دراسة مورفومترية للختوات التي تحمل
في الغدة الدقيقة نتيجة حقن مادة الميثيل ثيوبوراسيل
(سحص تقدير أقل جرعة التي عند ما لا يجدث أي تغيير مورفومترية)

محمد خيري

أجرى هذا البحث لتقدير أقل جرعة من مادة الميثيل ثيوبوراسيل التي يحقنها تحت الجلد في الفئران البيضاء.
لا يجدث أي تغيير هستولوجي في الخلايا الطلائية البيضاء
لسبيلات الغدة الدقيقة. وقد استخدم في هذا البحث عدد 80 فأر أبيض قسم إلى أربع مجموعات وكل مجموعة مكونة
من خمسة فأر وتم حقن هذه المجموعات بتركيزات مختلفة
من مادة الميثيل ثيوبوراسيل يوميا لمدة أسبوع بالإضافة إلى
المجموعة الخالية التي لم تحقن واستخدمت للمقارنة.

ولقد اتضح أنه عند حقن الفئران بتركيز (5 ملجم) سن
مادة الميثيل ثيوبوراسيل لا يحدث أي تغيير في طول الخلايا
 الطلائية المبطنة لسبيلات الغدة الدقيقة.

ولقد اتضح من الدراسة المورفومترية أنه بحقن الفئران بتركيز
(1 مجم من مادة الميثيل ثيوبوراسيل) يمكن علاج حالات
زيادة نشاط الغدة الدقيقة.)
EXPERIMENTAL STUDY OF HYPOTHYROIDISM IN RATS
WITH SPECIAL REFERENCE TO THE NO-EFFECTIVE DOSE
(With 1 Table & 1 Histogram)

By
M.K. IBRAHIM
(Received at 13/3/1983)

SUMMARY

The present work was designed to determine the dose at which no
morphometrical changes occur in the epithelial lining of the follicles
in the thyroid gland of rats experimentally injected with antithyroid
drug Methylthioaracil (M T U). Twenty-five rats were used in the
present experiment. They were divided into four groups A,B,C and
D of 5 animal each and were injected with (M T U) at a dose level
of 0.5, 0.1, 0.05 and 0.02 mg. per kg. body weight respectively. In
addition, a fifth group "E" of 5 animal was used as a control. It
was found that at a dose level of 0.05 mg. (M T U) per kg. body
weight, no morphometrical changes occur in the epithelial lining
of the thyroid follicles. Accordingly, a dose of 0.1 mg. (M T U) per
kg. body weight is to be recommended for treatment of hyperthyroi-
dism or to prepare a hypothyroid rat-model for comparative pathology.

INTRODUCTION

The functional state of the thyroid is assessed by different ways including morphometrical,
clinical and biochemical methods. Morphometrical study as a method for testing a medicament
and chemical substance was proved to be the best one when compared with the biochemical
and pharmacological methods (MESSOW et al. 1973). In an earlier work (IBRAHIM 1981), we
found that treatment of rats with a dose level of 0.1 mg. per kg. body weight of methylthioaracil
induced morphometrical changes in the epithelial cells that lined the follicles of the thyroid
gland compared with controls. In the present work we tried to determine the dose at which
no morphometrical changes occur in the epithelial lining of the follicles in the thyroid gland
of rats which have been administered this compound.

MATERIAL and METHODS

In the present work 25 wistar** rats (250-300 gm. body weight) were manipulated under
environmental condition of 22°C room temperature and were rationed ad libithum and adequately
supplied with tap water. The animals were regularly exposed to light for 12 hours per day.
The rats were divided into 5 groups A,B,C,D, and E of 5 animal each. The animals were individu-
ally treated daily with subcutaneous injection of 6 hydroxy-2-mercapto-4-Methyl pyramidin, Methyl-
thioaracil (M T U) for one week at dose level of 0.5, 0.1, 0.05 and 0.02 mg. per kg. body
weight for group A,B,C and D respectively. In addition a fifth group "E" of 5 animals was used
as a control.

** This experiment was done at the institute of pathology, Hannover (W G).

The thyroid glands were collected from the rats after they were sacrificed (by decapita-
tion) and were fixed in 10% neutral buffer formalin. Paraffin sections, 4-5 micron thickness,
were stained with haematoxilin and eosin. The histometrical parameter employed was measuring
the height of the epithelial cells lining the follicles of the thyroid gland. The histological slide
was then projected on a screen using a "karl zeiss" microscope to obtain a magnification of
500 fold. Each thyroid was represented in 5 serial sections. From each animal the epithelial
height of 50 follicles located centrally and 50 other follicles located peripherally were measured.
Statistical methods were carried out to postulate the changes given in each test. The mean
values of each measurement for different groups were statistically analysed.

