URIC ACID IN UTERINE FLUID AND BLOOD AS A DIAGNOSTIC AID IN CASES OF EXCESSIVE UTERINE BLEEDING

by

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The endometrium of the uterus is constantly bathed by uterine fluid—the normal composition of which is essential for the role it has to play in reproduction and normal physiology. Uric acid is an important end product of purine metabolism in the endometrium.

The recognition of uric acid as a constituent of uterine fluid was established by Engineer *et al*, 1968 and Das Gupta *et al* 1971 in women fitted with Lippes loop and in few cases of pathological bleeding, from the deposit over the loop. It has been reported by Engineer and Das Gupta (1974) and Chandra (1978) that uric acid in uterine fluid varies during different phases of menstrual cycle and exhibits a significant rise in cases of excessive uterine bleeding. Chief source of uric acid seems to be an increasd proliferation of tissues under the effect of oestrogen (Novak 1975). Furthermore, a rise in uric acid could be related to blood oestrogen titre (Llyod 1969).

An attempt was therefore made to understand the precise pathophysiology of excessive uterine bleeding by chemical analysis of uterine fluid.

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Material and Methods

This clinical—biochemical and histopathological study was undertaken in 160 cases admitted in or attending out patients department of Upper India Sugar Exchange Hospital and Nursing Homes in Kanpur.

Out of these, 20 (12.5%) cases having normal regular cycles were taken as controls. The remaining 110 (87.5%) cases presented with history of menstrual flow more than average as compared to their previous normal cycles. These included 35 (32.7%) cases of fibromyoma, 56 (50.9%) cases of dysfunctional uterine bleeding (ovular and anovular types), and 19 (17.3%) cases of adenomyosis.

A detailed clinical examination was carried out taking care to exclude cases of severe vaginitis, pelvic inflammation, cervical erosion, carcinoma and genital tuberculosis as in these cases level of serum uric acid is found to be altered.

The diagnosis in these cases was confimed by histological study of curettings whenever necessary.

Uterine fluid and blood was collected and subjected to biochemical analysis according to technique adopted by Engineer and Das Gupta 1974.

Obeservations

During normal menstrual cycle mean serum uric acid was observed to be signi-

ficantly higher than uterine fluid at $P < 0.001$ (Table I). Considerable variation between the proliferative and secretory phases of menstrual cycle was observed at $P < 0.001$. Higher values being observd for proliferative phase as compared to secretory phase.

In cases of excessive uterine bleeding, cases of fibromyoma had the lowest value of uric acid in uterine fluid. Highest uric acid concentration was observed for cases of adenomyosis. As shown in Table I in anovulatory type of dysfunctional uterine bleeding, the rise in uterine fluid uric acid when compared with the proliferative phase of controls was four folds. In ovular type, however, a seven and half time rise as compared with secretory phase of controls was observed.

TABLE I

Concentration of Uric Acid in Serum and Uterine Fluid During Normal Menstrual Cycle and in Cases of DUB

Subjects	Blood (Men ± S.E.)		Uterine fluid (Mean ± S.E.)	
	Proliferative	Secretory	Proliferative	Secretory
Control (20)	3.35 ± 0.15	3.27 ± 0.15	1.168 ± 0.15	0.577 ± 0.15
DUB (56)				
(a) Anovulatory (30)	4.11 ± 0.12	—	4.56 ± 0.12	—
(b) Ovulatory (26)	—	3.85 ± 0.13	—	4.27 ± 0.13

* DUB *Dysfunctional Uterine Bleeding.

A study of trend of uric acid in relation to days of menstrual cycle revealed a curvilinear trend in the first fifteen days of cycle in contrast to a linear pattern in the last fifteen days.

Maximum observed value being 2 mg% on 12th day of cycle, while a maximum of 1.57 mg% was estimated around the 10th day, difference being due to technical error. On the other hand, the linear trend observed in last half of the cycle had a significant correlation coefficient $r = 0.657$ at $P < 0.01$.

No change was observed between age, parity and uterine fluid uric acid. Serum uric acid showed no change with various phases of menstrual cycle.

In cases of excessive uterine bleeding uric acid in uterine fluid was significantly higher than that of controls at $P < 0.001$, though serum values were comparable with normal controls. Serum uric acid in anovular type of dysfunctional uterine bleeding was higher than that for controls but the rise was not statistically significant (Table II).

