ESTIMATION OF URIC ACID IN UTERINE FLUID AND BLOOD OF WOMEN WITH EXCESSIVE UTERINE BLEEDING

by

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Introduction

The self explanatory term excessive uterine bleeding is a symptom most frequently encountered in gynaecological practice. Though not a disease in itself but a symptom which explains other diseased conditions and specify the abnormalities of normal menstrual bleeding pattern. Due to wide variation in its etiology and mechanism a decided lack of unanimity exists among clinicians, as to the precise pathophysiology of excessive uterine bleeding.

Much emphasis was made on histological examination, but as the examination of curettings usually does not correspond to the actual endometrial process, the histological study of the endometrium is now augmented by qualitative hormone assays and chemical analysis, in order to obtain a better knowledge of the precise path-mechanism of excessive uterine bleeding.

Uric acid is the end product of purine metabolism, produced in the endometrium and found to vary in various cases of excessive uterine bleeding and also during different phases of menstrual cycle. Its estimation is done to see whether any variations in its level occurs in cases of excessive uterine bleeding. Rise of uric acid concentration of uterine fluid and of blood could be related to blood oestrogen titre (Lloyd, 1969) and also to assess whether estimation of uric acid in excessive uterine bleeding can act as diagnostic aid.

Material and Method

The clinico-biochemical and histopathological study was done in 100 cases, admitted in Zanana Hospital of S.N. Medical College, Jodhpur, during the year 1976. Out of these 100 cases, 10 had normal regular cycles 10 had lactational amenorrhoea and 10 were women of menopausal age group. The remaining 70 cases had excessive uterine bleeding, which was dysfunctional in 40 cases and associated with uterine pathology in 30 cases (20 cases were of fibromyoma and 10 cases of adenomyosis). Patients giving history of menstrual flow more than average as compared to previous normal menstrual cycles were taken as subjects in the present study.

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Complete history including present complaints, past history, menstrual history and obstetrical history alongwith careful clinical examination was carried out in every case. Moreover, the complaints were measured against the standard normal for the particular patient. Bimanual pelvic examination and speculum examinations were done. The diagnosis of dysfunctional uterine bleeding was made on the basis of negative findings, on bimanual and speculum examinations and was confirmed by histopathological examination of the curettings.

For the collection of blood and uterine fluid standard technique was employed adopted by Engineer *et al* (1974). Estimation of uric acid in blood and uterine fluid was done by Brown's technique. Endometrium was stained by the method of fixation, processing, cutting, mounting and staining with haemotoxylin and eosin of endometrial tissue and the tissue was studied.

Observations

Blood uric acid level in control cases during the proliferative and secretory phases did not differ significantly but in the uterine fluid, the uric acid level gave a significant variation in both the phases of menstrual cycle, being considerably higher in the proliferative phase than in the secretory phase (Table 1). In the cases of dysfunctional uterine bleeding of the anovulatory variety uric acid in the blood was found to be markedly higher than the level seen in the proliferative phase in control subjects. In the cases with ovulatory bleeding no deviation was recorded in the blood than the level seen in secretory phase of control cases. In the uterine fluid on the other hand, the uric acid concentration in both groups of cases registered highly significant increase. In the cases of anovulatory bleeding there was about 400% rise in uric acid concentration above the values in the proliferative phase of control subjects, while in the ovulatory cases the rise was 750% higher than that seen in the secretory phase of controls.

The concentration of uric acid in the blood of all the categories of subjects was of the same order and comparable to that of the controls. In the uterine fluid the uric acid level in 20 cases of fibromyoma was of same order as that seen in cases of anovulatory functional uterine bleeding (Table II).

In women of excessive uterine bleeding due to adenomyosis who came with menorrhagia of varied severity the concentration of uric acid in the uterine fluid was even higher than the values in cases of fibromyoma. Actually the uterine fluid

TABLE I

Concentration of Uric Acid in Serum and Uterine Fluid During Menstrual Cycle in Control Cases and Cases of Dysfunctional Uterine Bleeding

Uric Acid Concentration (mg/100 ml)

Subjects (No. of cases)	Blood		Uterine fluid	
	Proliferative phase	Secretory phase	Proliferative phase	Secretory phase
Control (10)	2.13 + 0.86	2.24 + 0.38	1.03 + 0.57	0.43 + 0.48
Case of D.U.B. (40)				
(a) Anovulatory (20)	3.15 + 0.37	—	3.85 + 0.33	—
(b) Ovulatory (20)	—	2.65 + 0.33	—	3.35 + 0.36

TABLE II

Uric Acid Concentration in Patients With Uterine Pathology, Lactational Amenorrhoea and Menopause

Subject	Uric Acid Concentration (mg/100 ml)	
	Blood	Uterine fluid
I With uterine pathology		
(a) Adenomyosis	2.67 ± 0.57	0.57 ± 0.42
(b) Fibromyoma	2.76 ± 0.33	3.85 ± 0.33
II Lactational amenorrhoea	2.33 ± 0.34	0.46 ± 0.36
III Menopause	2.45 ± 0.34	0.35 ± 0.33

uric acid values in cases of adenomyosis were the highest of all the groups studied. The uric acid concentration of the uterine fluid of lactational amenorrhoic and menopausal women was virtually the same and comparable to that of the normal secretory phase.

Discussion

This newer and interesting biochemical constituent estimation was done earlier by Das *et al* (1971); Kar *et al* (1968) in uterine fluid of women fitted with Lippes loop from deposit found on used devices. Chemical analysis revealed that alongwith other chemical constituents there was marked increase in proteins and non-protein nitrogen levels, irrespective of the stage of the cycle.

