TREATMENT OF EXCESSIVE UTERINE BLEEDING WITH CAPRAMOL

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Introduction

In clinical practice there is a need for adequate treatment of excessive menstrual blood loss to cure or prevent iron deficiency anaemia and to diminish the individual discomfort caused by a heavy blood loss. In 1959 Okamato described a synthetic amino-acid i.e. epsilon amino-caproic acid (EACA), which was useful for controlling various haemorrhagic conditions. It is a potent inhibitor of the activation of plasminogen to plasmin and consequently also of the breakdown of the fibrin polymer to its metabolities. In addition to its anti-fibrinolytic effect, EACA inhibits other endopeptidases e.g. chymotrypsin (Austen) also inhibits histamin release, therefore it is an anti-inflammatory and anti-allergic agent. It is known that the content of plasminogen activators is high in endometrial tissue (Albrechtsen, O., 1956, 1963). The concentration of these activators is highest on the first day of menstruation. The preliminary results of Rybo (1964) indicate that in functional menorrhagia, there is an increased endometrial content of these tissue activators for plasminogen. This may affect the coagulation and hence increase the loss of blood. Consequently, in menorrhagia there is theoretical justification for the use of EACA which inhibits the activation of plasminogen. Nilsson, *et al* (1961), Nilsson, *et al* (1964), Nilsson, (1964) and Gennser (1964) have shown that in menorrhagia reduction in the loss of blood can be obtained by administration of EACA.

Material and Method

The study was carried out in Government Hospital for Women, Amritsar, from May 1975 to December, 1975. Seventy patients admitted with excessive uterine bleeding were treated with capramol. The chief complaints of these patients were menorrhagia, polymenorrhagia and irregular profuse bleeding. Out of these, 60 patients were of dysfunctional uterine bleeding, 9 were with fibroid uterus and 1 of inversion uterus. Each patient was asked for detailed history and subjected to full clinical examination which was recorded on a proforma. Routine investigations of haemoglobin, urine, BT and CT were carried out in all patients.

Forty-six patients were put on oral capramol. Dose given was 5 gm/6 hourly for a maximum of 5 days. The other 24 patients were given intravenous capramol in the dosage of 2.5 gm/8 hourly for a maximum of 5 days. The drug was discontinued as soon as the bleeding was controlled. No other drug was used simultaneously to check the bleeding.

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The results were classified as follows:

Excellent: When the bleeding stopped totally within 48 hours of administration of drug.

Good: When bleeding reduced quite a bit within 48 hours and stopped totally in 72 hours.

Fair: When it took 3-4 days for the bleeding to stop completely.

Poor: When there was no response even with maximum safe limit of drug i.e. 5 gm/6 hourly for 5 days or bleeding recurred after stoppage of drug.

Side effects in the form of nausea, diarrhoea, abdominal pain etc. were noted. Haemoglobin levels of the patients were also built up during the course of treatment with blood transfusions and intramuscular iron injections to correct the anaemia caused by excessive bleeding.

Observations

Out of 70 patients kept under trial, 56 (80%) were of the age group of 30 to 50 years. Two patients were, unmarried under the age of 20 years as given in Table I.

TABLE I
Age Incidence

Age group in years	No. of patients	Percentage
Below 20 years	2	2.8
21–30 years	6	8.6
31–40 years	32	45.7
41–50 years	24	34.3
51 and above	6	8.6

Duration of bleeding was variable as shown in Table II. Thirty-two had profuse vaginal bleeding of 5 to 10 days. Thirty-five had menorrhagia, 29 patients had irregular bleeding and 6 were with polymenorrhagia. Two patients of the series were unmarried girls with puberty menorrhagia. Out of these two girls one had excellent and other had good response to capramol.

TABLE II
Duration of Bleeding

Duration of bleeding	No. of patients	Percentage
1– 4 days	17	24.3
4–10 days	32	45.7
11–20 days	10	14.3
21 and more	11	15.7

Sixty-eight out of 70 patients were married, and this disorder was more common in multiparous women as shown in Table III.

