INCREASED SENSITIVITY OF DETERMINATION OF CHROIONIC GONADOTROPIN WHEN IMPLANTED IN GELATIN CAPSULES

M. S. Parkan' and A. A. Molodyk

UDC 612.649.018-088.1

Implantation of gonadotropin in gelatin capsules allows doses of the hormone (0.1 i.u.) to be detected which are subthreshold with the ordinary injection method of administration.

* * *

In a previous paper [1] we described the results of investigations showing that the same dose of chorionic gonadotropin (CG), when implanted in capsules, causes a much greater increase in the weight of the uterus than if given in the usual way by injections over a period of three days.

We postulated on the basis of these results that if the gonadotropin to be tested is implanted in capsules, it can be determined in small doses which are below threshold for the ordinary method of determination and which cannot therefore be determined. In other words, we postulated that if the test gonadotropin is implanted, the resolving power of the method used for its determination, based on the increase in weight of the uterus, must be increased. This problem was studied in the present investigation.

EXPERIMENTAL METHOD

Experiments were carried out on 60 infantile noninbred female mice, divided into two groups. The animals of group 1 received CG by injection, while gelatin capsules containing CG were implanted in the body cavity of the mice of group 2. Depending on the dose of CG, the mice of both groups were divided into six subgroups. The animals of the first subgroup received a total dose of CG equal to 0.05 i. u., while the mice of subgroups 2, 3, 4, 5, and 6 received 0.1, 0.2, 0.4, 0.8, and 1.6 i.u. respectively. As in the previous investigation, to prolong the period of absorption of the gelatin capsules, formalin was added at the rate of 3 μg/g.

EXPERIMENTAL RESULTS

The results obtained are given in the table.

Changes in Weight of Uterus Depending on Doses and Mode of Administration of CG

total dose of CG (in i.u.)	weight of uterus of mice receiving CG			
	by injections		from capsules	
	absolute weight (in mg)	relative weight	absolute weight (in mg)	relative weight
0,05	14,7 (±2,1)	1,52 (±0,15)	17,1 (±3,0)	1,90 (±0,20)
0,10	15,2 (±2,4)	1,66 (±0,14)	44,1 (±7,2)	5,14 (±0,41)
0,20	17,3 (±3,6)	2,10 (±0,20)	75,3 (±8,6)	8,50 (±0,62)
0,40	24,5 (±4,2)	2,88 (±0,26)	81,2 (±9,2)	9,56 (±0,68)
0,80	32,6 (±5,4)	3,44 (±0,30)	92,2 (±6,3)	9,86 (±0,51)
1,60	4,77 (±8,1)	5,52 (±0,62)	98,8 (±7,7)	10,06 (±0,56)

Note. In all subgroups $P < 0.05$.

As the table shows, the expected results were obtained in a most demonstrative form. This may largely be attributed to the felicitous choice of subthreshold doses of CG. From our experience of working

Laboratory of Hormone Therapy, Institute of Experimental and Clinical Oncology, Academy of Medical Sciences of the USSR, Moscow (Presented by Active Member of the Academy of Medical Sciences of the USSR A. D. Timofeevskii) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 65, No. 1, pp. 123-125, January, 1968. Original article submitted April 27, 1967.

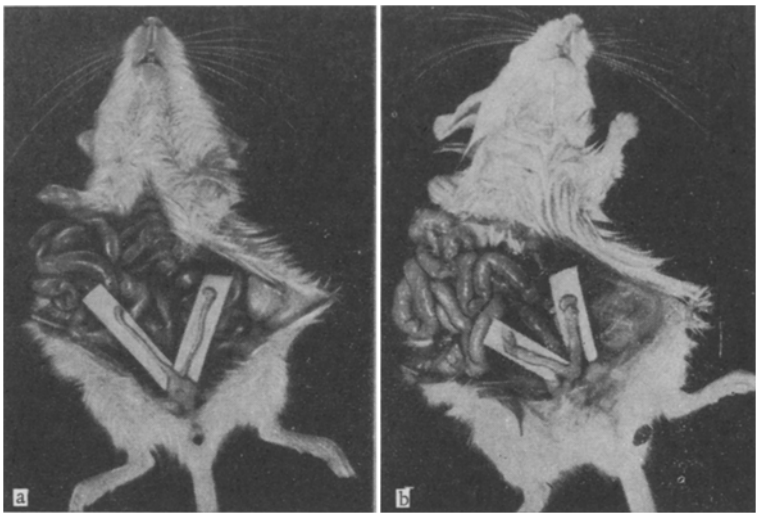

Fig. 1. Increase in size of uterus of mice following administration of 0.1 i.u. CG by injections (a) and by implantation in capsules (b).

with CG manufactured by the firm of Richter, we knew that 0.1 i.u. of this choriogonin does not produce changes in the weight of the uterus, yet nevertheless it was used in half that dose (0.05 i.u.), which was below threshold in experiments both with injections and with implantation of gelatin capsules. So far as the dose of 0.1 i.u. is concerned, while below threshold by the injection method, when implanted in a gelatin capsule it caused a greater increase in the weight of the uterus than a dose of 1 i.u. if the CG was given by injections. We know, for instance, that the unit of CG is usually taken to be the dose which doubles the weight of the uterus of infantile mice. The weight of the uterus of intact infantile mice weighing 8-10 g (at the end of the experiment) usually varied between 11 and 18 mg and, consequently, 1 i.u. of CG should increase the weight of the uterus to 22-36 mg, whereas in our experiment, when implanted in gelatin capsules, 0.1 i.u. of CG caused a still greater increase in weight of the uterus – on the average to 44 mg (see Fig. 1).

One special feature of our observations must be emphasized. If CG is incorporated in gelatin without the addition of formalin, capsules prepared in this way and implanted into mice are absorbed within 24 h. Clearly, besides the capsule, the CG is also absorbed, and in this case the weight of the uterus will be even smaller than if CG is given by injections, because the CG would act on the ovaries only for 24 h. The same results are obtained if an excess of formalin is added to the gelatin: such capsules take one week or longer to be absorbed, and consequently only part of the CG incorporated in the capsule is absorbed by the body. In this case the weight of the uterus is often smaller in mice receiving CG implantation in capsules. If, however, formalin is added to the gelatin for making the capsules at the rate of 3 μg/g, as we did in this case, such capsules are absorbed in the course of three days and only in individual mice can small pieces of capsule, or merely traces of them be found.

The results obtained are not only of theoretical, but also of practical interest. In pregnant women and patients with chorionepithelioma, CG is determined principally by the Ascheim–Zondek method [2], but this method cannot detect less than 2000 i.u./liter of urine. However, this concentration of CG is not found in pregnant women until the 5th week of pregnancy, and in the early periods of pregnancy this method cannot therefore be used. Furthermore, during treatment of chorionepithelioma, the need arises for detection of a much smaller quantity of CG. According to our observations, the discovery of 600-800 i.u. CG in the urine of patients is a characteristic sign of the presence of chorionepithelioma, but this concentration of CG cannot be detected by the Ascheim–Zondek method, whereas the method of implantation of CG in gelatin capsules can detect an even smaller amount of CG.

LITERATURE CITED

1. M. S. Parkan' and A. A. Molodyk, Byull. éksp. Biol., No. 9, 95 (1967).
2. B. Zondek, In the book: Hormones of the Ovary and Anterior Lobe of the Pituitary [Russian translation], Moscow (1938).