Research Article

DRUG PRESCRIPTION IN PREGNANCY: WISE OR WORRISOME

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ABSTRACT

Objective: To study the pattern of drug prescription among pregnant women referred to the antenatal care clinic of a tertiary care centre in India.
Method: It was a retrospective analysis of pattern of drug prescription in 1000 consecutive pregnant patients referred to antenatal clinic of the hospital between January 2016 and December 2016.
Results: Average number of drugs prescribed to each patient was 3.92 with a range of 1-15. In 49.9% patients drugs were prescribed empirically. Average number of empirical drugs prescribed per patient was 2.02 with a range of 0-9. In our study, 93.9 % patients received at least one FDA category A drug while 14.2 % patients received FDA category X drugs. In 142 patients receiving category X drugs, 94(66.1%) were prescribed these drugs empirically. Category X drugs was given to 57.4 % patients before 16 weeks of gestation. Iron was the most commonly prescribed drug in category A while Injection Human Chorionic Gonadotrophin was most commonly prescribed category X drug.
Conclusion: Caution should be exercised while prescribing drugs to pregnant women. Unindicated prescription of drugs leads to increased financial burden on the pregnant women while also exposing mother and fetus to deleterious effects of these drugs.

INTRODUCTION

Pregnancy is the period of altered physiological state in a woman's body. Drug prescription in pregnancy is a challenging task for the clinician not just because of the altered physiologic state but also because of the potential teratogenic effects of drugs on the fetus. The presumption to avoid all drugs during early pregnancy is unrealistic and multiple drugs may be required for the treatment of underlying medical, surgical or obstetric conditions.

Foetuses exposed to thalidomide developing phocomelia brought to the forefront the drug teratogenicity in 1960s. Drugs account for less than 1% of total congenital abnormalities. Hence in 1979, Food and Drug Administration classified various drugs used in pregnancy into five categories; categories A, B, C, D and X. This classification indicates the effect of various drugs on the fetus on the basis of available animal and human data. Category A is considered the safest and category X is absolutely contraindicated in pregnancy.

Despite adequate data on safety profile of drugs, available evidence shows that a surprisingly large number of drugs are prescribed to pregnant women. An international investigation sponsored by WHO showed that pregnant women ingest an average of three prescribed medications during pregnancy (range 1 – 15). [1]

The present study was conducted to analyse the pattern of drug prescription among pregnant women referred to the antenatal care clinic of a tertiary health care centre in northern India.

Experimental Section

Method

It was a retrospective observational study to analyse the pattern of drug prescription in 1000 consecutive pregnant patients presenting to the outpatient department of Maternal and Reproductive Health, SGPGIMS, Lucknow during January 2016 to December 2016. The drug prescriptions which these patients were following at the time of presentation were recorded in a predesigned proforma.

Demographic characteristics including age, socioeconomic status, drugs prescribed, FDA category, indications of prescription, gestational age at exposure, maternal and fetal complications encountered, if any, were recorded. Rationale of individual drug use was assessed. Empirical use was defined as use of drug without any definite indication.

RESULTS AND DISCUSSION

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RESULTS

The mean age of patients was 27 years (range 19-62 years). 36.7% women were primigravida. 31.4 % women presented to the OPD at less than 16 weeks of gestational age. Of the 1000 pregnant women referred to our OPD 13.3% were hypothyroid, 6.3 % had gestational diabetes mellitus, 2.5% had hypertensive disorders of pregnancy, 1.2 % had renal diseases and 1.1 % had anaemia at the time of referral to hospital. Average number of drugs prescribed to each patient was 3.92(range 1- 15). Majority of patients (65.6%) received 1-4 drugs and 1.6 % patients received 10 or more drugs (Table 1). Iron was prescribed to 88.4% patients and was the most commonly prescribed drug (figure 1). Drugs like progesterone, injection Human Chorionic Gonadotrophin and estrogen were prescribed to 69.7% pregnant women.

Analysis of rationality of drug prescription showed that 499 (49.9%) women received at least one drug which was prescribed without any definite beneficial effect reported in literature or was prescribed empirically. 41.7% of women received at least one drug empirically and 2.2% of women received more than five unindicated drugs (Table 2). As the number of prescribed drugs increased, the proportion of unindicated drugs also increased(figure 2). Most empirically used drugs were various forms of progesterone (like didrogesterone, micronized progesterone and hydroxyprogesteronecaproate) prescribed empirically to 30.3% patients. 15% patients were given multivitamins and protein supplements without any proven benefit (Table 3).

