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Uric acid excretion and surgery

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Surgical operation has long been considered capable of precipitating acute gouty arthritis (Hench, 1935; Linton and Talbott, 1943) but details of uric acid metabolism in this situation are unknown. This paper describes a study of postoperative uric acid levels in plasma and urine in a number of patients undergoing surgical operation.

Patients and methods

The initial study was carried out in a group of three men and three women each of whom was undergoing the operation of selective vagotomy for chronic peptic ulceration (Burge and Frohn, 1969). Further clinical details of this group are set out in Table I, Cases 1–6. Each operation was performed by the same surgeon under the

Table I *Clinical details of eleven patients*

Group	*Patient no.*	*Sex*	*Age (yrs)*	*Operation*	*Duration of anaesthesia (hrs)*	*Pre-medication*	*Anaesthetic agents*	*Post-operative drugs*	*Duration of post-operative I.V. infusion (hrs)*
I	1	F	62	Selective vagotomy Repair of hiatus hernia	2	Opiates	Thiopentone Gallamine Nitrous oxide	Pentazocine	72
	2	F	67	Selective vagotomy Pyloroplasty	2·5	Opiates	Thiopentone Gallamine Nitrous oxide	Opiates	36
	3	F	54	Selective vagotomy	1	Opiates	Thiopentone Gallamine Nitrous oxide	Opiates Perphenazine	36
	4	M	31	Selective vagotomy	2	Opiates Scopolamine	Thiopentone Halothane	Opiates Perphenazine	18
	5	M	32	Selective vagotomy Pyloroplasty	2	Opiates	Thiopentone Gallamine Nitrous oxide	Opiates	24
	6	M	42	Selective vagotomy	2·5	Opiates	Thiopentone Gallamine Nitrous oxide	Atropine Opiates	36
II	7	F	64	Left femoropopliteal disobliteration	3	Pethidine Promietha-zine	Thiopentone Suxamethonium Nitrous oxide Halothane	Opiates	6
	8	M	53	Selective vagotomy Pyloroplasty	2	Opiates	Thiopentone Pancuronium Nitrous oxide	Opiates	36
	9	M	67	Partial gastrectomy	3	Opiates	Thiopentone Halothane	Opiates	5 days
	10	F	56	Selective vagotomy	2	Opiates	Thiopentone Gallamine Nitrous oxide	Opiates	36
	11*	F	67	Selective vagotomy	2	Opiates	Thiopentone Gallamine	Opiates	48

* Urine collections for patient No. 11 were incomplete and only plasma levels were available.

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same conditions of premedication and general anaesthesia. Postoperative management was likewise uniform as regards drug administration and fluid balance.

In a second group of five patients, two men and three women, an intravenous infusion of glucose-saline was set up 6 to 12 hours before surgery (Table I, Cases 7–11). This was intended to offset any dehydration or ketosis occurring as a result of fluid and calorie deprivation before and during operation which could possibly influence urate excretion (Scott, McCallum, and Holloway, 1964). The infusion was maintained until adequate oral hydration was resumed. Apart from Case 9, who had had one attack of gouty arthritis several months previously, none of the patients in either group was hyperuricaemic or had suffered from gout.

Basal preoperative 24-hour uric acid excretion was measured in all patients while they were taking a diet containing less than 300 mg. purine daily, beginning at least 4 days previously. Urine collections were continued from the first postoperative day for a period of 5 to 6 days in most cases and for 10 days in a single patient. A low purine intake was maintained throughout.

Urine was collected in plastic bottles containing 1 to 2 ml. toluene as a preservative. Uric acid was measured spectrophotometrically by the enzymatic method of Liddle, Seegmiller, and Laster (1959) and creatinine by that of Edwards and Whyte (1958).

Results

PLASMA URIC ACID (Table II).

In neither group of patients was any consistent pattern of change discernible. In cases 5, 9, 10, and 11 there was a slight decrease in postoperative levels, in Cases 3 and 8 a slight increase, and in Cases 1, 2, 4, 6, and 7, very little change. In both groups mean levels tended to be lower during the postoperative period; the mean basal plasma uric acid for all patients was 4·5 mg./ml. and the mean level during the six post-operative days was 4·2 mg./ml.

URINARY URIC ACID (Table III, overleaf)

In Group I there was a two- to three-fold rise in uric acid excretion beginning on the first or second post-operative day. Of the five patients in Group II, urine collections were incomplete in Case 11 and data are not available. In the remaining four patients, however, there was a substantial increase in urinary uric acid in three (Cases 8, 9, 10) and a slight rise in the fourth (Case 7). The mean basal daily urinary uric acid for all patients was 380 mg., and the mean level during the six post-operative days was 628 mg.

URIC ACID CLEARANCE and URINARY URIC ACID: CREATININE RATIO

Patients from both groups therefore showed a substantial increase in postoperative uric acid clearance. There was no consistent change in urinary creatinine values, and the urinary uric acid: creatinine ratio rose postoperatively (Table IV, overleaf).

Discussion

From these results it is evident that the excretion of uric acid increases markedly during the week following abdominal operation.

There are a number of possible ways in which this effect might be produced. Increased production or mobilization of uric acid, due for example to rapid destruction of tissue nucleic acids, would result in an increase in urinary excretion, but if this were the case one might expect a tendency for the plasma level of urate to rise. A rise in plasma urate did occur in Cases 3 and 8, but in the others there was either no change or a fall in plasma urate, and the mean post-operative level was slightly lower than the pre-operative level.