Yangamachi and Chang (1963); Bhagat (1969); Sagiroglu and Sagiroglu (1970) stated that loops attract macrophages which are most efficient phagocytic cells ingesting dead or live cells, cellular debris and the non-absorbable material. They concluded that cell lysis by macrophages is responsible for the increased production of uric acid.

Engineer *et al* (1970) carried out a study of chemical composition of the deposit found on the Lippes loop after prolonged use and concluded the increased production of non-protein nitrogenous substances.

Engineer *et al* (1974) estimated uric acid in uterine fluid and blood of women with excessive uterine bleeding and stated that blood uric acid during the proliferative and secretory phases did not differ significantly. In uterine fluid the level was considerably higher in the proliferative phase than in the secretory phase. In cases of dysfunctional uterine bleeding of anovulatory varieties the blood uric acid level was found to be significantly higher than the level seen in the proliferative phase in control subjects. In cases of anovulatory bleeding there was about 400% rise in the uric acid concentration above the values in the proliferative phase of control subjects, while in the ovulatory cases rise was 800% higher than that seen in the secretary phase of control cases.

The uric acid level in cases of fibromyoma was of the same order, as that seen in cases of anovulatory functional bleeding. Uric acid of uterine fluid was even higher in patients with adenomyosis than in cases of fibromyoma. The uric acid concentration of uterine fluid of patients with lactational amenorrhoea and women of menopausal age was virtually the same and comparable to that of the normal secretory phase. This was sup-

ported by uniform increase in uric acid concentration of uterine fluid through the cycle in cases showing dysfunctional uterine bleeding, thinking that the endometrium of the patients may be exposed to a persistently high level of oestrogen (Llyod, 1969).

In the present study there was no significant difference in blood uric acid level during the secretory and proliferative phases of control cases. In the uterine fluid the uric acid level showed significant difference in both phases of menstrual cycle in control cases, being considerably higher in the proliferative phase than the secretory phase. The blood uric acid level in cases of dysfunctional uterine bleeding of anovulatory variety was found to be significantly higher than the level seen in the proliferative phase of control cases. There was about 400% rise in uric acid concentration above the values in the proliferative phase of control subjects, while in the ovulatory cases the rise was 750% higher than that seen in the secretory phases of controls. According to Engineer *et al* (1974), there was about 800% rise in ovulatory cases than the secretory phase of control subjects; except this all the observations coincide with the observations made by Engineer *et al* (1974). In adenomyosis cases the uric acid level in uterine fluid were the highest of all the cases studied and were nearly double to the level of patients showing dysfunctional uterine bleeding of both the types. Uterine fluid uric acid level in fibromyoma was of same order as in anovulatory functional uterine bleeding. The blood uric acid levels in adenomyosis and fibromyoma had no significant difference. The uterine fluid uric acid of lactational amenorrhoic and menopausal women was same and comparable to that of the normal secretory phase.

Thus in uterine pathology associated with bleeding, the uterine fluid level of uric acid is found to be significantly higher than that of the normal women, although the blood uric acid level does not show any marked rise above the control values. It confirms that uric acid value of uterine fluid reflects the status of the endometrium.

Summary

1. This clinical, biochemical and histopathological study was conducted in excessive uterine bleeding cases to recognize the better diagnostic aid for the condition. 70 cases were of dysfunctional uterine bleeding and 30 cases were control cases.

2. In normal healthy subjects uterine fluid uric acid value was found to be higher during the proliferative phase than in the secretory phase.

3. In patients with excessive uterine bleeding due to pathological conditions the uric acid level in uterine fluid was consistently higher than that of control proliferative phase.

4. In lactational amenorrhoea and menopausal cases the uterine fluid uric acid level was the same as that in the normal secretory phase.

5. The highest uric acid level in uterine fluid was found in cases of adenomyosis.

Conclusively chemical analysis are more reliable, more dynamic and more accurate than were morphological examination which can vary due to individuals interpretations. This estimation shows that uric acid value of uterine fluid appears to reflect the status of the endometrium and also perhaps the titre of blood estrogen.

References

1. Bhagat, S.: Jap. J. Pharma. **19: 427, 1969.**
2. Brown—Practical Clinical Biochemistry by Harold Varley, 4th ed. Arnold—Heinemann Publishers (India) Private Limited. 1969.
3. Das Gupta, P. R., Kar, A. B. and Engineer, A. D.: Am. J. Obst. & Gynec. **110: 543, 1971.**
4. Engineer, A. D., Das Gupta, P. R. and Kar, A. B.: Am. J. Obst. & Gynec. **106: 315, 1970.**
5. Engineer, A. D., Pushpa Mahajan, P. R., Das Gupta, Amiya, B. and Kar, A. B.: J. Obst. & Gynec. India. **24: 486, 1974.**
6. Kar, A. B., Engineer, A. D., Goel, R., Kamboj, V. P., Das Gupta, P. R. and Chowdhury, S. R.: Am. J. Obst. & Gynec. **101: 966, 1968.**
7. Llyod, C. W.: In text book of endocrinology. William, R. H. 4th edition, W. B. Saunders Co., Philedelphia, 1969.
8. Sagiroglu, N. and Sangiroglu, E.: Am. J. Obst. & Gynec. **106: 506, 1970.**
9. Yanagamachi, R. and Chang, M. C.: J. Reprod. Fertil. **5: 389, 1963.**