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Editorial

LASER THERAPY IN GYNECOLOGICAL CONDITIONS

Laser Therapy is one of the new modality of treatment in certain gynecological conditions. Laser is an acronym for Light Amplification by stimulated Emission of Radiation. As a point source of light energy the laser is more powerful than the sun. The most commonly used gases are carbon dioxide, argon, didynium, krypton, neon, and helium. The carbon-dioxide (Co2) laser is the most powerful and effective laser available today. Though known as CO2 laser, the gas is actually a mixture of 76 per cent helium, 15 per cent nitrogen, and 9 per cent carbon dioxide. Because of its wave length (10,600 nm), the CO2 laser can be used to vaporize a superficial lesion or as a "Laser Scalpel" to incise tissue. The CO2 laser is capable of destroying an extremely small or an extremely large area of tissue to any depth and with great precision. It delivers the laser beam to the superficial lesion with minimal pain and discomfort.

In Gynecology, the CO2 laser has been utilised for a variety of disorders e.g. cervical intraepithelial neoplasm (CIN), vaginal intraepithelial Neoplasia, Vulvar dystrophy and intraepithelial neoplasia, condyloma acuninatum, powderburn spots of endometriosis, in infertility surgery (like terminal salpingostomy for hydrosalpinx, tubotubal anastomosis, tackling the peritubal and periovarian adhesions), and Metroplasty and Myomectomy.

CIN Lesions of Cervix: CO2 laser therapy in this condition is simple, and can be done even in an outpatient clinic. The virtual absence of scarring and the rapid reepithelialization make it superior to cryosurgery in cases of CIN lesions of Cervix. The success rate is over 90 per cent in the management of this condition. Recurrence rates may be as low as or even lower than with cryosurgery. Even conisation can also be performed using lasers with a low complication rate, and providing tissue that is suitable for histopathological interpretation.

Vaginal intraepithelial Neoplasia: Laser therapy has been found useful in this condition. It produces localized destruction in a controlled manner on an outpatient basis, with minimal discomfort and no scarring. Of course continuous follow up is necessary.

Vulvar dystrophy and Intraepithelial neoplasia: Ablation of abnormal tissue can be attained using the CO2 laser without mutilation, and treatments can be used repeatedly if necessary. The end result is generally satisfactory, with scarring minimal. It is absolutely essential that adequate

diagnostic biopsies have been obtained before laser therapy is carried out.

Condyloma acuminatum: Laser therapy seems to be the treatment of choice in this condition. Both the female and male partners must be examined and all condyloma removed at one time to achieve high cure rates.

Powderburn spots of endometriosis: These can be fulgarated with vaporization with CO2 laser. Laser energy is dissipated in a limited fashion with minimal thermal damage to the adjacent tissue. CO2 laser therefore can be safely utilised for endometriosis on the surface of intestines.

Vaporization of endometriotic implants with argon laser has also been reported. Argon laser is selectively absorbed by the brownish implants of endometriosis. The development of the laser laparoscope might be useful for vaporization of adhesions and endometriotic implants through an endoscope without opening the abdomen.

Infertility Surgery: (A) *Terminal Salpingostomy for Hydrosalpinx*: The fallopian tube is distended with hydrotubation fluid and the distal end is examined under the microscope. The central dimple is noted and the CO2 laser is aimed and delivered. The hydrotubation fluid will escape. A glass rod is then introduced into the tubal opening so created. Radial incisions along the avascular line of fimbrial attachment are made with the CO2 laser. To maintain the patency of the newly created ostia, the mucosal flap is everted. Retraction of the flap's margin will create a "spontaneous laser eversion".

(B) *Tubo-tubal anastomosis*: The use of CO2 laser is to mainly prepare portions of the tube prior to anastomosis. The serosa and the muscular layer of the proximal and the distal portions of the tube are circumferentially incised with the laser. The mucosal layer is separated with a pair of microscissors. The anastomosis is then performed with 8-0 vicryl sutures, first muscularis and then serosa. The advantages of CO2 laser in this procedure are minimal bleeding, minimal oedema, and rapid healing.

(C) *Peritubal and Periovarian adhesions*: Vaporization of the adhesions with CO2 laser allows the surgeon to do an almost bloodless operation. The adhesions are lifted with a glass rod and vaporization performed along the rod. For adhesions that are inaccessible to direct laser beam such as those adhesions below the ovaries, it is proposed to have a front silvered surface mirror with integrated light bundle to reflect the laser beam. Direct vaporization of periovarian adhesions can also be done with low power density of laser.

