

COMPARATIVE STUDY OF TREATMENT OF MENORRHAGIA FOLLOWING CuT INSERTION BY ANTIPROSTAGLANDINS AND ANTIFIBRINOLYTIC AGENTS

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SUMMARY

Twenty eight patients suffering from menorrhagia following CuT insertion were evaluated. Each patient was studied for four-cycles and the response noted in terms of total blood loss, duration of bleeding and pelvic pain. No treatment was given in cycle I, in cycle 2 Aminocaproic acid (Tab. Hexalan-500 mg) thrice daily was given while in cycle 3 antiprostaglandin (Tab. Brufen 400 mg) thrice daily was given. In cycle 4 a placebo was given.

With antifibrinolytic agent the reduction in blood flow was significant 67 ± 13.6 ml ($p < 0.001$) while it was 96 ± 13.6 ml with antiprostaglandin therapy ($p < 0.01$). Duration of flow was not significantly reduced by any therapy. Though the reduction of blood flow was significant with antifibrinolytic agents, the subjective relief in pelvic pain and discomfort was more with antiprostaglandins.

Antiprostaglandin treatment is therefore suggested first and if this fails to reduce blood loss than antifibrinolytic treatment should be tried. However, further trials are advocated to assess the synergistic effect to the two treatments.

Introduction

Excessive menstrual blood loss is a common complaint and a major reason of anaemia in woman using Copper T. It is well established from controlled clinical investigations with quantitative assessments that treatment with antifibrinolytic drugs decreases menstrual blood loss (Nilson and Rybo, 1971; Callendar *et al*, 1979). Recently treatment

with prostaglandin inhibitor has also proved effective in diminishing bleeding in patients with menorrhagia associated with Copper T (Guilleband *et al*, 1978; Rybo *et al*, 1981).

In this study a comparison of reduction of bleeding by antiprostaglandins and antifibrinolytic agents is presented.

Material and Methods

Thirty two patients complaining of excessive menstrual blood loss following Copper-T insertion were evaluated. Of

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these 28 were found to be suffering from menorrhagia (defined as blood loss more than 80 ml). One female was excluded as she had her Copper-T removed before the end of the study. Thus the total number of patients studied was twenty seven. Eleven patients had Copper-T inserted at least 6 months previously, the rest had it for more than a year. All these women were parous with a mean age of 28 years (ranging from 19 to 36 years). They all had normal findings on pelvic and general examination.

All these women were studied during four consecutive menstrual cycles. In the first cycle their menorrhagia was assessed. In the second cycle they received oral antifibrinolytic agent (Aminocaproic Acid marketed as Tab. Hexalan, 1 tab. thrice daily for 5 days). In the third cycle antiprostaglandin agent (Brufen 1 tablet thrice daily) was given for 5 days. A placebo (vitamin C) was given in the last cycle.

The following responses were noted in each cycle—

(i) Total blood loss; (ii) Number of days of bleeding; (iii) Pelvic pain.

No iron supplements were used during the trial. A haemoglobin assessment was performed at the beginning and then at the end of the study for all the patients.

The women were given seven consecutively numbered polythene bags for each menstrual cycle in which the used

standard size sanitary pads were collected daily. Bag No. 1 was used from onset of menses to the next day. Bags 2-6 were during successive days as required.

The daily blood loss was calculated by weighing the pads. The blood loss was evaluated by noting the increase in weight of the pad. Every 1 gm increase in weight accounted for a blood loss of 1.0 ml.

Results

(i) *Menstrual blood loss*: Mean blood loss during the placebo treated cycle and during no treatment cycles was 131 ± 14 ml and 133 ± 15 ml respectively.

There was significant reduction in blood loss when the candidates took antifibrinolytic agents. The mean blood loss being 67 ± 13 ml. When the patients took antiprostaglandin the mean blood loss was 96 ± 13 ml.

(ii) *Duration of Flow*: Neither the antifibrinolytic agent nor the antiprostaglandin significantly reduced the number of days of bleeding. During the pre-treatment and placebo cycles, the duration of flow was 5 ± 2 and 6 ± 2 days respectively. In cycle 2 it was 4 ± 1 and in cycle 3 it was 5 ± 1 days.

