since adequate respiration took several days to return, respiration was supported artificially. Hypertension and tachycardia did not recur. Recovery was gradual but uneventful. He was discharged 35 days after admission.

Comment

Labetalol was effective in controlling the circulatory effects of adrenergic stimulation from tetanus in this patient, and may be more advantageous than other forms of management using either alpha- or beta-adrenergic blocking drugs. Continuous infusion, although expensive, ensures a reasonably sustained effect and offers a practical alternative to intermittent intravenous or oral administration. Nevertheless, decurarisation should be performed cautiously and adequate doses of atropine must be given. This regimen merits further study.

[1] Stoddard, J C, *Intensive Therapy*. Oxford, Blackwell, 1975.
[2] Keilty, S R, *et al*, *Lancet*, 1968, **2**, 195.
[3] Benedict, C R, and Kerr, J H, *British Medical Journal*, 1977, **2**, 806.
[4] *British Journal of Clinical Pharmacology*, 1976, **3**, suppl No 3, p 681.

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Failure of labetalol to prevent hypertension due to clonidine withdrawal

Abrupt withdrawal of clonidine treatment may be complicated by a severe rebound rise in blood pressure accompanied by symptoms of sympathetic overactivity, severe headache, and increased circulating catecholamine concentrations.[1 2] The rise in blood pressure usually occurs within 24-48 hours after withdrawing the drug[3] but may be delayed for up to 14 days.[4] Blood-pressure control and reversal of the symptoms may be achieved by reintroducing clonidine or giving α-adrenoceptor-blocking agents. Although symptoms may be abolished by beta-blockers, rebound hypertension may be potentiated because of unopposed sympathetic vasoconstriction.[2 3] The use of labetalol, a compound that antagonises both α- and β-adrenoceptors, has been proposed for treating clonidine withdrawal and other hypertensive conditions characterised by increased sympathetic activity.[3 5] We report on a patient in whom severe rebound hypertension developed during gradual clonidine withdrawal and concurrent labetalol treatment.

Case report

A 41-year-old woman with a history of pyelonephritis and analgesic abuse had had high blood pressure for about eight years. Adequate control had been achieved by her general practitioner with clonidine 150 μg three times daily. She reported that she became "agitated" when she missed or delayed taking her tablets. She presented to hospital with a severe headache and impaired consciousness after having had no clonidine for 22 hours. She was restless, and her blood pressure was 300+/145 mm Hg and pulse rate 55 beats/min. Ocular fundi showed papilloedema with haemorrhages and exudates. The lower limbs were extended, muscle tone increased, and tendon reflexes exaggerated with extensor plantar responses. Hypertensive encephalopathy was diagnosed. An immediate attempt was made to reduce the blood pressure initially with intravenous diazoxide and, when this proved unsuccessful, with nitroprusside infusion. Satisfactory blood-pressure control was subsequently maintained by reintroducing clonidine 150 μg three times daily. After discharge blood-pressure control deteriorated and labetalol 100 mg three times daily was added. Good control was achieved with this combination, though moderate postural hypotension occurred.

Gradual withdrawal of the clonidine treatment was attempted, beginning at the rate of 150 μg every five days. When the patient was reviewed after taking the last dose of clonidine she felt well and her blood pressure was well controlled. Labetalol was continued at the same dose. Three days later, however, she presented again to hospital complaining of severe headache and restlessness. Her blood pressure was 230/170 mm Hg. No neurological abnormalities were present. After intravenous diazoxide was given the pressure remained raised at 230/130 mm Hg. Oral clonidine was then restarted. After four hours the blood pressure was 136/96 and after six hours 110/86 mm Hg. It was considered unwise to attempt to withdraw clonidine again, and the patient was discharged on this drug with good blood-pressure control.

Comment

This case report shows that the hypertensive crisis precipitated by withdrawing clonidine may not be prevented by gradual withdrawal and concurrent administration of labetalol. Interestingly, rebound hypertension was delayed until the last, small dose was stopped. Perhaps further stepwise reduction using 25-μg tablets (Dixarit) would have been preferable.

The effectiveness of intravenous labetalol as emergency treatment has been documented[3 5] but experience with oral administration is limited. Larger doses of labetalol might have been more protective. These were not given in this case because of the degree of blood-pressure reduction achieved and the postural effects already present. Because only partial α-antagonism is attained with labetalol, breakthrough may occur when the catecholamine response is excessive. Under these circumstances the vasoconstrictor effect is likely to be augmented by the more potent beta-blocking action of the drug. Further experience is needed before oral labetalol may be recommended for use in patients in whom clonidine is to be discontinued.