Metroplasty and Myomectomy: These also can be carried out with CO2 laser. The ability of the laser beam to seal blood vessels is beneficial for those usually bloody operations. Thermal stimulation of the collagen in the wall of the vessels results in hemostasis. The technique essentially requires skill and precision.

Thus laser surgery is an important additional modality of treatment in some of the gynecological conditions, whenever such facilities are available. A good understanding of the basic concepts of laser physics and a familiarity with the laser instruments are mandatory for the laser surgeon. A well acquainted operation theatre staff will be very useful in carrying out successful, safe laser surgery. All flammable and explosive material must be removed from the laser area, and protective coverings for the eyes must be worn by all personnel. Innovating simpler, less bulkier instruments, and development of flexible CO2 laser transmission fibre that can be utilized through an endoscope will be extremely beneficial.

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MATERNAL TOXAEMIA AND FOETAL GONADAL ACTIVITY WITH SPECIAL REFERENCE TO PROLACTIN—I. OVARY

by

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SUMMARY

The maternal serum prolactin (PRL) level and foetal ovarian morphology in 25 cases including 15 of toxaemia of pregnancy and 10 non-toxaemic pregnancy have been studied. Follicular maturation of the foetal ovaries were found in 86.6% toxaemic cases. The maturation ranged from early follicular maturation to cystic atresia and theca luteinisation. A steady increase in the maternal serum PRL level was observed in these cases according to the degree of follicular maturation. In the control series no maturation was found in 80% cases and maternal serum PRL level was not as high as in the toxaemic cases.

Toxaemia of pregnancy is perhaps the most common single complication of pregnancy prevalent in the developing countries. Various factors have been incriminated in its genesis such as different toxins, placental ischaemia, neuromuscular disorder, endocrine imbalance involving posterior pituitary, increased renin-angiotensin, chorionic gonadotrophins, disseminated intravascular coagulation, immunological factors etc. (Browne and Veall, 1953; McKay *et al* 1953; Hunter and Howard, 1960; Brust *et al* 1948; Kumar 1962; Morris *et al* 1964; Masani *et al* 1967; Petrucco *et al* 1974). Recently, high level of prolactin (PRL) in the maternal blood has been demonstrated in cases of toxaemia of pregnancy (Horrobin, 1975; Friese, 1977) and is considered as one of the principal aetiologic factor. Morphology of the foetal gonads in cases of toxaemia of pregnancy has not been widely studied. Maturation of the foetal ovarian follicles were the notable observations as published in this field (Govan and Mukherjee, 1950; Pryse-Davies and Dewhurst, 1971). However, the cause of such maturation is not yet settled with certainity.

In the present study, we have attempted to establish the relation between morphological changes in the foetal ovaries and

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serum prolactin level in the toxaemic mothers. Maternal prolactin level has been considered as the pilot factor which gives reflection of the same in the foetal blood.

Material and Methods

The present study comprises of examination of 25 mothers (in labour) including 15 cases of toxaemia of pregnancy serving the test series and the remaining 10 were the non-toxaemic cases included as the control series. The age group in both the series were between 16 to 40 years and included both primi and multigravida. The probable causes of foetal death in the control series were cord prolapse, placenta praevia, post maturity and/or difficult breech delivery.

For the estimation of prolactin level, maternal blood was collected during labour and the separated serum was kept at -20°C till the prolactin was assayed. The level of prolactin was measured by radio-immunoassay technique (Hwang *et al* 1971) (The human prolactin standard and antisera were kindly supplied by K. Mashiter of Hammersmith Hospital, London).

The ovaries were collected from the still born foetuses within 6 hours of delivery for the histological examination. The gross features, viz. weight, dimensions, presence of cysts etc., were noted. The specimens were then sectioned in longitudinal axis and fixed in 10% buffered formol saline. The tissues were processed routinely, stained by haematoxylin and eosin stain and were examined under light microscope.

Results

I. *Non-Toxaemic (Control) Series*

Weight and dimension of the foetal ovaries varied as follows; Weight: 15 mg to 125 mg (mean: 59.3 mg), Length: 12 to 20 mm (mean: 15.1 mm) and breadth 3 mm to 5 mm (mean 3.9 mm). Gross examination did not show any cystic elevation on the surface.