TABLE III
Parity

Parity	Number of patients	Percentage
Nullipara	4	5.9
One child	4	5.9
2-5 children	42	61.8
6-10 children	18	26.4

Regarding the dosage of capramol required to arrest the bleeding, it was variable as given in Table IV.

TABLE IV
Duration of Drug Given

No. of days	Number of patients: Oral administration	Number of patients: Intravenous administration	Total
1	9	9	18
2	14	4	18
3	12	7	19
4	4	2	6
5	7	2	9

In 2 patients bleeding was stopped with single dose of capramol. Patient with inversion uterus required only 15 gms of oral capramol for complete stop-

page of bleeding. Nine patients of fibroid uterus were put on capramol, 4 had excellent response, 1 good, 3 fair and 1 had poor response.

In this trial 64 (91%) patients out of 70 showed favourable results with capramol. Excellent results were obtained in 36 patients, good in 16, fair in 12 and poor in 6 patients.

In all the 6 patients who had poor response with capramol, curettage was done. Out of these endometrium of 4 patients showed proliferative phase while in 2 it was secretory phase.

Hystectomy was done on 12 patients, 9 with fibroid uterus and 3 with dysfunctional uterine bleeding with failed response. All these patients were above 35 years of age. Haultains' repair was done in the patient with inversion of uterus.

Side effects with capramol therapy were recorded in 15 cases out of 70. These symptoms were nausea in 7, dizziness in 10, diarrhoea in 1 and allergic manifestations in the form of flushing of face noted in 1 case. Headache and abdominal pain was not complained of by any of the patients. Only 2 cases out of 24 on intravenous capramol had side effects as dizziness. Rest of the 13 cases were with oral capramol therapy. Some patients complained of more than 1 side effects.

TABLE V
Side Effects With Capramol Therapy

Side effects	Number of patients		
	With oral therapy	I/V therapy	Total
Nausea	7	—	7
Dizziness	8	2	10
Diarrhoea	1	—	1
Headache	–	—	—
Abdominal pain	–	—	—
Allergic manifestation	1	—	1

Discussion

Epsilan-aminocaproic acid has been proved to be of value in treatment of menorrhagia (Nilsson, *et al* 1961 Nilsson, *et al* 1964; Nilsson, 1964; Gennser, 1964; Nilsson, and Rybo, 1965; Nilsson and Bjorkman, 1965).

In the present series favourable response was observed in 91%. Albrechtsen (1963) reported 87% favourable results. Linz (1967) 100% favourable results in his series of 50 patients.

Poor results were obtained in 6 patients out of 70 i.e., 8.6% in the present series.

Side effects were observed in 15 patients out of 70 under trial i.e. 21%. These symptoms were nausea in 7, dizziness in 10, diarrhoea in 1 and allergic manifestations in 1. Much lower incidence of side effects has been reported by some of the authors. Albrechtsen found that in 6% treatment had to be discontinued because of toxic effects. Nilsson and Rybo (1971) found a much higher incidence of side effects i.e. 53%, 91 out of 172 patients.

In the present study favourable results with capramol in cases of fibroid uterus were recorded in 8 cases out of 9. Nilsson and Rybo, (1971) have also found satisfactory response in cases of fibroid uterus with capramol therapy.

Summary and Conclusion

Seventy patients with excessive uterine bleeding were treated with capramol, 60 cases were with dysfunctional uterine bleeding, 9 with fibroid uterus and one with inversion uterus. Out of 70 patients, 46 had oral capramol therapy and 24 had intravenous injections of capramol.

Dose of oral capramol given was 5 gm/6 hourly maximum upto 5 days i.e. total dose not exceeding 100 gms. With intravenous dose given was 2.5 gm/8 hourly maximum for 5 days i.e. total dose not exceeding 35 gms. In all, 64 (91%) cases had fair to excellent results with capramol therapy. Only 15 (21%) patients had side effects, 2 patients on intravenous therapy and 13 on oral therapy. Only 1 patient had severe dizziness; others had mild to moderate side effects. Side effects are much less with intravenous preparation of capramol.

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