RESULTS

Data of the morphometrical parameters of the epithelial lining of the thyroid follicles
was shown in table 1 and represented in histogram 1. Statistical analysis of these data revealed
a high significant increase (P/ 0.001) of the average value of the epithelial height in group
A which has been given the high dose of M T U as compared with the control group. Group
B revealed also a significant increase of the average value of the epithelial height (P/ 0.01)
as compared with control. These significant changes of the epithelial height were prominent
in the centre of the gland as well as in the peripherally located follicles (group A and B).
Both group C and D showed no significant changes of the epithelial height either centrally
or peripherally as compared with the control group.

DISCUSSION

The functional activity of the thyroid gland can be determined by different means, one
of which is histometry. SELYE (1953) and MESSOW et al. (1973) stated that the epithelial height
reflects the functional state of the gland. METTHIESEN, et al. (1975) found moreover that,
when compared with the biochemical finding, the epithelial height as a histological parameter
was more sensitive in Wistar rats treated with oral application of M T U.

In the present work we used different dose-levels of M T U in an attempt to determine
the "no-effective level", i.e., the dose at which no morphometrical changes occur in the thyroid
gland. HANSEN (1977), by oral application of M T U, found that in Wistar rats the "no-effective
level" was 0.5 mg. per kg. body weight. In the present work we have found that subcutaneous
injection of M T U at a dose of 0.05 mg. per kg. body weight induced no morphometrical changes
in the rat thyroid. The difference between our results and that of HANSEN (1977) is related
most probably to the route of administration and emphasized the conclusion of KOPF (1952)
that the effect of antithyroid drug depends not only on the dose but also on its duration and
route of application. By oral administration, the small intestine metabolised large amount of
M T U before reaching the blood (BRUGGEMANN et al. 1952) and therefore, higher doses are
required.

Accordingly, a dose level of 0.1 mg. M T U per kg. body weight (the dose above the
no-effective level; group B) is recommended for treatment of hyperthyroidism or preparing
a hypothyroidised rat-model for experimental comparative pathology. Our results are of impor-
tance from the point of view that at this low level other side-effects of the drug can be minimiz-
ed to the greatest extent.
In the present study, the location difference of the epithelial reaction has been taken in consideration. Our result showed that the epithelial cells that lined the centrally located follicle reacted more clearly than those located peripherally (Histogram 1). This is similar to that recorded by Messow et al. (1973) and Hansen (1977). These location difference may be related to variations in the concentration of iodine in different parts of the thyroid gland. Nadler (1954) stated that the thyroid gland of children is greatly resembling those of rats and found that high absorption of iodine occurs more in the centre of the gland.

REFERENCES


| Table (1) |

<p>| Relative measures of epithelial height (central and peripheral) |</p>
<table>
<thead>
<tr>
<th>Groups</th>
<th>X</th>
<th>S.D</th>
<th>X</th>
<th>S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>central</td>
<td>central</td>
<td>peripheral</td>
<td>peripheral</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>11.032</td>
<td>± 0.323</td>
<td>8.420</td>
<td>± 0.458</td>
</tr>
<tr>
<td>B</td>
<td>7.940</td>
<td>± 0.235</td>
<td>5.490</td>
<td>± 0.073</td>
</tr>
<tr>
<td>C</td>
<td>7.336</td>
<td>± 0.018</td>
<td>4.940</td>
<td>± 0.038</td>
</tr>
<tr>
<td>D</td>
<td>7.432</td>
<td>± 0.043</td>
<td>4.950</td>
<td>± 0.025</td>
</tr>
<tr>
<td>Control</td>
<td>7.100</td>
<td>± 0.284</td>
<td>5.160</td>
<td>± 0.085</td>
</tr>
</tbody>
</table>

X = mean
S.D = standard deviation
x = P/0.05
xx = P/0.01
xxx = P/0.001
of different dose-levels of M.T.U.
the following of the thyroid gland centrally and peripherally under the effect

Histogram (1): showing the average height and standard deviation of the epithelial cells lining

GROUPS

Epithelial-height (relative value in mm)

12
16