On histopathological examination, 8 out of 10 cases (80%) did not show any follicular maturation; the follicles consisted entirely of primordial follicle with one or two layers of granulosa cells. The stromal cells were spindle shaped and blood vessels were congested. In the remaining 2 cases (20%), moderately matured follicles lined by 4-7 layers of granulosa cells, but without any ova were noted.

Prolactin level: The average maternal prolactin level in this group was 235.3 ng/ml with a range of 21.2 to 392 ng/ml. Two cases, which showed atretic follicles, had high level of prolactin (320 and 392 ng/ml) (Table I).

II. *Toxaemic (Test) Series*

The foetal ovaries of this series were greater in all dimension and weight as compared to the control group. The variation of length, breadth and weight were as follows: Weight; 45-380 mg (mean 140 mg), Length; 12-27 mm (mean 15 mm) breadth; 4-7 mm (mean 5.6 mm). The surface of the ovaries were studded with multiple cysts in 3 out of 15 cases.

On histological examination, signs of follicular maturation was observed in 13 cases (86.6%). These cases were divided in to the following groups according to the degree of maturity.

Group A. Early maturation: This is characterised by follicles containing a healthy ovum surrounded by 3-5 layers of granulosa cells possessing distinct cell membrane and deeply staining nuclei with moderately developed theca interna. Two cases showed changes limited to this

TABLE I

Foetal Ovarian Follicular Changes and Average Maternal Serum Prolactin (PRL) Level

Foetal ovarian follicular changes	Non-toxaemic series (10 cases)			Toxaemic series (15 cases)		
	No. of cases	Average maternal serum PRL level ng/ml (Range)	Percentage	No. of cases	Average maternal serum PRL level ng/ml (Range)	Percentage
No maturation	8	205.8 (21 2-320)	80	2	243.9 (217.8-270)	13.3
Early maturation only (Group A)	Nil	—	—	2	302.5 (290-315)	13.3
Advanced maturation (Group B)	Nil	—	—	4	386.6 (318-532)	26.6
Cystic atresia and atretic follicles (Group C)	2	356 (320-392)	20	5	414 (247-610)	33.4
Theca luteinisation (Group D)	Nil	—	—	2	415 (395-435)	13.3

stage only, whereas the rest showed associated advanced features of maturation.

Group B. Moderate to advanced maturation (*Fig. 1*): More advanced stage of maturation was seen in this group than the preceeding group. The antra were well developed, the ova with prominent cumuli were lined by 6-10 layers of well developed granulosa cells. Theca interna was prominent and in 1 case there was haemorrhage in the layers. Four cases (26.4%) belonged to this group.

Group C. Cystic atresia of follicles (*Fig. 2*): Five cases (23.3%) were included in this group. Cystic follicles were observed in 3 cases and in another 2 cases there was complete atresia. In 2 ovaries the surface was studded with multiple cysts. The ova in the follicles were absent. The granulosa cell layer was thin. Theca interna was well developed. In 1 of the cases, the cysts were so large that the overlying cortex was highly compressed with atrophic primordial follicles.

Group D. Theca luteinisation (*Fig. 3*): In these cases, the theca interna was much proliferated and highly vascular. Groups of cells were swollen and became more epithelioid with translucent cytoplasm and small spherical nucleus—suggesting luteinisation. Such features were observed in 2 cases (13.2%) in association with cystic atretic follicles. In 1 case, the dilated cysts contained blood.

Serum prolactin level: The average serum prolactin level in the toxaemic series was 369 ng/ml with the range from 217.8 to 610 ng/ml. The level of serum prolactin in the different groups according to the

foetal ovarian follicular maturation has been depicted in Table I.

Discussion

Govan and Mukherjee (1950) first described the morphological changes in the ovaries in still born foetuses of toxaemic mothers. The changes varied from early follicular maturation to the theca luteinisation in majority (92%) of their cases. Interestingly, such changes were conspicuously absent in the babies of the non-toxaemic mothers except only in 13.9% cases where early follicular maturation was noted. Increased foetal ovarian maturation in toxaemic cases was also observed by Pryse-Davies and Dewhurst (1971).

