COMPARATIVE STUDY OF COPPER IUDs

by

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A decade of international research effort has been focussed on improvement in the performance of bioactive Copper IUD s. Copper T 200—the first of the Cu T devices to undergo clinical trials—has been variously modified during the last few years in an effort to improve efficacy or increase longevity. The copper surface area was increased in Cu T 380 A with the idea that this may have better and long lasting contraceptive efficacy. In Cu T 220 copper sleeves were used to overcome the problem of fragmentation of copper wire and to impart greater rigidity to the device (Population reports, 1973). Copper Y device of Dr. Soonawala was designed with the idea of minimising expulsions.

A comparative study of 4 copper devices-Cu T 200, Cu T 220, Cu T 380 and Cu Y device—was undertaken in the Peripheral Contraceptive Testing Unit of Indian Council of Medical Research, at Madurai to evaluate their performances.

Material and Methods

Two hundred and fifty women wearing Cu T 200 mm^2 device, 227 wearing Cu T 220, 281 wearing Cu T 380 A and 119 wearing Y Cu were taken up for the study. All these women were followed up at 1 month, 3 months, 6 months, 9 months, 12 months and 18 months.

Observations

Table I shows net cumulative termination rates at 6, 12 and 18 months. Continuation rate was lower with Cu Y and Cu T 380 A as compared to Cu T 200 and Cu T 220. Expulsion rate and termination rate due to expulsion were higher with Cu T 200 and Cu T 380 A. Incidence and removal rate for menstrual disorders were highest with Cu T 380 A.

Pregnancy

There were 2 pregnancies with Cu T 200 and none in the other groups (Table II). The lower pregnancy rate with Cu T 220 and Cu T 380 A might be due to the presence of Copper on the horizontal limb in the devices so that the zygote encountered inimical effect of Copper as soon as it entered the cornual region. Cu T 220 is atleast as effective in preventing pregnancy as Cu T 380 A, alteast upto a period of 18 months. So, the higher content and release rate of Copper in Cu T 380 A seems to be unnecessary for achieving contraceptive efficacy upto this period.

Expulsions

Event rate for expulsion was the least with Cu Y. Among the Copper T devices Cu T 220 had the least expulsion rate;

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TABLE I

Comparative Study of Copper Devices—Cu T 200, Cu T 220, Cu T 380 A and Cu Y Net Cumulative Termination Rate at 18 Months

	T. 200	T. 220	T. 380	Y Cu	T. 200	T. 220	T. 380	Cu Y	T. 200	T. 220	T. 380	Y Cu
	6 months				12 months				18 months			
Pregnancies	0.4	0.0	0.0	0.0	0.9	0.0	0.0	0.0	0.9	0.0	0.0	0.0
Expulsion	3.4	3.0	4.4	1.9	4.6	4.1	7.1	4.1	6.3	5.5	8.0	4.1
REMOVALS												
Menstrual disorder	2.1	2.5	6.4	4.8	4.1	5.0	10.2	6.9	5.2	5.8	12.6	6.9
Pain	0.2	0.5	0.4	0.9	0.2	0.5	0.4	0.9	0.2	0.5	0.4	0.9
Wants Pregnancy	2.1	2.6	0.8	0.9	3.4	4.4	4.9	1.9	8.6	7.3	8.1	4.4
Personal	7.2	9.8	8.1	4.8	9.7	14.5	13.7	7.9	12.6	18.1	18.2	10.4
Thread came adrift	0.0	0.0	0.0	7.6	0.0	0.0	0.0	12.2	0.0	0.0	0.0	17.0
Removal Rate	11.6	15.4	15.7	19.0	17.4	24.4	29.2	29.8	26.6	31.7	39.3	39.6
Closure Rate	15.4	18.4	20.1	20.9	22.9	28.5	36.3	33.9	33.8	37.2	47.3	43.7
Continuation Rate	84.6	81.6	79.9	79.1	77.1	71.5	63.7	66.1	66.2	66.8	52.7	56.3
No.	194	181	216	97	180	153	165	87	121	112	139	24
Months use	1352	1227	1491	672	2484	2223	2634	1234	3306	3018	3551	1475
Lost for follow up	2.7	2.5	3.1	2.2	3.9	3.7	4.9	3.5	5.2	5.3	5.5	5.1

