the different subgroups. There is an obvious inverse correlation between sperm concentration and ICSH excretion (Fig. 5).

**DISCUSSION**

It is known that a primary pituitary failure is associated with a low total gonadotrophin excretion whereas a high excretion indicates a primary gonadal defect. It is also generally agreed that both FSH and ICSH have to be simultaneously present to complete human spermatogenesis. Some of the published observations (Gemzell & Kjessler 1964; Heller & Clermont 1964; Martin 1967)

<table>
<thead>
<tr>
<th>Group Sperms million/ml</th>
<th>Symbol</th>
<th>No. of patients</th>
<th>ICSH excretion in urine (µg/24 h)</th>
<th>Statistical comparison between mean values of groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean value</td>
<td>Fiducial limits of stand. error of mean ($P = 0.05$)</td>
</tr>
<tr>
<td>Azoospermia 0</td>
<td>A</td>
<td>80</td>
<td>2.41</td>
<td>2.11–2.74</td>
</tr>
<tr>
<td>Oligospermia &gt;0–20</td>
<td>B</td>
<td>92</td>
<td>1.88</td>
<td>1.61–2.18</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>47</td>
<td>1.34</td>
<td>1.12–1.62</td>
</tr>
</tbody>
</table>
suggest that FSH may have a predominant effect on spermiogenesis whereas ICSH seems to have a somewhat more complex effect, exerted in part at least via the interstitial Leydig cells. The ICSH has been alleged to be of importance for the nutrition of the germinal epithelium by some kind of influence on the seminiferous tubular apparatus. Any alteration, actual or relative, in the pituitary secretion of ICSH or FSH might therefore imply abnormal gamete production resulting in impaired sperm concentration.

Determinations of ICSH excretion values in the present series of 219 males have only disclosed 2 cases with a clearly low or prepubertal excretion level (lower than 0.3 µg/24 h).

This is in striking contrast to the number of patients found with an increased
Severe oligospermia
>0-20 x 10^6 sperms/ml
92 cases

Fig. 3.
The distribution of ICSH excretion values in patients with severe oligospermia, up to 20 million sperms per ml (Group B). The dotted line indicates the distribution of Group C (Fig. 2) for comparison.

ICS

0.1 0.2 0.5 1.0 2.0 5.0 10 20 ICSH µg/24h

Per cent

Aspermia
80 cases

Fig. 4.
The distribution of ICSH excretion values in patients with azoospermia (Group A). The dotted line indicates the distribution of Group C (Fig. 2) for comparison.

ICSH excretion, presumably due to gonadal failure. From these results it would appear that only a few patients with impaired spermatogenesis would benefit from replacement therapy including gonadotrophins with ICSH activity, at least from a theoretical point of view.

When the patients were grouped primarily according to their ICSH excretion values it became evident that the proportion of patients with azoospermia in-
The relative distribution of patients with different sperm concentration in relation to urinary ICSH excretion values in 219 males. The figures inside the diagram are expressed as a percentage of the number of patients included in each group.

Increased, the higher the level of ICSH excretion, as seen in Fig. 5. The reverse was found to be true for patients with more than 20 million sperms per ml. This seems to imply some correlation between sperm concentration in the ejaculate and ICSH excretion in the urine.

There are several possible explanations for such a correlation. Any disturbance in the regular feed-back mechanism related to a primary defect in the germinal epithelium is known to give an increased excretion of total gonadotrophins. This general increase appears to be partly due to an increase in ICSH excretion. The ratio of FSH/ICSH increase is still unknown and is being investigated. There might, however, also exist several other defects in the regulation of gonadotrophin production, and/or release, leading to a raised ICSH excretion in the urine. Such an increase could in turn be responsible for over-stimulation of the gonadal structures resulting in decreased gonadal functional capacity.

Further evaluation of these aspects requires the simultaneous investigations of testicular morphology in addition to sperm concentration and hormone analyses and these are being undertaken at present.
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