While Govan and Mukherjee (1950) implicated maternal pituitary gonadotrophin as the cause for foetal ovarian change, Pryse-Davies and Dewhurst (1971) were of opinion that human chorionic gonadotrophin (HCG) of the mother was the responsible factor. HCG has a combined follicle stimulating and luteotrophic action, and that latter effect was considered to be predominent with large doses and conspicuous theca luteinisation in the adult ovary has been reported (Segaloff *et al* 1951). However, foetal level of HCG is much less than that of the maternal circulating level and earlier authors (Geist, 1933; Brown *et al* 1941) opined that HCG is unable to stimulate the foetal ovary and hence they rejected the possibility. HCG secreted by the trophoblasts with large molecular size reaches the maternal system by diffusion much more readily that the foetal one and this selective passage of gonadotrophin to the mother serves the purpose of protecting the foetal gonads from excessive stimulation. Other workers (Govan and Mukherjee, 1950, Peters *et al* 1975) also thought that HCG is unable to stimulate the foetal ovary. Recent postulation involves that foetal gonadal maturation is due to the action of prolactin (PRL). Recently, PRL has been established as a separate specific anterior pituitary gonadotrophic hormone and with the advent of specific radio immunoassay, the study of its role in different conditions, health and disease, is being possible (Loewenstein *et al* 1971; Friesen *et al* 1972, Horrobin 1977).

McNatty *et al* (1974) have observed presence of PRL in the follicular fluid at various stages of menstrual cycle. Progressive rise of serum PRL with a peak level at 38-40 weeks of gestation has also been observed (Tyson *et al* 1972, Jaffe *et al* 1973, Schenker *et al* 1975). The cause of such rise in pregnancy is not clear. Further Hauth and associates (1978) have demonstrated high plasma PRL level in foetuses older than 36 weeks and PRL being a low molecular weight protein can easily cross the placental barrier and in toxamia the foetal level rises to a great extent. Thus it might be reasonably presumed that the foetal ovaries are exposed continuously to the high concentration of PRL.

In our study, the average serum PRL level in the toxaemic mother were much higher than that of the non-toxaemic ones. Such observations in toxaemia of pregnancy has been reported also by Horrobin (1975) and Friese (1977). PRL is known to be related with fluid and electrolyte balance. High level of PRL leads to sodium, potassium and water retention along with increased aldosterone secretion followed by hypertension and oedema (Horrobin *et al* 1971; Manku *et al* 1973; Nassar *et al* 1974) and hence the role of PRL in the genesis of toxaemia of pregnancy is not beyond consideration.

In our present work, we have aimed to

find a correlation between the foetal ovarian maturity and PRL level in the mother. Eight of the 10 foetal ovaries (80%) among the non-toxaemic (Control) cases did not show any evidence of maturation of ovarian follicles and the average PRL level in their mother's blood was much less when compared to the high level in the two cases showing foetal ovarian follicular maturation. However, no obvious cause could be attributed to the high PRL level in these two cases.

In the toxaemic group however, the relation between the degree of follicular maturation and maternal PRL level was significant. Only in 2 out of 15 cases (13.3%) there was no follicular maturation and the maternal PRL levels were relatively lower. Moderately raised maternal serum PRL level was detected in the 2 cases showing early follicular maturation only. In the remaining cases, where more advanced degree of follicular maturation (Group B) to cystic atresia of follicles (Group C) and theca luteinisation (Group D) were observed, a steady rise in the average maternal serum PRL level than the preceeding group was noticed.

The significant relationship between the foetal ovarian maturation and maternal PRL level as observed in our present study, opens up a new channel to question whether the maturation is due to a direct action of PRL on the ovaries or due to increased production of oestrogen. Poindexter *et al* (1979) have demonstrated presence of PRL receptor in the ovary leading one to postulate the former hypothesis of direct stimulation by PRL. Conversly oestrogen is also known to stimulate PRL secretion either directly or indirectly (Friesen *et al* 1972; Yen *et al* 1974). Whatever may be the pathway of action, it may reasonably be concluded that PRL has got significant role in the foetal ovarian maturation and considering the observations in our present study, it seems highly alluring to have a suggestive impression that ovarian maturation in the foetuses born to toxaemic mothers, is directly related to the high maternal serum PRL level.