TABLE II

Event Rates

	6 months				12 months				18 months			
	T. 200	T. 220	T. 380	Cu Y	T. 200	T. 220	T. 380	Cu Y	T. 200	T. 220	T. 380	Cu Y
Post Insertional bleeding	4.9	5.2	6.8	5.4	4.9	5.2	6.8	5.4	4.9	5.2	6.8	5.4
Menstrual Disorders	6.6	7.2	16.8	9.2	12.1	15.5	28.2	18.9	15.6	18.1	34.2	19.2
Leucorrhea	3.8	4.2	3.9	4.5	4.9	4.8	4.7	5.2	5.4	5.6	5.8	5.9
Pain	3.2	3.5	3.9	4.5	4.6	4.6	4.9	5.2	5.7	5.8	5.4	5.9
Pregnancy	0.4	0.0	0.0	0.0	0.9	0.0	0.0	0.0	0.9	0.0	0.0	0.0
Expulsion	5.6	4.2	5.9	1.9	7.8	5.3	8.7	4.1	9.5	5.3	9.6	4.1

expulsion rates of Cu T 200 and Cu T 380 A were similar (Tables I and II). The theory that the added rigidity imparted by Cu sleeves on the vertical limb would reduce the expulsion rate of T devices gains support from these clinical observations.

Side Effects

Menstrual side effects were more common with Cu T 380 A. Menstrual disorders were least among Cu T 200 users. Irrespective of the device, incidence of menstrual disorders decreased with increasing duration of device in utero (Table II). Removal rate for menstrual disorders paralleled the incidence of menstrual disorders (Table I). Other minor side effects like abdominal pain, backache, leucorrhea did not vary with the type of device (Table II).

Removal Rate

Removal rate for menstrual side effects were highest with Cu T 380 A, almost thrice that of Cu T 200; Cu T 220 and Cu T 200 had almost similar removal rates for menstrual disorders. Removal rates for personal reasons—mainly lack of confidence in IUD and planning pregnancy were similar in all the devices. The thread attached to Soonawala's device quite often got detached. At times patients brought the expelled thread with the knot still intact. Whenever the thread was missing we sounded the uterine cavity to confirm the presence of the device in utero and removed the same with either a straight artery forceps or endometrial biopsy curette. This accounted for 17% of removal of Soonawala device and contributed to lower continuation rate with Cu Y (Table I).

Discussion

Among the four devices under investigations, Cu T 200 seemed to have fared better than Cu T 380 A and Cu Y. Clinical trials from India and elsewhere have conclusively proved that contrary to the earlier belief Cu T 200 retains its contraceptive efficacy atleast upto a period of 4 years (Orlans 1974; Malhotra *et al* 1977; Prema *et al* 1978). Thus the need for removal and reinsertion every 2 years does not exist and preclude the wide use of Cu T 200 in developing countries.

Cu T 220 appeared to be a safe and effective contraceptive. Side effects with this device were similar to that seen with Cu T 200. Larger trials might be needed to find out whether the small differences in pregnancy and expulsion rates are consistantly seen. Contraceptive efficacy and side effects with Cu Y device was comparable to Cu T 200, but Cu Y had a lower expulsion rate. The main disadvantage with Cu Y device was the thread coming a drift. It is neither feasible nor desirable to leave in utero an untailed device and keep sounding the uterine cavity during each followup visit to ensure that the device is in utero. Removal of devices because of loss of thread accounted for the poor continuation rate with Cu Y. If this snag is overcome, it is possible that this indegenously manufactured device may have continuation rates comparable to Cu T 200.

Use of Cu T 380 A was associated with higher incidence of menstrual side effects and higher removal rate for menstrual side effects. Timonen (1976) had demonstrated that among Cu T 200 device wearers the release rate of Cu was 127 μg/day in those who had menorrhagia but only 47 μg/day in those with normal menstrual cycle. The higher release rate of Cu from Cu 380 A may therefore be the reason for the higher incidence of men-

strual disorders in Cu T 380 A wearers.