[1] Hunyor, S N, *et al*, *British Medical Journal*, 1973, **2**, 209.
[2] Bailey, R R, and Neale, T J, *British Medical Journal*, 1976, **1**, 942.
[3] Reid, J L, *et al*, *Lancet*, 1977, **1**, 1171.
[4] Vanholder, R, *et al*, *British Medical Journal*, 1977, **1**, 1138.
[5] Agabiti Rosei, E, *et al*, *British Journal of Clinical Pharmacology*, 1976 (Supplement), **3**, 809.

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Antiplasmin concentrations after surgery: failure of alpha$_2$-antiplasmin to rise in patients with venous thrombosis

The antiproteases α_2-macroglobulin, α_1-antitrypsin, C1 inactivator, and antithrombin III all show antiplasmin activity. Recently a new fast-acting antiplasmin, α_2-antiplasmin, has been recognised as the major fast-acting antiplasmin.[1] Impaired fibrinolytic activity has been noted after operation in patients who develop deep vein thrombosis (DVT)[2] so that increased antiplasmin concentrations might be expected in such patients. We have therefore measured concentrations of the three major antiplasmins—α_2-antiplasmin, α_2-macroglobulin, and α_1-antitrypsin—in ten patients who developed positive ^{125}I-fibrinogen scans after major surgery and 15 patients with negative scans.

Patients, methods, and results

Plasma was collected half an hour before surgery and on the first and second days after operation from 25 patients undergoing major gynaecological surgery in a clinical trial evaluating anticoagulant prophylaxis.[3] Twenty patients were initially studied: 11 were receiving subcutaneous low-dose heparin 5000 units twice daily and nine were receiving subcutaneous saline as a placebo. Patients were screened for the development of deep vein thrombosis by scanning daily with ^{125}I-fibrinogen scan for one week. α_2-Antiplasmin, α_2-macroglobulin, and α_1-antitrypsin concentrations were measured by rocket immunoelectrophoresis using specific antisera (α_2-antiplasmin antiserum was kindly donated by D Collen, University of Leuven). Five of these original 20 patients showed positive scans (three patients on saline and two on heparin). Five further patients who had isotopic DVT were included in the study and all five were in the saline group.

α_2-Antiplasmin values(%) before and after surgery

Case No	Day before surgery	Two days after surgery	P
	Heparin, no thrombosis		
1	104	120	
2	116	137	
3	80	106	
4	137	155	
5	111	111	0·01
6	91	95	
7	100	116	
8	130	140	
9	88	98	
	Saline, no thrombosis		
10	113	152	
11	103	115	
12	100	107	
13	100	108	0·02
14	97	126	
15	83	121	
	Heparin, thrombosis		
16	95	95	0·5
17	98	98	
	Saline, thrombosis		
18	112	120	
19	120	85	
20	115	120	
21	83	95	0·5
22	125	135	
23	77	77	
24	88	92	
25	109	135	

Fifteen patients were also screened before and after operation for plasmin-α_2-antiplasmin complexes[4] using antiserum again kindly donated by D Collen.

Both heparin-treated and saline control groups showed a similar rise in α_2-antiplasmin concentration after surgery. In the 15 patients who did not develop positive fibrinogen scans α_2-antiplasmin concentrations also rose, and the increase was highly significant by day 2 (see table). In contrast, in the 10 patients with positive scans there was no significant rise in α_2-antiplasmin concentration. Thrombotic patients on the second day after surgery had significantly lower α_2-antiplasmin concentrations than non-thrombotic patients ($P=0{\cdot}05$ using unpaired t test). No plasmin-α_2-antiplasmin complexes were found in preoperative or postoperative plasma in any of the 10 thrombotic and five non-thrombotic patients studied. Mean α_2-macroglobulin concentrations fell after operation but this fall reached statistical significance only in the thrombotic group (day before treatment *v* day 2 after treatment: $P=0{\cdot}01$, nine paired results; day before treatment *v* day 1: $P=0{\cdot}02$, ten paired results).

α_1-Antitrypsin concentration rose in all patients after surgery, and both thrombotic and non-thrombotic groups showed a similar significant rise.

Comment

This study shows that in patients without evidence of venous thrombosis α_2-antiplasmin concentration rises after operation. Low-dose heparin treatment did not modify this rise. Reduced fibrinolytic activity has been observed in surgical patients who develop DVT.[2] It has been suggested that increased fibrinolytic inhibitor concentrations might account for this reduced fibrinolysis. We have, however, been unable to show abnormally increased concentrations of α_2-antiplasmin, α_1-antitrypsin, or α_2-macroglobulin in patients who developed postoperative venous thrombosis. Paradoxically, significantly lower concentrations of α_2-antiplasmin were found after operation in these patients. These lower concentrations of α_2-antiplasmin do not seem to be due to consumption by plasmin during secondary fibrinolysis. Fibrinolysis has been observed previously to be reduced rather than increased in similar patients,[2] and we found no evidence of plasmin-α_2-antiplasmin complexes in our thrombotic patients, which would have been expected if the fibrinolytic system had been activated.