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References

1. Brown, W. E., Bradbury, J. T., Arbor, A. and Metzger, I.: Am. J. Obstet. Gynec. **41**: 582, 1941.
2. Browne, J. C. M. and Veall, N.: J. Obstet. Gynaec. Brit. Emp. **60**: 141, 1953.
3. Brust, A. A., Assali, N. S. and Ferris, E. B.: J. Clin. Invest. **27**: 717, 1948.
4. Friese, S.: M.D. Thesis, University of Gromingen, 1977. Quoted from Horrobin, D.F., 1977.
5. Friesen, H., Hwang, P., Guyda, H., Tolis, G., Tyson, J. and Myers, R.: In Prolactin and Carcinogenesis. 4th Tenovus Workshop. Eds. Boyns, A.R. and Griffith, K. Cardiff, U.K., 1972. Alpha Omega Alpha Publishing, p. 64.
6. Geist, S. H.: Am. J. Obstet. Gynec. **26**: 588, 1933.
7. Govan, A. D. T. and Mukherjee, C. L.: J. Obstet. Gynaec. Brit. Emp. **57**: 525, 1950.
8. Hauth, J. C., Parker, C. R. Jr., MacDonald, P. C., Porter, J. C. and Johnston, J. M.: Obstet. Gynaec. **51**: 81, 1978.
9. Horrobin, D. F.: Med. Hypothesis. **1**: 153, 1975.
10. Horrobin, D. F.: Prolactin. Vol. 5, 1977. Edinburgh, 1977. Churchill Livingstone, p. 152.
11. Horrobin, D. F., Lloyd, I. J., Lipton, A., Burstyn, P. G. Durkin, N. and Muiruri, K. L.: Lancet. **2**: 352, 1971.
12. Hunter, C. A. Jr. and Howard, W. F.: Am. J. Obstet. Gynec. **79**: 838, 1960.

13. Hwang, P., Guyda, H. and Friesen, H.: Proc. Natl. Acad. Sci., U.S.A.: 68: 1902, 1971.
14. Jaffe, R. B., Yuen, B. H., Keye, W. R. and Midgley, A. R.: Am. J. Obstet. Gynec. 117: 755, 1973.
15. Kumar, D.: Am. J. Obstet. Gynec. 84: 1323, 1962.
16. Loewenstein, J. E., Marez, I. K., Peak, G. T. and Daughaday, W. H.: J. Clin. Endocrinol Metab. 33: 217, 1971.
17. Manku, M. S., Nassar, B. A. and Horrobin, D. F.: Lancet 2: 1261, 1973.
18. Massani, Z. M., Sanguinetti, R., Gallegos, R. and Raimondi, D.: Am. J. Obstet. Gynec. 99: 313, 1967.
19. McKay, D. G., Merrill, S. J., Weiner, A. E., Hertig, A. T. and Reid, D. E.: Am. J. Obstet. Gynec. 66: 507, 1953.
20. McNatty, K. P., Sawers, R. S. and McNeilley, A. S.: Nature (London). 250: 653, 1974.
21. Morris, R. H., Vassalli, P., Beller, F. K. and McCluskey, R. T.: Obstet. Gynec. 24: 1964.
22. Nassar, B. A., Manku, M. S., Reed, J. D., Tyson, M. and Horrobin, D. F.: Brit. Med. J. 2: 27, 1974.
23. Peters, H., Byskov, A. G., Himelstein-Braw, R. and Faber, F.: J. Reproduc. Fertil. 45: 559, 1975.
24. Petrucco, O. M., Thomson, N. M., Lawrence, J. R. and Weldon, N. W.: Brit. Med. J. 1: 473, 1974.
25. Poindexter, A. N., Buttram, V. C. Jr., Besch, P. K. and Smith, R. G.: Fertil. Steril. 31: 273, 1973.
26. Pryse-Davies, J. and Dewhurst, C. J.: J. Pathol. 103: 5, 1971.
27. Segaloff, A., Sternberg, W. H. and Gaskill, C. J.: J. Clin. Endocrinol. 11: 936, 1951.
28. Schenker, J. G., Ben-David, M. and Polishuk, W. Z.: Am. J. Obstet. Gynec. 123: 834, 1975.
29. Tyson, J. E., Hwang, P., Guyda, H. and Friesen, H. G.: Am. J. Obstet. Gynec. 113: 14, 1972.
30. Yen, S. S. C., Ehara, Y. and Siler, T. M.: J. Clin. Invest. 53: 652, 1974.

See Figs. on Art Paper I