The hypothesis that Cu release rate and contraceptive efficacy are related to each other has been challenged in the last few years. Gibor (1973) showed that release rate of copper from Cu T 200 decreased from 55.0 μg/day at 6 month to 8.9 μg/day at 21 months without affecting the contraceptive efficacy. Marangoni *et al* (1976) showed that inspite of large differences in release rate of copper there was no difference in pregnancy rates between Cu T 30, Cu T 120, Cu T 200 and Cu T 340 when copper coil was evenly distributed throughout the uterine cavity. Thus, it is possible that Cu T 380 may not be a more effective contraceptive than Cu T 200. The second theoretical advantage with Cu T 380 A was that it may retain its contraceptive efficacy for periods longer than 4 years. In India long-term follow-up of cases beyond 4-5 years is extremely difficult. The need for removal or loss of contraceptive efficacy after 4 years will atleast ensure that women do have a check-up once in 4 years. The potential hazards of wearing a bioactive device for periods longer than 5 years and never having a check-up is an effective deterrant against use of IUDs which retain contraceptive efficacy for upto a decade. Thus, Cu T 380 A does not seem to possess any practical advantage over Cu T 200.

Parallel clinical trials with Cu T 200, Cu T 220, Cu T 380 A and Cu Y showed that:

1. Cu T 200 was a fairly effective contraceptive with minimal side effects.
2. Cu T 220 was more effective in preventing pregnancy. It had the least expulsion rate among Cu T devices. Menstrual side effects though more common with Cu T 220 than with Cu T 200 were less when compared to Cu T 380.
3. Cu T 380 was an effective contraceptive but high expulsion rate and high incidence menstrual disorders lead to poor continuation rate.
4. Cu Y was an effective contraceptive with minimum expulsion rate. Menstrual disturbances were not very common. The detachment of the thread while device was in utero contributed to maximum removals and poor continuation rate.

References

1. Copper IUDs—performance upto date Population reports Series B No. 1, 1973.
2. Gibor
Quoted in Population reports Series B. No. 1, 1973.
3. Malhotra, U., Saxena, N. C., Choudhury, S. D. and Tejuja, S.: Proc. of 7th Asian Congress in Obst & Gynec. Bangkok 1977 pp 453.
4. Marangoni, P., Rodriguez, G. and Faundes A.: Contraception 13: 715, 1976.
5. Orlans, F. D.: Contraception. 10: 543, 1974.
6. Prema, K., Gayatri, T. L. and Philips, F. S.: J. Obst & Gynec. India. 28: 949, 1978.
7. Timonen, H.: Contraception. 14: 25, 1976.

girl) died of thalassaemia and 1 daughter was still suffering from the disease. Her parents were well.

On examination, she had slight anaemia. Liver and spleen were not palpable. On 14-5-71, she delivered spontaneously. Bood examination showed Hb. 10 Gms. per cent, hypochromia and reticulocyte one per cent. There was no foetal haemoglobin. X-ray skull showed no abnormality.

Case 2

Mrs. S. M., primigravida, aged 24 years and carrying 20 weeks was admitted on 27-7-72 in Eden Hospital complaining of palpitation and swelling of legs.

She suffered from splenomegaly since her childhood when she was treated by haematologist and diagnosed as a case of Hb. E-thalassaemia. There was no significant family history. General examination showed severe anaemia. Liver and spleen were respectively 2 and 4 fingers breadth palpable below the costal margin. Anaemia was microcytic hypochromic in type with Hb. 4 Gms. per cent and marked anisocytosis and poikilocytosis. Foetal haemoglobin level was 18 per cent of total. Bone marrow was hyperplastic. X-ray showed some evidences of demineralisation.

To keep Hb. level to about 8 Gms. per cent, she was given, at intervals, 2100 ml. blood transfusion. She also received folic acid. On 9-12-72 she gave birth to a fresh stillborn male baby weighing 1.7 Kg. She was advised splenectomy for hypersplenism.

Case 3

Mrs. J. G., a 2nd gravida, aged 22 years, was admitted in Eden Hospital on 9-10-72 while carrying 16 weeks for severe anaemia. She had 1200 ml. blood transfusion in the puerperium of her last pregnancy in January, 1971, though she had no abnormal haemorrhage. The baby was boy, alive and well.

