EFFECTS OF AN ANTIPROSTAGLANDIN DRUG ON HUMAN FALLOPIAN TUBES IN VIVO

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SUMMARY

The Authors studied 17 patients with patent tubes, normal ovulation and Rubin's test results. In the following cycle, this test was repeated divided into two phases. The first followed the normal procedure; the second started 10′ after the e.v. administration of 50 mg of an antiprostaglandin drug (Ketoprophen).

The results highlighted the capability of this drug to alter the activity of human tubes. A general increase was observed in the amplitude and frequency of tubal contractions.

The Authors finally analyse the possible clinical use of this drug in the treatment of the tubal pathology.

Prostaglandins are known to perform many functions in the physiopathology of reproduction ([1]). They act, for example, on hypothalamus-hypophysis-ovarian functions ([2]), cyclical endometrium modifications, tubal functions and uterine contractility.

Attempts have been made to use them in various fields such as men's infertility-contraception, pre-term pregnancy interruption and induced term-delivery. But they have been clinically successful in the two last indications only, notably in induced abortion at the 2nd trimester ([1]).

INTRODUCTION

Prostaglandins are known to perform many functions in human physiopathology. They have been experimentally used in various fields ([1]): hypothalamus-hypophysis-ovarian functions ([27]); endometrium cyclical physiology; men's infertility-contraception ([3]); tubal conceptive and contraceptive functions; uterine contractility; pre-term pregnancy interruption and induced term-delivery.

But they have been clinically used in the two last indications only, notably in induced abortion at the 2nd trimester ([1]).

As many pathologic conditions are associated with changes in the prostaglandin tissue concentration ([1]), a lot of research has been started to obtain antiprostaglandin substances or find other substances si-

Table 1. — *Clinical requirements met by the women included in the test-group.*

- Hysterosalpingography:
  normal, with regard to tubal patency
- Rubin's test:
  normal, with regard to basal-tone and peristalsis.
- Ovulation:
  present (Tab. 2).
- Anamnesis:
  recording no previous gastroduodenal pathology.

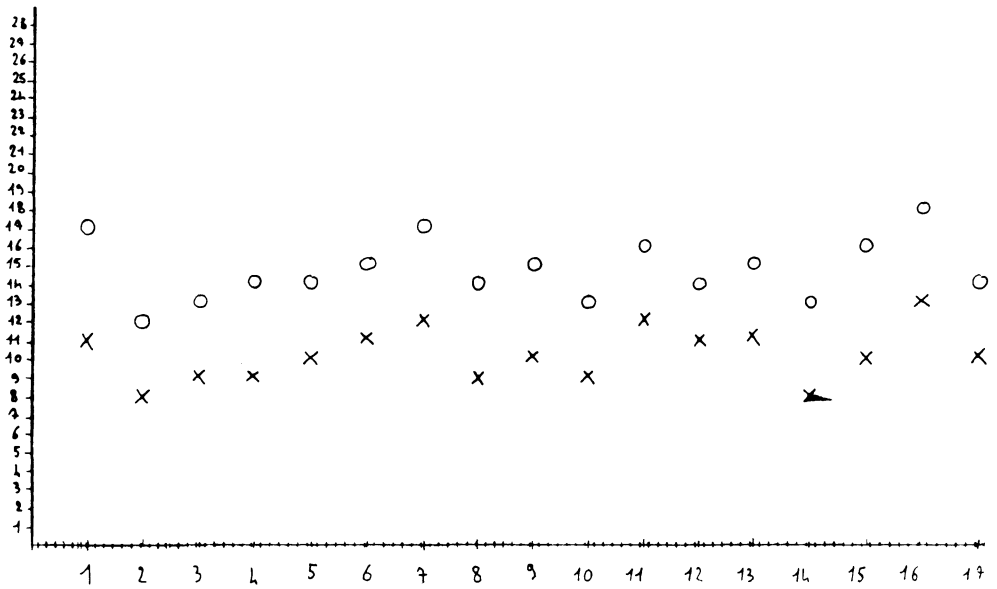

Table 2.

milar to prostaglandins to control their action ([4]).

With regard to the field of tubal motility, the results of our previous studies concerning the action of PG F_2 ([5]) on the tubes, have highlighted, in agreement with other Authors ([6, 7]), the inhibiting action of these substances on the tubal peristaltic activity. This activity does not depend on the dose but rather on the menstrual phase.

It reaches its maximum in the preovulation period, probably to favour fecundation, whereas in other phases, PG F_2 can perform even an opposite action.

The tubal peristaltic action has been recognized as the most important among the mechanisms governing the ovum capture, fecundation and subsequent implantation ([8]).