(iii) *Pelvic pain*: Seventeen of our patients complained of pelvic pain. This pain was not relieved by placebo or Hexalan. When given Brufen, fifteen of

TABLE I
Showing Mean Blood Loss in Different Cycles

Cycles	Mean blood loss in ml.	Significance of differences as compared with placebo
1. Control pre-treatment	133 ± 15.6	
2. Antifibrinolytic	67 ± 13.6	$P > 0.001$
3. Antiprostaglandin	96 ± 13.4	$P > 0.01$
4. Placebo treatment	131 ± 14.8	$P > 0.05$

TABLE II
Showing Duration of Menses in Difference Cycles

Cycles	Duration of menses in days	Significance of difference as com- pared with placebo
1. Control pre-treatment	5 ± 2	
2. Antifibrinolytic	4 ± 1	P > 0.05
3. Antiprostaglandin	5 ± 1	P > 0.05
4. Placebo treatment	6 ± 2	

these seventeen patients had marked relief in their pain.

(iv) *Subjective effect of therapy:* Restriction of activity, pelvic pain and discomfort were common complaints of these Cu.T users. Eleven patients reported subjective relief of varying degree in cycle 3, while in cycle 4, subjective relief was obtained only by four patients.

(v) *Haematology:* Although no iron supplements were used in the study, the mean haemoglobin concentration remained the same i.e. 9.6 gm per cent.

Discussion

Spacing of family and family planning are two very important goals of India. Due to poverty and poor socio-economic conditions the certainty of alive baby reaching adulthood is not very much. Most women in these adverse environment are not keen to undergo sterilisation. Thus Cu.T or any IUCD is popularly accepted especially amongst the educated masses. Menorrhagia, pelvic pain and discomfort affect its popularity adversely. Menorrhagia till recently was treated with good diet and iron supplements. These were not really useful and the over-worked Indian women usually had her Cu.T removed and sooner or later another baby was conceived.

Excessive and prolonged menstrual bleeding is the major complication associated with IUCD and the main reason for having it removed (Cohen and Gibor, 1980).

The intense fibrinolytic activity in the endometrium around the IUCD (Larsson *et al*, 1975; Bonner *et al*, 1976) and the reduction in menstrual blood loss during antifibrinolytic therapy (Nilsson and Rybo, 1971; Cohen and Gibor, 1980) suggest that increased fibrinolysis in the endometrium could be at least one reason for heavy blood loss in IUCD users.

The human endometrium contains several prostaglandins which may play a role in the regulation of menstrual bleeding (Abel, 1979). This theory is supported by reports of increased endometrial concentrations of PGE or PGE₂ in women with dysfunctional uterine bleeding (Haynes *et al*, 1980; Smith, *et al*, 1981).

The IUCD seems to increase endometrial prostaglandin level (Miller and Kasonde, 1976), partly due to prostaglandin production by macrophages accumulating on the surface of the device. The significant decrease in blood loss in women with an IUCD during the administration of prostaglandin synthesis inhibitors eg. naproxen (Davies *et al*, 1981; Rybo *et al*, 1981) ibuprofen (Roy and Shaw, 1981) suggest that prostaglandin

may also be important in IUCD—induced menorrhagia.

In the presence of two effective treatments available for reduction of menstrual bleeding in IUCD users, the question arises as to which regimen is preferable.

Our comparison shows that antifibrinolytic agents decrease bleeding more than prostaglandin inhibitors. However the number of days of flow is unaffected. Pelvic pain and discomfort, experienced frequently by IUCD users responded significantly to antiprostaglandins.

Antiprostaglandin treatment is preferable economically also. On the basis of these comparisons we would suggest antiprostaglandin treatment to be tried first. If this fails to reduce blood loss satisfactorily, then antifibrinolytic agents should be tried.

Further studies are required to assess the synergistic effect of combination of antiprostaglandin and antifibrinolytic agents for better results in terms of menorrhagia, pelvic pain and discomfort, thereby reducing the major side effects of IUCD and further increasing its acceptability to the users.

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