Examination showed severe anaemia. Liver and spleen were palpable beneath the costal arch 1 finger and 2 fingers breadth respectively. Anaemia was microcytic hypochromic in type with Hb. 2.5 Gms. per cent, marked anisocytosis, poikilocytosis, and basophilic stippling. There were 10 normoblasts per 100 W.B.C. In consultation with haematologist she was treated with repeated small blood transfusions (900 ml), iron and folic acid. As the anaemia was found refractory to treatment, electrophorectic study was done on 17-2-73 which revealed the case as one of Hb. E-thalassaemia.

She gave birth to a live premature female on 22-2-73 which died on 26-2-73.

Case 4

Mrs. U. D., a third gravida aged 24 years was admitted in Eden Hospital on 12-10-72 while carrying 28 weeks complaining of extreme weakness. She had no living child, the first baby died one hour after birth of asphyxia and the second child was stillborn in a peripheral hospital. Her family of parents, brothers and sisters were all well.

She had mongoloid facies, moderate anaemia and just palpable spleen. Her Hb. was 6.5 Gms. per cent and peripheral smear showed marked hypochromia, anisocytosis, poikilocytosis and occasional myelocytes. Marrowgram showed normoblastic hyperplasia. Radiograph of skull showed faint striations (hair-on-end appearance). Foetal Hb. constituted 12.5% of total. Electrophoresis revealed it to be intermediate type of thalassaemia.

She was treated with folic acid and 600 ml. blood transfusion.

On 22-12-72 an emergency caesarean section was done for foetal distress. A live female baby was born weighing 3.2 Kg.

N.B. She was again admitted with her next pregnancy in 1974 when she received 900 ml. blood transfusion and caesarean section with tubal sterilisation was done.

Case 5

Mrs. J. M., primigravida, aged 24 years and carrying 28 weeks was admitted in Eden Hospital on 27-1-73 complaining of palpitation and weakness. Her younger brother was thalassaemic.

She was severely anaemic and had just palpable spleen. Anaemia was microcytic hypochromic having Hb. 5.8 Gms. per cent. Reticulocytes numbered 20 per cent, and there were target cells. Foetal haemoglobin was 20% of total. Marrowgram showed erythroid hyperplasia. Normoblasts of various stages increased. Electrophoretic study showed intermediate type thalassaemia.

She was treated with blood transfusions (900 ml.) and folic acid. On 5-2-73, she delivered prematurely a live baby weighing 1.4 Kg. The baby died after 24 hours.

Case 6

Mrs. S. P., third gravida, aged 24 years and carrying 28 weeks was admitted in Eden Hospital on 9-5-73 complaining of palpitation, weakness and oedema, not responding to treatment outside.

In her first and second pregnancies, she attended the antenatal clinic of her village hospital regularly. She suffered from refractory, oedema in both the pregnancies and delivered prematurely stillborn babies in both her first and second pregnancies.

She had mongoloid facies and marked pallor and oedema. Haemolgobin was 5.5 Gms. per cent—microcytic hypochromic in type. Foetal haemoglobin was 26.3 per cent of total. Marrowgram showed hypercellular marow with extreme normoblastic hyperplasia. Radiograph of skulll showed slight inrease of diploic spaces with granular appearance. Electrophoresis cliniched the diagnosis to Hb. E-thalassaemia. She was treated with blood transfusions (600 ml.) and folic acid. She delivered prematurely on 26-6-73 a live male baby weighing 1.8 kg. The baby died on the 4th day.

Comment

Incidence of thalassaemia has been reported to be varying between 4 to 20 per cent in Mediterranean countries (Willoughby, 1973). Chatterjee (1968) has reported the incidence of thalassaemia in Bengalees as approximately 3.7 per cent. In Eden Hospital, out of nearly 50,000 obstetric admissions, we have met with 6 cases of thalassaemia in association with pregnancy.

During pregnancy, thalassaemia is diagnosed by relevant history, splenomegaly, haemogram, marrogram, roentgenogram and electrophoresis. Clinical features vary widely depending upon the nature and extent of abnormality in the globin moiety in a particular subject.

In heterozygous inheritence (trait) expressed as thalassaemia minor or milder forms as thalassaemia minima, the subjects are mainly symptomless. Diagnosis is made by a chance blood examination which reveals low haemoglobin and high red cell count. The subjects have foetal haemoglobin in the region of 1-4 per cent but sometimes as high as 40 per cent.