We have therefore tried to evaluate the action of an antiprostaglandin drug (Ketoprophen), following the procedure

Table 3. — *Methods to determine ovulation.*

Cases	Cervical scores (*)	Ovulation days (*)	Progesterone in the lutheal phase (**)		
1/BC	12	14°	21,14	17,30	18,50
2/FC	10	12°	14,40	11,90	23,00
3/SF	11	13°	10,80	14,80	18,00
4/DR	12	14°	16,00	13,40	19,10
5/NF	11	14°	18,00	21,00	13,50
6/IN	12	15°	22,40	56,50	18,00
7/GL	12	17°	38,70	12,00	20,00
8/DR	11	14°	12,00	17,60	39,00
9/CR	10	15°	15,40	18,00	16,80
10/BV	11	13°	21,00	18,30	20,80
11/LF	10	16°	14,00	18,30	17,00
12/RA	11	14°	20,60	21,50	15,60
13/PM	10	15°	13,60	25,30	15,60
14/TA	10	13°	17,30	16,80	12,70
15/PR	11	16°	21,00	14,00	17,20
16/IM	11	18°	16,00	16,40	19,20
17/DP	11	14°	18,00	17,20	16,80

* Performed in the month preceding Rubin's test (V.N. 10).

** Dosage repeated for three cycles.

Table 4.

Case	Basal Diagnosis	Pre-administration diagnosis	Post-administration diagnosis
1	Normal record	Initial spasm followed by patency record. Increased base-tone. Regular, medium-amplitude oscillations.	Initial spasm followed by patency record. Increased base-tone. Regular, medium-amplitude oscillations.
2	» »	Patency record. Regular base-tone. No oscillations.	Patency record. Regular base-tone. Regular, medium-amplitude oscillations.
3	» »	Patency record with increased base-tone. Irregular, small oscillations.	Unchanged.
4	» »	Stenosis record (spasm).	Initial spasm followed by patency record. Regular base-tone. Regular medium-amplitude oscillations.
5	» »	Normal record.	Normal record. Increased peristalsis with regular, medium-amplitude oscillations.
6	» »	Patency record. Scarce oscillations.	Patency record. Normal base-tone. Regular, medium-amplitude oscillations.
7	» »	Normal record.	Normal record.
8	» »	Normal record.	Significant increase in oscillation frequency and amplitude.
9	» »	Patency record. Almost no oscillation.	Patency record. Small increase in oscillation frequency and amplitude.
10	» »	Spastic stenosis record. No oscillations.	Unchanged.
11	» »	Patency record. Regular base-tone. Very wide irregular oscillations.	Patency record. Regular base-tone. Medium-amplitude regular oscillations.
12	» »	Normal record.	Unchanged.
13	» »	Functional stenosis record.	Normal record.
14	» »	Patency record. Increased base-tone. Irregular, small oscillations.	Normal record. Regular tone and oscillations.
15	» »	Spasm record. Scarce, irregular and small oscillations.	Spasm record. Regular peristalsis and base-tone.
16	» »	Patency record. Regular base-tone. Reduced peristalsis.	Normal record.
17	» »	Patency record. Small, irregular and scarce oscillations. Regular base-tone.	Patency record. Reduced base-tone. Small and scarce oscillations.

used in our previous work ([5]) to verify the possible PG inhibiting action on the tubal activity.

CLINICAL CASES

We studied 17 cases meeting the clinical requirements listed in Table 1. They were all nulliparous patients, average age 28, weight between 45 kg and 60 kg and height between m 1.50 and m 1.70. In the test-period, condoms were used during sexual intercourses.

The following procedure was applied: 4/6 days before ovulation (0 day), a basal Rubin's test (Tab. 2) was performed (insufflation pressure: 100 mmHg; duration of CO_2 insufflation: 3′; insufflation volume: 30 ml³/min, plus a 1′ record after stopping the flow, to evaluate the outflow).

Table 5.

Record changes	No cases/tot. cases	%
a) Unchanged records	4/17	23.53%
b) Resolution of occlusions of likely functional origin	2/3	66.66%
c) Increase in the base-tone	3/17	17.65%
d) Decrease in the base-tone	0	0
e) Increase in the frequency of oscillations	3/17	17.65%
f) Decrease in the frequency of oscillations	0	0
g) Increase in the amplitude of oscillations	.10/17	58.82%
h) Decrease in the amplitude of oscillations	1/17	5.88%
i) Records showing an overall increase in the activity of tubal muscles	.12/17	70.59%

In the following cycle, this test was repeated but divided into two phases: the first followed the usual procedure; the second started 10′ after the e.v. administration of 50 mg of Ketoprophen. We used Fikentscher-Semm equipments with manual calibration and a 40 cm/min paper-flow speed. E_2, progesteron and hPrl hormonal dosages were performed by RIA for three consecutive cycles to check the occurrence of ovulation. Ovulatory results were obtained as far as the luteal progesteron rise was concerned (Tab. 3). In the month preceding the test, a cervical score was performed according to Insler's rating, with ovulatory results in all the examined cases (Tab. 2).

In some cases, the diagnosis disagreed with the previous basal record. This was due to the decision to avoid the antispastic pre-medication that is usually done before the recording to control the frequent spastic phenomena. Our aim was avoiding any interference with the action of the studied drug during the test (Tab. 4).

