

## THROMBOSIS AND ORAL CONTRACEPTIVES

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Oral contraceptives were introduced for general use in 1960 and since then have been widely used all over the world. Seigal (1969) and Valrie (1976) remarked that relative risk of deaths from vascular occlusive disease was higher among women using oral contraceptives. The relationship between oral contraceptives and vascular occlusive disease is very controversial. Most of the studies carried out are retrospective and these show positive correlation between the two. Since these products are widely used, hence their safety is to be evaluated in great detail. We observed 2 cases of thrombophlebitis of the lower extremity within a short period of 3 months following use of the combined pill (Ovral and Voldys).

### CASE REPORT

#### Case 1

Mrs. N. aged 23 years C.R. No. 640, attended gynaec. O.P.D. on 30th March, 1977 with the complaints of pain on walking and swelling of the left leg for the last 5 days. She was taking Ovral for the last 3 months as a contraceptive measure. She had full term normal delivery in this hospital about a year back. There was no previous history suggestive of thrombophlebitis or diabetes.

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#### Examination

Average built young girl, B.P. 110/70 mm Hg. Pulse 84/mt. regular. Heart and Lungs were normal. Abdomen examination revealed no positive findings. On local examination there was a swelling of the left leg below the knee joint, pitting oedema, tenderness of calf muscle, Hoffman's sign +Ve. The right leg appeared normal. Investigations: Hb. 12 gm% TLC 8000/cu.mm. DLC poly. 61, L 23, M 2, E 9. Platelet count adequate, clotting time 4 minutes. Liver function tests: Serum bilirubin 0.4 mgm%, Serum Protein 6.8 gm%, albumin 3.2 gm%, globulin 3.2 gm%, fibinogen .4 gm%. Blood Alkaline phosphatase 3.3 units (Bodonsky's), Serum Amylase 160 units (Somogi). Sugar 70 mgm%.

Patient was put on complete bed rest, anti-coagulants, antibiotics and analgesics and she responded to the treatment.

#### Case 2

Mrs. K., aged 45 years, was admitted in this hospital on 9-5-1977 with history of irregular vaginal bleeding for the last 6 months. She used to get vaginal bleeding at interval of 15-22 days lasting for 7-10 days, with excessive flow. At the time of admission she was bleeding for the last 20 days. There was no past history suggestive of thrombophlebitis.

**Menstrual History.** Menarche at 14 years, past cycles, 3-4/30 days regular.

**Obstetric History.** Married 30 years back, sterile.

On Examination general condition was fair, anaemic, pulse 96/mt. regular. B.P. 110/70 mm Hg. Heart and Lungs were normal. Abdominal examination revealed no positive findings. On vaginal examination, uterus was nor-

mal in size, mobile, firm in consistency with clear fornices.

In view of her anaemia she was put on anti-anaemic treatment and hormones (Voldys) on 11-5-1977. Within a month of starting this drug she developed swelling of left leg starting from the foot and gradually spreading upwards involving the thigh. There was pain associated along with the swelling. Local examination revealed marked swelling of the left leg, pitting oedema +, marked tenderness of calf muscle, Hoffman's sign +ve. She was diagnosed as a case of thrombosis of the deep vein of the leg and was put on heparin, antibiotics, rest and analgesics. The hormones were immediately stopped. She responded to treatment. Investigations: Hb. 6 gm%, blood urea 19 mgm%, blood sugar 80 mgm%, serum electrolytes Na 142 meq/L, K 4.8 meq/L., Cl 100 meq/L. ECG Normal; Screening Chest, Normal. Alkaline phosphatase 3.5 units (Bodonsky's), Serum Amylase 170 units (Somogi).

#### *Review of Literature and Discussion*

Jordan (1961) reported the first case of pulmonary embolism following the use of 'Enovid' in a patient of endometriosis. Since then, many case histories have been published indicating that oral contraceptives increase the risk of vascular occlusive disease. An *ad hoc* committee in 1963 advised 'comprehensive and critical' studies to evaluate the association between the two. Number of retrospective studies were carried out. Vessey and Doll (1968) reported eight times more risk among users of oral contraceptives. Drill and Calhoun (1968) noted that incidence of thrombophlebitis among large group of women from local population and those women on oral contraceptives was same. Drill (1972) after reviewing the prospective study supported the above findings. An *ad hoc* Committee (1963), Advisory Committee Obstetrics and Gynaecology (1966) and report of W.H.O. Scientific group found no definite evidence on which to incriminate these hormones to cause thromboembolism.

British Committee on safety on drugs issued a recommendation in December, 1969 that Oral contraceptives containing less than 50 ugm Oestrogens should be normally prescribed. According to the W.H.O. scientific report, (1973) the risk of venous thrombosis is 3-4 times less owing to most of the contraceptives now with 50 ugm of Oestrogen. Valrie (1976) remarked that there was risk with the newer, lower dose pills—though it was less. In both of our patients the Oral Contraceptive administered had the content of the oestrogen 50 ugm.

The mechanism by which thromboembolism occurs during the use of oral contraceptives is not known. Oestrogens probably play a major part as has been pointed out by Daniel and Bloom (1968). There is an increase in factor II, III and V and decreased fibrinolytic activity. These changes are produced by Oestrogen, Mollinson and Howie (1970). There is maximal concentration of fibrinogen, plasminogen and spontaneous fibrinolytic activity during middle of the treatment and decrease towards the end of the treatment. This periodic imbalance can lead to thrombosis. According to the report of the W.H.O. scientific group (1971), increased response to aggregating agent adenosine diphosphate shown by platelets in women on oral contraceptives and in patient with manifest Occlusive vascular disease is due to abnormality in phospholipids in low density lipoprotein.

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