Discussion

Engineer *et al* 1968, Das Gupta and Engineer 1971, during extensive study on uterine fluid of women fitted with Lippes loop reported the presence of uric acid as a new constituent of uterine fluid alongwith an increase in protein and non-protein nitrogen levels, irrespective of stage of cycle. An increase in uric acid so observed was attributed to the cellular lysis by macrophages which are attracted by the loop (Yangamachi and Chang 1963; Bhagat 1969) Das Gupta and Engineer 1971 isolated uric acid from the deposit over the loop and in cases of pathological bleeding in women fitted with Lippes loop. This preliminary observation led Engineer *et al* 1974 and Chandra 1978 to establish the role of uric acid in cases of

TABLE II

Uric acid in Blood and Uterine Fluid in Cases of Excessive Uterine Bleeding

Case Type	No. of cases	Uric acid in mg% Blood	Uterine fluid	F Value
Fibromyoma	35			
Range		2.5 to 4.8	1.4 to 5	
Mean		3.40	3.90	
C.D.		).3226*		
Dysfunctional Uterine Bleeding (Anovular)	30			
Range		2.8 to 5.8	2.9 to 5.4	
Mear		4.11	4.56	
C.D.		0.3485*		
Dysfunctional Uterine Bleeding (Ovular)	26			124.83***
Range		2.8 to 5.4	3.2 to 5	
Mean		3.8[illegible]	4.27	
C.D.		0.3743*		
Adenomyosis	19			
Range		3.4 to 5.2	4.8 to 6.2	
Mean		3.45	5.56	
C.D.		0.4390*		

C.D. Critical difference *Significant at $P < 0.05$ ***Significant at $P < 0.001$

excessive uterine bleeding. Chief source of uric acid seems to be an increased proliferation of tissues under effect of hormones.

In the present study, cyclical variation of uric acid in uterine fluid was observed, being higher in the proliferative phase than secretory phase of menstrual cycle (Table I). The possible explanation for this is that cyclical variation of oestrogen may be responsible for higher values in proliferative (oestrogen dominant) than secretory (low, oestrogen, progesterone dominant) phase.

A study of trend of uric acid revealed a curvilinear pattern in the first fifteen days and a linear trend with significant correlation co-efficient in the last fifteen days of cycle. Maximum observed value for uric acid was on 12th day of cycle which in turn is coincident with high oestrogen level at this time of the cycle.

Appreciable rise in uterine fluid uric acid from normal controls was observed in cases of excessive uterine bleeding.

There was about 400% rise in uric acid concentration in anovulatory type of dysfunctional uterine bleeding above the values for proliferative phase of controls, while a 750% rise higher than the secretory phase was observed in ovular types of dysfunctional uterine bleeding. This observation is in complete agreement with that of Chandra 1978 but Engineer and Das Gupta 1974 had reported a higher rise of 800% uterine uric acid in ovular type of dysfunctional uterine bleeding.

The study of uric acid in cases of dysfunctional uterine bleeding revealed a uniform increases in uric acid concentra-

tion of uterine fluid, suggesting that the endometrium of such patients may be exposed to persistently high levels of oestrogen (Llyod 1969). A rise in uric acid may thereby be related to blood oestrogen titre. Further, our observation of increased uric acid content of uterine fluid in cases of fibromyoma, adenomyosis and dysfunctional uterine bleeding may be explained by coincident hyperoestrogenemic state associated with such cases of menorrhagia.

Higher values of uric acid in adenomyosis and fibromyoma may be due to the tumour tissue acting as an additional source of uric acid (Engineer and Das Gupta 1974). Besides, the tumour may be regarded as local pronounced manifestation of oestrogens to proliferate fioroblasts (Bullough 1946).

We observed that there was no rise in serum uric acid in cases of excessive uterine bleeding in contrast to the rise in uterine fluid. This may be due to a possibility that the rise in serum uric acid is too small to produce a recordable difference.

Thus, in uterine pathology associated with bleeding, the uterine fluid uric acid is found to be significantly higher than that of normal women although blood uric acid fails to show any rise.

Conclusion

The present study thus confirms the role of uric acid in uterine fluid as a reliable index for assessing hormonal status of endometrium, and perhaps the titre of blood oestrogen also. As chemical analysis is more accurate and reliable than histological examination which may differ due to individual interpretations, quantitative assessment of uric acid in uterine fluid can serve as a better diagnostic aid.

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