Ulutin[5] observed a parallel rise in both plasminogen activator concentrations and antiplasmin activity in normal subjects after pharmacological fibrinolytic enhancement. If plasminogen activation determines the α_2-antiplasmin concentration then the lower values we observed during postoperative thrombosis may reflect reduced plasminogen activation. Patients with idiopathic recurrent venous thrombosis have been shown to have defective activator release, so a similar defect may be more commonly seen as part of the cause of venous thrombosis in patients with a moderate risk undergoing major surgery. Our findings therefore seem to support the view that there is a failure of fibrinolytic response in patients who develop postoperative venous thrombosis, with a consequent failure of α_2-antiplasmin stimulation.

[1] Collen, D, and Wiman, B, in *Fibrinolysis: Current Fundamental and Clinical Concepts*, ed P J Gaffrey and S Balkuv-Ulutin, p 17. London, Academic Press, 1978.
[2] Mansfield, A, *British Journal of Surgery*, 1972, **59**, 754.
[3] Taberner, D A, *et al*, *British Medical Journal*, 1978, **1**, 272.
[4] Collen, D, *et al*, *European Journal of Clinical Investigation*, 1977, **7**, 21.
[5] Ulutin, O N, *Journal of Clinical Pathology*, 1972, **25**, 619.

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ONE HUNDRED YEARS AGO It is generally believed and taught that suprapubic or hypogastric puncture of the bladder, for the relief of retention, is an operation better honoured in the breach than in the observance. My own experience refutes this tradition. During last ten years, I have performed it in seventeen cases with invariably good result. In some cases, the cannula has been kept in for weeks, till the urethra had been again rendered permeable by nature or art. I have never seen any bad consequences from the operation; it has succeeded in every case. There are those who will argue against this inexorable logic of facts. Some of my cases were *in extremis* at the time of puncture—"given up." Perineal section, or urethrotomy, is easier said than done, and it is an unjustifiable proceeding in any but skilled hands. Presuming that suprapubic is as safe as rectal puncture—and my own experience affirms that it is—it is to be preferred to the latter as being more easily performed and better allowing subsequent drainage—a difficult matter *per rectum* for any length of time. Facility of performance is an important point in its favour. My first case was that of a pauper patient with old-standing stricture, hitherto successfully treated by dilatation with bougies. He had allowed this treatment to fall into abeyance, thinking he was cured. An attack of retention was the result, and all ordinary means—medical and surgical—failed to overcome the difficulty. I went prepared to evacuate *per rectum*, but finding my patient—worn out by agony and exhaustion—cold, insensible, pulseless, and evidently shuffling off this mortal coil as fast as he could, it was impossible, with the only assistance at hand—an imbecile old woman—to get him into position for this operation. He was a large, heavy subject, apparently breathing his last, and lay like a log. It was impossible to get at him.The belly was invitingly prominent and tense. Time was precious. Without further consideration, I plunged in the instrument, withdrew the trocar, tied in the cannula, and touched the edges of the wound with lunar caustic. Something like a gallon of strong-smelling urine escaped, and eight hours afterwards, the old fellow had a good breakfast—the first for many days—and was downstairs by the fire, smoking his pipe. In three weeks' time, without the slightest interference, bladder and urethra were again able to do their work, the cannula was withdrawn, the fistula covered with a fold of dry lint, and in about a week the artificial vent had closed. This patient has been since operated on in the same way successfully, refusing to submit to "splitting" or "cutting," and occasionally neglecting to present himself for dilatation. Where circumstances permit, and the conditions are favourable, it is of course better to restore the urethral passage at once; but where there is any doubt or difficulty, suprapubic puncture is easy, safe, and effectual, and I prefer the curved rectal instrument for this operation. Previous incision through the integument is better avoided. The edges of the puncture (or incision, if that be practised) should be "touched up" with lunar caustic for the purpose of soldering them together, but, as a matter of fact, I have seen no bad result where this nas not been done. The aspirator is all very well, but is not always at hand or in order, and the operation may have to be repeated several times; therefore, if the trocar operation be equally safe, it is preferable. The bladder trocar and cannula are to me, as a surgeon, what the midwifery forceps is to me as an accoucheur. Neither should be used without sufficient cause. (*British Medical Journal*, 1879.)