The comparison of the records (Tab. 4) showed that 4 of them had remained unchanged (23.53%); 2 were normal

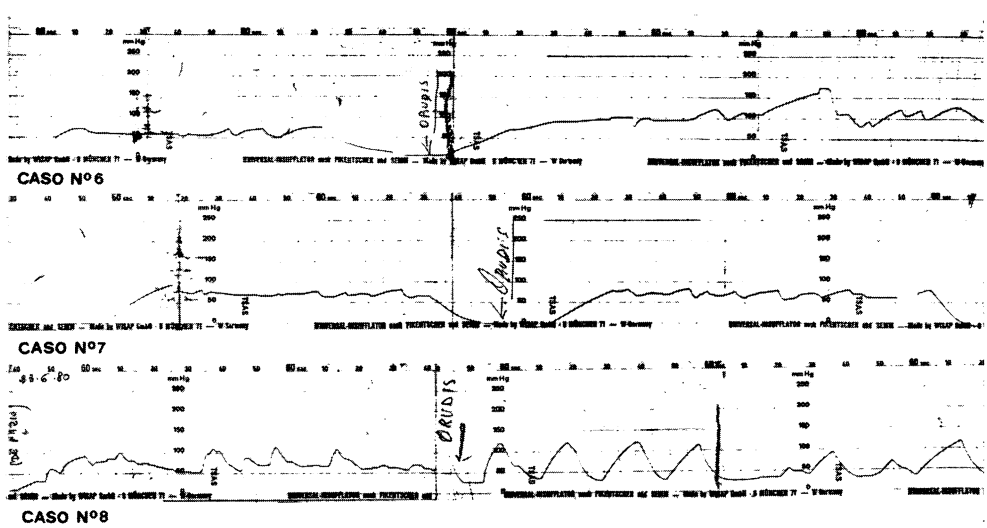

Fig. 1.

both before and after the administration; 1 showed a stenosis, probably of functional origin and 1 was just within the normal-range limit. In 3 cases (17.65%) the base tone rised; it decreased in no case. In 10 cases (58.82%) the contraction amplitude increased; it decreased in just 1 case. Similarly, the contraction frequency increased in 3 cases (17.65%) and decreased in no case (66.66%). 2 out of 3 records showing occlusion, probably of functional origin, became normal.

5 patients (29.41%) reported hot flushes after the drug administration. One of them also reported moderate and temporary gastralgia (Tab. 5).

DISCUSSION

The results of our study clearly show that a general administration of this drug can alter the activity of human tubes. In line with the results of our previous experiences ([5]), PG F_2 Prostaglandins, locally administered in vivo, tend to decrease the tubal peristaltic activity in the pre-ovulation period. Consequently, the administration of an antiprostaglandin drug is likely to increase the tubal peristalsis.

In all our test-cases, systematic administrations of Ketoprophen increased both the frequency and the amplitude of tubal contractions (Tab. 4) (Fig. A).

Therefore, assuming that an increased tubal contractility before the ovulation favours the oocyte's capture ([6]), we can suppose that this antiprostaglandin drug plays a positive pro-conception role in this phase of the menstrual cycle.

However, the uterotubarian insufflation (Rubin's test) provides an overall evaluation of the tubal activity, but no information on the contractility of the various segments ([7]). The previous assumption must therefore be confirmed by further studies, both in vivo, using endotubal cannulae according to Coutinho and Coll.'s technique ([9]), and in vitro, on tissues taken from different tubal segments.

As a matter of fact, previous studies have shown that the various tubal tracts respond differently to the administration of exogenous substances. This response is also influenced by the menstrual phase and the kind of prostaglandin that is used ([9, 10]).

BIBLIOGRAPHY

1) Arrata W. S. M., Tsai A. Y. M.: *J. Reprod. Med., 20*, 84, 1978.
2) Warberg J., Eskay R. L., Poter J. C.: *Endocrinology, 98*, 1135, 1976.
3) Abbatiello E. R., Kaminsky M., Weisbroth S.: *Int. J. Fertil., 21*, 82, 1976.
4) Guyonnet J. L., Julou L.: « Relations entre l'activité inhibitrice sur la syntese de la R.C.S. et des prostaglandines et l'activité anti-inflammatoire dans les cas du kétoprofene et de quelques autres anti-inflammatory non stéroidiques ». 8° Congrès Européen de Rheumatologie. Helsinki (Juin 1975).
5) Rustichelli S., Chiappa A., Mariatti M.: *Min. Gin.*, In press.
6) Afzelius B. A., Canner P., Mossberg B.: *Fertil. Steril., 29*, 72, 1978.
7) Coutinho E., Siegler A., Swolin K., Suzuki S.: «Fallopian tube physiology». From: « Nineth world congress on fertility and sterility. Thirty-third annual meeting of the american fertility society ». April 12-16 1977, Miami.
8) Coutinho E. M., Maia H. S.: *Fertil. Steril., 22*, 539, 1971.
9) Takeda T., Tsutsumi Y., Hara S., Ida M.: *Fertil. Steril., 30*, 79, 1978.
10) Lindblom B., Hamberger L., Wiqvist N.: *Fertil. Steril., 30*, 553, 1978.