CREATININE IN SERUM AND UTERINE FLUID OF WOMEN WITH EXCESSIVE UTERINE BLEEDING

by

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Menorrhagia is a frequent and common symptom of gynaecological problems, and conditions like fibromyoma, adenomyosis and dysfunctional uterine bleeding have a major contribution in its aetiology. As a consequence the biochemical changes associated with altered endometrial histology and metabolism of such cases is reflected directly by changes in the uterine mileu.

The most important remaining end product of amino acid catabolism is creatinine derived from creatine present in the body tissues. Levels of creatinine reflect muscle development activity. According to Novak (1975) the rhythmic muscular contractility of the uterus reaches its peak during the phase of oestrogenic dominance.

An attempt was, therefore, made to understand the precise pathophysiology in such cases of menorrhagia by quantitative estimation of creatinine in uterine fluid.

Material and Methods

The study was undertaken in 145 cases, out of which 30 with normal menstrual cycle served as controls. The remaining 105 cases presenting with menorrhagia were subjects for this study. These included cases of fibromyoma, dysfunctional uterine bleeding and adenomyosis diagnosed clinically or revealed on histopathology. A detailed history and clinical examination was undertaken for clinical evaluation of cases, care being taken to exclude cases with fever, starvation, diabetes and muscular dystrophy from the study as creatinine levels are altered in these conditions.

Histological examination of endometrial curettings was done wherever necessary. Uterine fluid was collected by the technique described by Engineer and Das Gupta, 1974. For uterine fluid, specimens drawn from 5 cases were pooled to make a volume of 1 ml. and then the mean value per case was compared with mean serum creatinine value.

Estimation of creatinine in blood and uterine fluid was done by a technique described in Bray's clinical laboratory methods (1962) with certain modifications. Creatinine in serum and uterine fluid was estimated during both phases of menstrual cycle.

Observations

As shown in Table I, mean serum creatinine was significantly higher than mean creatinine uterine fluid at $P < .001$.

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TABLE I

Creatinine in Serum and Uterine Fluid in Relation to Menstrual Cycle

Phases of Menstrual Cycle	Serum creatinine	Creatinine in Uterine Fluid	'P' Value	
Proliferative	0.76	0.168	2.11	NS
Secretory	0.72	0.144		
Mean creatinine	0.74	0.156	587.76	xxx
C.D.	0.048			
Standard error of media means and phase means	0.024			

N.S.—Non significant
XXX—Significant at P $<$.001.

Age had no effect on creatinine concentration. However, creatinine in uterine fluid showed a significant increase with increasing parity, highest value being for para 3 and 4.

As shown in Table III creatinine in uterine fluid was significantly higher than that for normal controls at P $<$ .001. Highest creatinine concentration in fluid was observed for cases of fibromyoma at P $<$ .05. A significant variation between mean serum creatinine and creatinine in

TABLE II

Creatinine in Serum and Uterine Fluid of Normal Controls in Relation to Parity

Parity Groups	Serum proliferative	Secretory	Uterine fluid proliferative	Secretory	Parity means
P_0 — 2	0.547	0.642	0.160	0.130	0.371
P_3 — P4	0.900	0.782	0.170	0.160	0.582
P_5 — and above	0.920	0.740	0.180	0.132	0.493
F Value	1576.61	XXX			

XXX—Significant at P $<$.001.

TABLE III

Creatinine in Serum and Uterine Fluid in Cases of Excessive Uterine Bleeding

Case type	No. of cases	Serum creatinine ± S.E.	Creatinine uterine fluid ± S.E.	'P' value
1. Fibromyoma	30	0.778 ± 0.021	0.273 ± .020	
2. Dysfunctional uterine bleeding	55			
(i) Anovular	35	0.692 ± 0.029	).212 ± 0.31	6.38X
(ii) Ovular	20	0.665 ± 0.036	0.225 ± 0.036	
3. Adenomyosis	20	0.980 ± 0.051	0.192 ± 0.051	

S.E.—Standard error.
X—Significant at $<$.05

uterine fluid was observed in all cases of excessive uterine bleeding.

Discussion

Engineer and Das Gupta (1974) and Chandra (1978) observed a significant increase in uric acid in uterine fluid in cases with excessive uterine bleeding. Chief source of uric acid seems to be an increased proliferation of tissues under effect of Oestrogen (Novak, 1975). Rise in uric acid due to altered urine metabolism was found to be related to hyperoestrogenaemia associated with cases of menorrhagia.

Creatinine in uterine fluid is a new and interesting constituent under study. Creatinine is derived from creatine present in the tissues by breakdown of the latter during muscular contraction. It is well known that uterine contractiliy reaches its maximum peak during phase of oestrogen dominance. Creatinine in uterine fluid may thus reflect the hormonal status of the endometrium.

We observed no statistically significant rise in uterine fluid creatinine during proliferative and secretory phases of menstrual cycle (Table I). In normal subjects uterine fluid creatinine was considerably lower than corresponding serum value at $P < .001$. Age had no effect on creatinine concentration in normal controls. However, creatinine concentration was observed to increase with increasing parity. Highest value being for para 3 and 4. Variation between the parity means may be because of increased uterine bulk with increasing parity leading to high output of creatinine from breakdown of creatine in the muscle.

In cases of excessive uterine bleeding, creatinine in uterine fluid was considerably higher than that of normal controls at $P < .05$, though serum creatinine level was comparable with that of controls.

Highest value of creatinine was observed in case of fibromyoma. This may be attributable to an increased muscle mass as a result of the tumour itself and also because of an increased contractility of the uterus in an attempt to expel the tumour. The latter however is more true for submucous fibroids. Increased contractility may cause increased breadown of creatine to creatinine. Further, an increased proliferation of fibroblasts (Bullough, 1946) in the manifestation of local pronounced action of oestrogen. Hence, rise in creatinine may indirectly reflect the associated hyperoestrogenemia in these conditions.

In both anovulatory and ovulatory type of dysfunctional uterine bleeding, uterine fluid creatinine was significantly higher than that of controls though no change was observed between anovulatory and ovulatory types.

In adenomyosis also, the creatinine content of uterine fluid was significantly higher than that of normal controls at $P < .05$. The rise in creatinine content of uterine fluid may be explained by coincident hyperoestrogenemic state associated with such cases. Increased contractility of the uterus during oestrogen dominance may result in increased creatinine content of fluid.

Conclusion

Our observation of increased creatinine content of uterine fluid in cases of excessive bleeding in conditions associated with hyperoestrogenemia reflect indirectly the hormonal status of the endometrium. This is further confirmed by our observation of increased levels particularly in cases of fibromyoma where increas-

ed muscle bulk and proliferation of fibroblasts is secondary to high oestrogen levels. Thus creatinine content of uterine fluid can serve as a parameter for assessing hormonal status of endometrium.

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