SERUM COPPER AND CERULOPLASMIN IN WOMEN USING COPPER CONTAINING INTRA-UTERINE CONTRACEPTIVE DEVICE

by

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SUMMARY

The present study was undertaken to find out the copper loss from CUT 200 over the period of its use and also to find out the systemic spillage of copper which could be harmful to the body.

Study group included 118 patients studied over a period of 1 year (March 1980 to April 1981) and was further divided in two groups. In the first group results were analysed considering the levels during that particular month. In the 2nd group serial estimations were done. Few devices were removed within 2 months and 1 year of insertion and were weighed to find out the systemic spillage.

Serum copper and ceruloplasmin values estimated in control group were 109.96 ± 16.76 mg/100 ml. and 32.29 ± 4.93 mg/100 ml. respectively. There was no significant change in levels of copper and ceruloplasmin in different months of use CUT 200 and also in serial estimations when compared to control. The release rate per 24 hours for first 2 months was 49.0 ± 19.92 ug while it was 27.16 ± 3.93 ug for 1 year which is only 1-2% of daily copper intake.

The study concludes CUT 200 is harmless to the body and its efficacy goes on decreasing with the period because of the constant loss of copper from the device.

Introduction

The new generation of medicated intrauterine contraceptive devices were introduced in search of an ideal spacing contraceptive which is safe with minimal side effects and maximum antifertility action.

The incorporation of 120 mg of copper in the device with release of 20-25% of this amount during first year of life raises the question of its systemic absorption and subsequent deposition in various organs leading to its harmful effects. In this con-

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text, the present study was undertaken to study the following:

1. Normal copper and ceruloplasmin values in Indian women.

2. Systemic spillage of copper which can be harmful because of its use for a longer duration.

3. Copper loss from the device and its relationship with the duration of device in sites.

Material and Methods

This study was carried out for a period of one year (March 1980 to April 1981). The cases were selected from patients attending OPD and family planning clinic, Deptt. of Obstetrics and Gynaecology JNMCH, AMU, Aligarh. A total of 142 patients were studied and divided into two groups:

I. control group: Twenty-four normal, non-pregnant women of reproductive age group were free from any evidence of disease were included in this group.

II. study group: This group includes patients using copper T-200 as a contraceptive method. This group is further subdivided into two groups:

(a) In this group estimations were done 1 month (26), 2 months (6), 3 months (15), 6 months (21), 9 months (33), 12 months (21) after insertion of device and results were analysed considering the levels during that particular month.

(b) In this group were included the cases who came for follow-up and whose serial estimations were done:

(i) In 8 cases estimations were done before inserting the device, after 1 month and 2 months of insertion.

(ii) In 15 cases, the estimations were done before insertion of device, after 2 months and 3 months of insertion.

(iii) In 10 cases, the estimation were done before insertion of device, after 2 months and 6 months of insertion.

Blood samples were taken between 6th-10th day of menstruation. All cases taken were interval cases i.e., 3 months after delivery and abortion.

Few devices were removed within 2 months and 1 year of insertion and were weighed to find out the average release rate.

Method

The estimation of ceruloplasmin in serum was done by the method of Ravin (1961). Principle of this method lies in finding the extent of oxidation of PPD (Paraphynylene diamine dihydrochloride) by serum ceruloplasmin in 0.4 M sodium acetate buffer, PH 5.5 and this was taken as a measure of concentration of this metelloprotein.

The optical density measured near 530 nm was converted directly into mg% of ceruloplasmin in serum by multiplying it with Holmberg Lamell factor which is 37.5.

Concentration of ceruloplasmin in serum (in mg%) = (O.D) 530 nm X 87.5. The copper content of the serum was determined using the equation.

$$\text{Concentration of copper in serum (in mg\%)} = \frac{3.20 \times \text{ceruloplasmin in mg\%}}{0.94}$$

Observations

Maximum number of cases (79.66%) who opted for CUT 200 as contraceptive device were of age group 21-30 years (79.66%), 31-40 years (15.25%) and in the age group under 20 years (5.08%). 30.51% of cases were second para, 27.12% were fourth para or more, 24.48% cases were third para and only 17.08% were first para.

Discussion

Serum copper ceruloplasmin values estimated in control group were 109.96 ± 10.76 mg/100 ml and 32.29 ± 4.93 mg/100 ml respectively. These values are somewhat near to values of earlier workers like like Lahey *et al* (1953), Wintrobe, Cartwright and Gubler (1953).

The above Table shows that there is no statistical significant alteration in mean serum values of copper and ceruloplasmin in any of the months following insertion when compared to control.

The above Table shows that there was no statistical significant change in mean serum values in cu and cp even in serial estimation in different cycles.

