

DRUG INDUCED GANGRENE OF FOREARM

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INTRODUCTION

Novalgin has been used for many decades as antipyretic. It is known to cause serious toxic effects, particularly bone marrow depression. A case is reported where the drug has directly been implicated in causing gangrene of forearm in a young man. In search of a few books of Pharmacology and Therapeutics and some recent literature no such incidence was found; or reported before.

CASE REPORT

A 38 years old male patient presented to a private clinic and complained of swelling of left forearm extending from below elbow up to the finger tips. Tingling sensations spread over the same area and he was unable to move his fingers. He had a history of an injection of Novalgin (Dipyron) intravenously into the median cubital vein by a local Medical technician three days previously

On examination his left forearm was swollen (31.5 cm circumference measured at a point five centimeter below the intercondylar line) as compared to the right (circumference 30 cm).

The skin looked slightly red tinged. The forearm was warmer than the normal side. The radial pulse was

palpable and was normal in character. The ulnar pulse could not be felt. Sensations were slightly diminished. The wrist was held in palmer flexed position and the patient could not dorsiflex it. Abduction and adduction of the fingers were normal but he could neither extend nor flex them. A provisional diagnosis of thrombophlebitis and neuritis was made. The patient was admitted into the hospital. Investigations revealed normal haemoglobin, platelet, white cell and red blood cell count. Haematocrit was also normal.

Prothrombin time and partial thromboplastin time were done as base line investigations. The patient was heparinized with 30,000 units of heparin and continued with 1000 international units per hour infusion. Arm was elevated on a drip stand. Twenty four hours later there was no improvement and the forearm looked very tense.

Venogram, Doppler and other sophisticated tests were not performed at the hospital. A clinical diagnosis of compartmental syndrome was made so the patient was advised fasciotomy. Unfortunately the patient refused to have the operation and requested for discharge. He was personally persuaded but he left the hospital against medical advice. One week later he returned to

Accident and Emergency dept. of the same hospital with deterioration of his condition. The doctor on duty advised him to consult a Neurosurgeon.

The patient attended private clinic of a Neurosurgeon who instead referred him to a Vascular surgeon. The Vascular surgeon advised admission and investigations but the patient left that hospital again, against medical advice. A week later he reported to a local general practitioner with gangrene of his hand extending up to a point 9cm below elbow. He underwent a below elbow amputation. Histology confirmed gangrene of the tissues with thrombosis in veins.

DISCUSSION

Novalgin (Dipyron, Analgin, Antipyrin) is a Pyrazolone compound¹ used in cases of pyrexia and hyperpyrexia. Its chemical name is Sodium N-(1, 5 demethyl-3-oxo-phenyl-pyrazoline-4-yl)-N-methyl-lamino-methane-sulphonate.⁴

There is limited information available about the pharmacokinetics of Novalgin. Side effects of the drug includes severe agranulocytosis and prolongation of prothrombin time.

Agranulocytosis more commonly occurs in patients who receive the drug for long time but this toxicity may occur in sensitive individuals after a single dose. Agranulocytosis which occurs in around 1% of cases is characterized by a marked decrease in the neutrophil count without a significant decrease in the count of Erythrocytes. Neutropenia is detectable within 30 minutes of a test dose of Aminopyrine. Anti-aminopyrine antibodies have been demonstrated in the serum of a patient with granulocytopenia and so it is postulated that this side effect may be due to the rapid peripheral destruction of leuko-

cytes and not from direct interference with bone marrow function.²

Wessel et al reported a case of hypokalaemic periodic paralysis provoked by Ambene (a drug containing Lidocain, Dexamethasone and Novalgin). But this effect was found to be due to the combination of lidocaine and dexamethasone.⁵ It has been suggested that a combination of aminopyrine (a pyrazolone) and a nitrite orally administered to certain strains of mice, may produce a carcinogen called Dimethylnitrosamine.⁶ While Inai et al tested orally administered aminopyrine to B6C3F1 mice in a controlled trial without showing statistically any significant difference in the incidence of Tumours (Hepatocellular carcinoma, Malignant lymphoma, Lymphoid leukaemia) between the control group and those given oral aminopyrine.⁷

Satoshi Takeno et al have reported embryotoxic effects caused by aminopyrine in mice. Malformations like Omphalocele and Club foot were noted in two Strains of mice (C57BL/6N and DBA/2N).⁸

B. Jaremin reported two cases of dermatological syndromes after they took acetylsalicylic acid, Paracetamol, Amid-ophenazone and Bactrim (A combination of a Sulphonamide and Trimethoprim), though it was not clear that these particular side effects were due to amidophenazone only.⁹ SL Mathur and CS Bhargave reported three deaths in a period of one year due to possible sensitivity to analgin (dipyron).¹⁰

Noskov SM reported megaloblastic pancytopenia in a female patient after she received methotrexate and amidopyrine for Rheumatoid disease. The author held that the effect was due to the combined action of the two drugs.¹¹ It is concluded that dipyron and

other members of the pyrazolone group are very toxic. The Venous Gangrene caused by the intravenous administration of dipyrone into the median cubital vein of forearm as happened in our case is not reported in the literature searched from January 1980 to April 1994. In 1938 "Over the counter sale" of aminopyrine (a pyrazolone) was banned in the United States of America.³ The drug is practically non existing in Europe and North America. In many countries of Asia and Africa, unfortunately, this drug is still widely used by Dispensers, Medical Technicians and General practitioners.

The drug is freely available in the markets in the developing countries. At the same time practically no effective control system exists in these countries, therefore, the drug is misused. It is, therefore, suggested that the free use of dipyrone must be controlled. Probably its use is not justified even in cases of hyperpyrexia. Cold sponging may save these patients from serious toxic effects of the drug. Studies are needed to evaluate the effects of pyrazolones on the veins and arteries.

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