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Thrombocytopenia induced by nalidixic acid

Over the years the Netherlands Centre for Monitoring of Adverse Reactions to Drugs has received six case reports on patients with profound but transient thrombocytopenia probably induced by nalidixic acid (Negram, Mictral). The table gives the details of these patients.

Cases

Characteristically thrombocytopenia developed within 10 to 15 days of treatment with nalidixic acid, 4 g daily, and rapidly recovered after stopping the drug (table). All patients had platelet counts below 30×10^9/l and serious impairment of blood coagulation, haemorrhagic symptoms being recorded in five. In one case immediate relapse of thrombocytopenia on rechallenge with a single dose of 1 g nalidixic acid provided the proof for a causal relation. One patient concomitantly had a generalised rash. The bone marrow was studied in two patients and showed active megakaryopoiesis.

Comment

Case observations on patients with thrombocytopenia induced by nalidixic acid do not appear to have been described. The rare occurrence of thrombocytopenia is, however, briefly mentioned in the data sheet on Negram (in the Netherlands, but not in Britain) and in the sixth edition of *The Pharmacological Basis of Therapeutics*.[1] According to a report from the Australian Drug Evaluation Committee three cases of thrombocytopenia suspected to be induced by nalidixic acid were reported there during 1964-71.[2] The Committee on the Safety of Medicines has been notified of eight similar cases (J C P Weber, personal communication, 1984).

Apart from the positive result on rechallenge in one patient, several observations suggest a causal relation with nalidixic acid—in particular the rapid and complete recovery when the drug was discontinued. In two patients underlying disturbances of haematopoieses were excluded by examination of bone marrow. Urinary tract infections are not known to be associated with thrombocytopenia. No other suspected drugs than nalidixic acid were known to have been used. Although no specific tests were done, the induction time of 10 to 15 days, the rapid recovery, the active bone marrow, and the concomitant rash in one patient are consistent with an allergic reaction resulting in peripheral destruction of platelets. Nalidixic acid is excreted mainly by the kidneys, and it may be relevant that five of these patients were over 65 and that two of them had clearly impaired renal function.

It is concluded that the use of nalidixic acid is associated with the risk of developing sudden and severe thrombocytopenia. Although this reaction seems to be rare, there may have been considerable underreporting. The notification of similar occurrences to national drug authorities is recommended.

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Early onset scoliosis: a call for awareness

School screening programmes, carried out routinely in the United States and established in a few centres in the United Kingdom,[2] have identified many children with spinal deformities. These deformities, however, are generally mild curves, and controversy exists about the need for their detection. A report by the British Orthopaedic Association and the British Scoliosis Society concluded that more data are required before school screening throughout the United Kingdom can be recommended.[3] If school screening is to be adopted children at special risk need to be identified. I therefore reviewed all patients with infantile idiopathic scoliosis or congenital scoliosis who had attended a regional scoliosis service to see whether diagnosis had been delayed and the appropriate advice or treatment offered.

Patients, methods, and results

I reviewed the case records and radiographs of 139 patients seen during 1976-83. Thirty nine had progressive infantile idiopathic curves and 100 congenital curves, representing 8% and 21% respectively of all new referrals. Ages at diagnosis, at referral for specialist advice, and at referral to the scoliosis clinic were recorded. The circumstances of diagnosis and subsequent management were noted. The severity of curvature was measured from the first available radiograph and from radiographs taken at the initial visit to the scoliosis clinic.

The table shows the results. In both groups a delay of over five years occurred between initial diagnosis and referral to the scoliosis service. Accepting that informed advice is needed when a curve is 40° or more in a child aged over 2, then in 21 children with idiopathic curves the delay was excessive. In 16 of these the diagnosis was made by a parent, in three by a

Details of patients with reactions to nalidixic acid

Case No	Age and sex	Daily dose of nalidixic acid (g)	Other drugs	Platelet count ($\times 10^9$/l)	Complications	Time relation*		Other factors
						Interval	Course	
1	53 F	4	Sodium bicarbonate	16	Petechiae, epistaxis, vaginal bleeding	10 days	5 days	Impaired renal function, serum creatinine 370 μmol/l (4·2 mg/100 ml)
2	91 M	4		6	Bleeding time over 15 minutes	14 days	5 days	Renal insufficiency, serum creatinine 625 μmol/l (7·1 mg/100 ml), rash
3	75 F	4	Digoxin	27	Petechiae	15 days	About 6 days	Treated with prednisolone; sternum puncture: active megakaryopoiesis
4	66 F	4		7	Ecchymosis	3 days	1 week	Relapse of thrombocytopenia 32×10^9/l on rechallenge with 1 g nalidixic acid
5	73 F	4	Insulin	9	Purpura	12 days	5 days	
6	81 F	4		6	Ecchymosis	12 days	4 days	Sternum puncture: active megakaryopoiesis, increased number of plasma cells. After recovery: normal bone marrow

*Interval = interval between starting nalidixic acid and development or discovery of thrombocytopenia. Course = interval between stopping nalidixic acid and recovery of thrombocytopenia.