Table II *Pre- and postoperative plasma uric acid levels*

Group	*Patient no.*	*Plasma uric acid (mg./100 ml.)*								
		Basal preoperative readings			*Postoperative days*					
					1	*2*	*3*	*4*	*5*	*6*
I	1	4·0	5·6	5·8	5·7	—	5·6	4·7	4·5	4·5
	2	5·2	3·9	—	—	4·4	—	—	3·9	—
	3	1·9	—	—	2·6	3·8	2·9	—	1·9	2·6
	4	4·9	4·9	—	4·8	6·6	4·4	4·5	—	—
	5	5·4	—	—	4·4	—	—	4·5	—	4·4
	6	4·6	4·6	4·7	5·3	4·9	2·9	4·5	5·0	4·4
	Mean	4·3	4·7	5·2	4·5	4·9	3·9	4·5	3·8	4·0
	S.D.	1·3	0·7	0·7	1·2	1·2	1·3	0·1	1·4	0·9
II	7	3·5	—	—	4·1	3·8	3·5	3·1	3·6	2·8
	8	3·7	3·7	2·6	5·8	5·3	5·6	5·7	5·6	5·3
	9	5·6	5·4	5·8	4·5	4·2	3·7	3·7	—	3·5
	10	5·1	4·8	4·3	4·2	4·2	4·2	4·6	4·8	—
	11	3·6	3·2	3·9	1·4	1·7	2·4	3·5	—	—
	Mean	4·3	4·3	4·2	4·0	3·8	3·9	4·1	4·7	3·8
	S.D.	0·8	0·9	1·1	1·4	1·3	1·0	1·0	2·6	0·9

Table III *Pre- and postoperative uric acid excretion*

Group	Patient no.	*Urinary uric acid (mg./24 hrs)*								
		Basal preoperative readings			*Postoperative days*					
					1	*2*	*3*	*4*	*5*	*6*
I	1	421	406	—	—	899	586	372	378	422
	2	445	480	—	962	901	552	950	714	—
	3	52	—	—	788	607	444	488	739	388
	4	345	—	—	—	400	355	551	—	—
	5	376	—	—	772	963	849	—	1000	393
	6	407	242	—	—	872	661	739	632	390
	Mean	341	376	—	840	773	574	620	692	398
	S.D.	133	99	—	92	204	159	203	201	20
II	7	325	—	—	475	302	415	391	465	470
	8	449	573	570	1050	998	793	651	751	—
	9	393	292	221	328	520	888	735	752	848
	10	488	302	351	233	505	655	459	547	657
	Mean	414	389	381	521	581	687	559	629	658
	S.D.	60	130	143	317	256	181	139	125	156

Table IV *Pre- and postoperative urinary uric acid: creatinine ratio*

Group	Patient no.	*Ratio*								
		Basal preoperative readings			*Postoperative days*					
					1	*2*	*3*	*4*	*5*	*6*
I	1	0·5	—	—	—	0·9	0·8	0·8	0·6	0·6
	2	0·6	—	—	0·8	1·0	0·9	1·0	0·8	—
	3	0·4	—	—	0·6	0·8	1·0	0·7	1·3	0·5
	4	0·2	—	—	—	0·3	0·5	0·8	—	—
	5	0·3	—	—	0·5	0·5	0·5	—	0·4	0·3
	6	0·4	—	—	—	1·1	0·7	0·6	0·6	0·5
	Mean	0·4	—	—	0·6	0·8	0·7	0·9	0·7	0·5
	S.D.	0·1	—	—	0·1	0·2	0·4	0·4	0·3	0·1
II	7	0·3	—	—	0·3	0·4	0·4	0·4	0·4	0·5
	8	0·3	0·4	0·4	0·4	0·5	0·5	0·2	0·4	—
	9	0·3	0·3	0·2	0·3	0·3	0·5	0·7	0·63	0·8
	10	0·4	0·3	0·4	0·7	0·3	0·7	0·5	0·6	0·7
	Mean	0·32	0·33	0·32	0·53	0·38	0·53	0·45	0·51	0·6
	S.D.	0·07	0·05	0·09	0·3	0·3	0·08	0·18	0·1	0·1

A second possibility is that the raised excretion of uric acid is the result of a renal mechanism, which accords with the increased urate clearance found in most patients. There are several agents which might be responsible. The effect of anaesthetics on urate excretion is unknown and it is conceivable that the actual procedure of vagotomy and intestinal manipulation could influence urate excretion. In this context it is of interest that the one patient who had a non-abdominal operation (Case 7) failed to show much change in plasma or urinary urate. Corticotrophin and cortisone are known to have uricosuric properties (Forsham, Thorn, Prunty, and Hills, 1948; Gutman and Yü, 1950; Ingbar, Kass, Burnett, Relman, Burrows, and Sisson, 1951) and elevated postoperative plasma levels of endogenous corticosteroids (Sandberg, Eik-Nes, Samuels, and Tyler, 1954; Helmreich, Jenkins, and Swan, 1957) may be an important factor. Again, all patients received intravenous infusions of glucose or glucose-saline postoperatively, and this may have had a further contributory effect (Talbott, 1943).

Whatever the mechanism, there is clearly a major disturbance in the dynamic equilibrium of urate in the postoperative period, and this may be responsible for attacks of acute gout similar to those severe attacks which can occur in the early stages of treatment with allopurinol or uricosuric drugs (Scott, Hall,

and Grahame, 1966). Alternatively, postoperative gout may be induced by a completely different mechanism, for example, a transient alteration in the relationship between urate crystals and biomembranes of the type described by Weissmann, Rita, and Zurier (1971). It is evident that further work is required to investigate these complex factors.

Summary

An increase in postoperative uric acid excretion was found in ten patients undergoing surgery. Usually two- or three-fold, the increase commenced within 48 hours of operation and persisted for several days. There was no consistent change in the plasma level of urate or urinary creatinine excretion. Possible mechanisms are discussed, together with their relationship to the occurrence of postoperative gouty arthritis.

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