STUDY OF ADVERSE REACTIONS OF METRONIDAZOLE IN INDIAN PATIENTS

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SUMMARY

Present study was an attempt to evaluate epidemiological profile of adverse reactions of metronidazole and factors influencing them. The study included 1112 indoor patients at all India Institute of Medical Sciences Hospital, New Delhi. The patients were in the age group of 15-63 years. Overall incidence of adverse reactions was 23.10%. Metronidazole produced metallic taste in 16.39%, nausea and vomiting in 8.99%, anorexia in 14.92% and headache in 17.28%. All reactions were reversible. Incidence of ADRs has been found to be higher in Indian population as compared to Western population (Kavousi 1979 and Catterall 1977).

Key Words - Adversereactions, metronidazole.

INTRODUCTION

Over a period of last 20 years metronidazole has earned a reputation of being a safe drug. (Kristenson and Freedman 1988). The indications for the use of metronidazole have expanded since its introduction. Currently it is being used to treat many conditions, including anaerobic microbial infections. (Koch-Weser and Goldman 1980). Pre-operative intravenous single dose administration of this drug significantly reduces the incidence of infection after vaginal and abdominal hysterectomies and caesarean sections. (Jackson et al 1979). Other indications for its use are giardiasis and amoebiasis for which metronidazole is given orally. The incidence of untoward effects associated with metronidazole is reported to be low (Catterall 1977). These include furring of tongue, glossitis and stomatitis and may be associated with candidiasis (Koch-Weser and Goldman 1980) (Molavi A, et al 1982). Reversible neutropenia is seen only rarely. (Y. Le Febure Y and Hesseltine H. C. 1965). Neurological side effects - including sensory polyneuropathy, manifested by paraesthesiasataxia and incordination have been reported in a few

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patients after high dose administration given for prolonged period. Convulsions and encephalopathy have also been reported after high doses (Kusumi R. K. et al, 1980). Metronidazole is also reported to be carcinogenic (Beard C. M. 1988).

MATERIAL AND METHODS

One thousand one hundred and twelve adult patients ranging between 15-63 years of age admitted in All India Institute of Medical Sciences Hospital and who received metronidazole were included in this study. These patients were observed for adverse drug reactions during their stay in the hospital. Five hundred and twenty three patients received metronidazole through intravenous route, 513 received orally and 76 cases were initially given metronidazole by intravenous route followed by oral administration. Intravenous metronidazole was given in Gynecology for one day as prophylaxis. Seventy six patients were given this drug parenterally followed by oral administration when favourable conditions prevailed. Clinical picture and drug history were recorded in detail. Patients were seen and interviewed daily by both the clinician and the investigator regarding occurance of adverse reactions. Information was collected using a prepared proforma. Relevant laboratory investigations were done whenever required.

RESULTS

Table I shows type of ADRs seen with metronidazole administration. The anorexia was the commonest symptom (14.92%) followed by metallic faste (9.35%) dryness of

Table I

Incidence of ADRs of metronidazole (according to route)

	I/V	Oral (5-7 days)	I/V + Oral
No. of Patients	523	513	76
Patients with ADR	108 (20.72%)	185 (35.98)	29 (38.4)
Nausea	106 (20.26)*	41 (7.99)	8 (10.5)
Nausea and vomiting	42 (8.03)	48 (9.3)	5 (6.57)
Metallic taste	40 (7.73)	116 (22.6)*	28 (36.8)
Anorexia	14 (2.76)	130 (25.3)*	19 (25.0)
Dry mouth	24 (4.67)	45 (8.7)*	7 (9.21)
Diarrhoea	6 (1.14)	8 (1.55)	2 (2.63)
Abdominal cramps	16 (3.05)	37 (8.2%)*	6 (7.89)
Heavy feeling of body	—	13 (2.5)	—
Cough	12 (2.20)	7 (1.36)	1 (1.3)
Headache	23 (4.39)	74 (14.6)*	—
Giddinesss	3 (0.57)	7 (1.36)	—

Percentage in bracket
* $p < 0.001$

mouth (9.35%) and nausea (8.99%). Very few patients had vomiting which was self limiting.

The overall incidence of ADRs with intravenous, oral and I/V plus oral routes were 20.72%, 35.98% and 38.4% respectively.

Route of administration affected the time of onset of adverse reactions. With I/V route giddiness occured within 15-20 minutes, nausea between 2-12 hours, loss of appetite on 2nd day, collicky abdominal pain in 35 hours diarrhoea on 3rd day and irritant cough appeared 36 hours after the initiation of therapy.

Patients on oral route complained of metallic taste on 3rd day after the first dose. Loss of appetite was observed on 5th day. Onset of headache was early in 1.36% and late in 5.92% of patients. In patients where it was an early symptom it lasted for 18-24 hours though metronidazole was not withdrawn. In the second group headache disappeared only after the drug was withdrawn.

Table II gives the incidence of adverse reactions of metronidazole in relation to the sex of the patients. Females were more susceptible to the ADRs compared to males ($P < 0.01$).

All adverse reactions of metronidazole was completely reversible. Anatacids relieved abdominal pain while cough sedatives were needed to control cough.

No case of neuropathy, encephalopathy and cardiopathy was noticed.

DISCUSSION

In this study the incidence of ADRs is significantly higher than that reported by Kavousi

Table II

Incidence of ADRs of metronidazole according to sex of Patients

	Males	Females	Total
No. of Patients	418	694	1112
No. of Patients with ADRs	81 (19.25)	175 (25.21)	256 (23.10)
GIT Symptoms			
Metalic taste	52 (12.42)	130 (18.93)	182 (16.39)
Nausea and vomiting	36 (8.61)	64 (9.22)	100 (8.99)
Diarrhoea	3 90.71)	13 (1.87)	16 (1.43)
Dry mouth	32 (7.65)	12 (10.37)	104 (9.35)
Abdominal cramps	24 (5.94)	49 (7.06)	73 (6.56)
Anorexia	68 (13.87)	108 (15.56)	166 (14.92)
CNS			
Headache	16 (3.82)	65 (9.36)	81 (7.28)
Giddiness	1 (0.02)	7 (1.0)*	8 (0.71)
Cough	4 (0.95)	7 (0.70)	11 (0.98)

Percentage in bracket
* $p < 0.01$

(1979). Bad taste in mouth was the predominant complain followed by anorexia. Earlier reports on ADRs of this drug are from the Western hemisphere where individuals due to habit of social drinking are less sensitive to bitter and metallic tastes. Barring nausea, intravenous route produced significantly lower incidence of ADRs as compared to oral route. This is due to short duration of therapy by parenteral route. In addition oral metronidazole was employed in Medical wards where it was given along with other antimicrobials to treat mixed (aerobic and anaerobic infection) infections. This combination is likely to be responsible for giving higher incidence of ADRs. Metronidazole administered orally is almost completely absorbed from the intestinal tract. The absorption rate varies in different individuals (Molavi et al 1966). It is likely that absorption rate in our population is better and clearance rate slower which was responsible for higher incidence of ADRs. It is suggested that dosage of this drug be further reduced.

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