Intermediate grade thalassaemia also is characterised by anaemia and polycythaemia. The subjects may show hepatosplenomegaly and typical bony changes like "hair on end" in the enlarged diploe of skull bones and osseous demineralisation as found in the thalassaemia major.

In homozygous state, foetal haemoglobin is present to the extent of about 50-90 per cent and there are varying grades of anaemia, severe microcytic hypochromic anaemia with anisocytosis, poikilocytosis, polychromasia and characteristic target cells. Haemoglobin A_2 is raised in all cases of thalassaemia minor and some cases of thalassaemia major.

In heterozygous conditions when two dissimilar abnormal haemoglobins are inherited, the symptoms are variable. The clinical and haematological features of Hb. E-thalassaemia are almost same as thalassaemia major but less serious and the subjects may cross to adult life.

Diagnosis may be particularly difficult in mild varieties. Blood picture may be consistent with iron-deficiency anaemia. Failure of response to haematinics, suspicion and special tests of Singer and electrophoresis clinches the diagnosis. There is preponderance of foetal haemoglobin in homozygous state and Hb. A_2 in thalassaemia minor. In Hb. E-thalassaemia, E comprises 60-80 per cent of the total. In the present series of 6 cases, 2 were known thalassaemics, 1 had history of thalassaemia in the family while haematinic-resistant anaemia (mongoloid facies in 2) and subsequent special examinations clinched the diagnosis in 3 others.

Obstetric performance of thalassaemic patients have not yet been properly studied. Successful pregnancy in thalassaemic is rare and once pregnancy has occurred, effort must be made to keep the level of haemoglobin to about 8 gms. per cent. Repeated blood transfusion, though having no effect on the course of the disease, temporarily increases the general well-being of the patient (but there is danger of haemosiderosis to develop). As the anaemia is refractory to iron-therapy, iron may be dangerous to precipitate haemosiderosis. The over-proliferative (though defective) erythropoiesis may contribute to produce folic acid deficiency and folic acid therapy may help.

Thalassaemics are very prone to infection which may precipitate haemolytic crisis too. Infection must be prevented. There is doubt whether pregnancy can provoke haemolytic crisis. In none of our 6 cases was there any haemolytic crisis, but anaemia was exaggerated during later weeks of pregnancy.

Splenectomy might benefit patients if haemolysis is marked, if there is evidence of excessive destruction of transfused blood or there is hypersplenism. In 1 of our 6 cases (case 2), splenectomy was advised because of hypersplenism.

Labour is to be conducted taking all precautions for a severely anaemic mother. Since haemolytic crisis may occur, large quantity of blood transfusion may be necessary at the time of delivery There is no scope for caesarean section for thalassaemia per sé. In 1 of our cases, caesarean section was done for superadded foetal distress. Four out of 6 babies had perinatal death.

Pregnancy with thalassaemia is a dangerous association because of the highly increased risk of maternal and foetal mortality. Until and unlss ready methods are available which will permit manipulation of gene, thalassaemia can not be controlled. If marriage between two heterozygous traits can be prevented by premarital examination, the occurence of the disease can be controlled but this will mean marriage between a normal and a heterozygous which will produce trait in community. The possibilities may be summarised as follows:

(i) If the affected person marries one with same trait, about 75 per cent children will be affected and 25 per cent will be thalassaemia major.

(ii) If an affected person marries a normal person, about 50 per cent children will be affected.

Question of induction of abortion and/or permanent sterilisation will definitely arise, particularly when both the parents are thalassaemic.

References

1. Britton, C. J. C.: Disorders of the Blood, ed. 10, J. & A. Churchill Ltd., London, 1969.
2. Chatterjee, J. B.: Cal. Med. J. 65: 117, 1968.
3. Dacie, J. V.: The Haemolytic Anaemias, Part I, ed. 2, J. & A. Churchill Ltd., London, 1970.
4. Willoughby, M. L. N.: Text Book of Paediatrics by Forfar, J. O. and Arneil, G. C., ed. 1, Churchill Livingstone, Edinburgh & Lond. 1973.