The above Table shows that the copper loss within 2 months of insertion was 2 ± 1.15 mg and the release rate was 49.0 ± 19.92 mg/24 hours. Cooper loss within one year of insertion was 10.2 ± 0.75 mg and the release rate was 27.16 ± 3.03 ug/24 hours. (Vashist 1979; Ravin 1961; De Jorge *et al* 1965 and Burzek *et al* 1979).

In the present study it has been noted that there is no significant change in levels of copper and ceruloplasmin values in different months of use of CUT 200 when compared with the levels of control. In a small group of patients in whom serial estimation were done, also showed no statistical difference in mean values of copper and ceruloplasmin.

TABLE I

Statistical Analysis or Values of Serum Copper ceruloplasmin in Different Months Following CUT and Their Comparison With Control (Group I and II A)

Months following insertion	No. of cases	Mean serum cu levels mg/100 ml.	Mean serum cp values mg/100 ml.	Comparative significance between	df. P	Remarks
1st	26	100.308 ± 16.956	32.0 ± 5.40	Control and 1st month	48>0.05	NS
2nd	06	102.0 ± 4.817	30.0 ± 1.41	Control and 2nd month	28>0.05	NS
3rd	15	108.53 ± 11.946	31.867 ± 3.52	Control and 3rd month	37>0.05	NS
6th	21	106.386 ± 12.646	30.480 ± 3.5	Control and 6th month	43>0.05	NS
9th	33	106.3 ± 15.81	31.21 ± 4.59	Control and 9th month	55>0.05	NS
12th	21	104.76 ± 14.356	30.7 ± 4.17	Control and	43>0.05	NS
Control	24	109.96 ± 16.76	32.29 ± 4.93	—	—	—

TABLE II

Statistical Analysis of Values of Serum Copper Ceruloplasmin in Serial Estimations (Group IIB)

Group	Period in months following insertion	No. of cases	Mean serum Cu values	Mean serum cp values	Comparative significance between	df. p	Remarks
I	Before insertion	8	87.875 ± 34.320	29.500 ± 03.891	—	—	—
II	1st	8	109.25 ± 11.915	32.00 ± 35.05	Before Insertion and 1st	14>0.05	NS
	2nd	8	105.625 ± 11.538	31.000 ± 3.381	Before Insertion and 2nd	14>0.05	NS
	Before insertion	15	82.260 ± 23.39	25.733 ± 3.305	—	—	—
	2nd	15	83.933 ± 24.642	26.600 ± 3.019	Before Insertion and 2nd	28>0.05	NS
	3rd	15	80.333 ± 23.218	25.600 ± 2.746	Before Insertion and 3rd	28>0.05	NS
III	Before insertion	10	91.20 ± 12.299	26.800 ± 3.645	—	—	—
	2nd	10	93.20 ± 12.299	27.400 ± 2.836	Before Insertion and 2nd	18>0.05	NS
	6th	10	92.40 ± 8.262	27.100 ± 2.469	Before Insertion and 6th	18>0.05	NS

TABLE III

Copper Loss From CUT Devices Within 2 Months and One Year of Insertion

Period	No. of cases	Copper loss (mg)	Range	Release ug/24 hrs.
Within 2 months	4	2 ± 1.15	1.0 - 3.0	49.0 ± 19.92
1 year of insertion	6	10.2 ± 0.75	9.0 - 12.0	27.16 ± 3.03

Our findings are similar to those of Hagenfeldt (1972) who also did not show any significant change in the mean values of serum copper. However, there values were higher than our values. This could be because the sample of population studied was different and the method used for estimation too was different (neutron activation analysis), Brain Daunter and Elestein (1973) also did not find any significant change in levels of serum copper in their study.

Copper loss from the device within first 2 months was 2.0 ± 1.15 mg and 10.2 ± 3.03 mg for one year use of device. The release rate per 24 hours for first two months was 49.0 ± 19.92 μg while it was 27.16 ± 3.03 μg/24 hours for one year. These values are near to those of Hagenfeldt (1972). She has also reported a release of 28.7 μg/24 hours in one of her studies which are also near to our values. The release within 2 months of insertion was definitely more than that for 1 year. This observation is in accordance with that of Hagenfeldt (1972) who also reported high release rate for first 2 months.

Conclusion

From the study we conclude:

1. The copper containing lu CDS are harmless even if kept in uterus for a longer period. There is no significant systemic spillage of copper from the device, as the amount of copper released per 24 hours in one year (27.16 ± 3.03 μg/100 ml) constitutes only 1-2% of copper intake per day estimated to be necessary to maintain a normal copper balance.

2. Since the copper is being constantly lost from the device its efficacy goes on decreasing with the period since the contraceptive effect is only through the copper ions.

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