93.9 % pregnant women were administered USFDA category A drug and 14.2% women were exposed to FDA category X drug in pregnancy. Iron was the most commonly prescribed drug in category A while Injection Human Chorionic Gonadotrophin (HCG) was the drug most commonly prescribed in category X. In the 142 patients receiving category X drugs, 94 (66.1 %) received drugs without any potential benefit (Table 4). Of these 94 patients receiving Category X drugs empirically, 57.4 % patients were exposed to their deleterious effects before 16 weeks of gestation which is the period of maximal teratogenesis (Table 5).

Overall fetal or neonatal complications in the form of congenital malformations, stillbirth, neonatal death, fetal growth restriction and oligohydramnios were noted in 23.1 % women. It was noticed in 15.9%, 21.9% and 20.4% of women exposed to FDA categories B, C and X drugs respectively.

Table 1 Number of drugs prescribed to pregnant women

No. of drugs	Number of patients
1	168
2	193
3	165
4	132
5	110
6	77
7	65
8	33
9	22
10	8
>10	16
Average no. of drugs : 3.927	
Range of no. of drugs : 1- 15	

Table 2 Percentage of patients receiving unindicated drugs

Number of unindicated drugs	Percentage of patients (n=499)
1	41.7
2	26.2
3	18.1
4	8
5	3.8
>5	2.2

Table 3 Commonly prescribed empirical drugs

Name of drug	Percentage of patients receiving the drug empirically
Progesterone supplements	30.3%
Human Chorionic Gonadotropin	9.5%
Estrogen	3.3%
Isoxsuprine (tocolytic)	5%
Multivitamins and protein supplements	15%
Antibiotics	1.2%

Table 4 Number of patients receiving drugs empirically

Category of Drugs	Number of Patients (A)	Number of patients receiving drugs empirically (%)
A	939	210 (22.3)
B	438	265 (60.5)
C	269	188 (69.8)
D	31	3 (9.6)
X	142	94 (66.2)

Table 5 Prescription of unindicated drugs before or after 16weeks of gestation

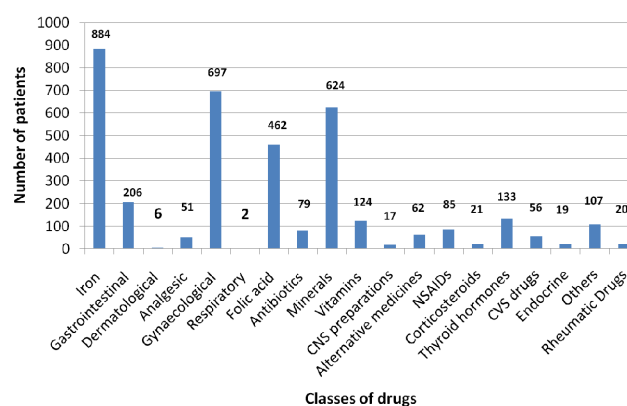| Drug Category	Number of patients receiving empirical drugs (A)	Emperical drugs > 16wks (B)	Emperical drugs <16wks (C)	Percentage %(C/A)
A	210	175	35	16.67
B	265	171	94	35.47
C	188	135	53	28.2
D	3	1	2	66.67
X	94	40	54	57.44

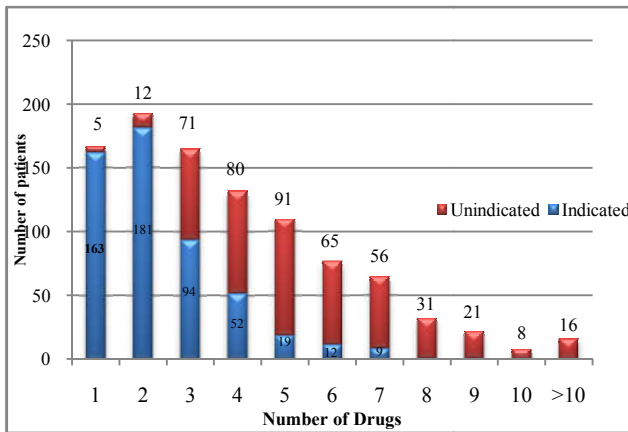**Figure 1** Various classes of drugs prescribed to pregnant women

Figure 2 Comparison of indicated versus unindicated/empirical drugs

DISCUSSION

Prescribing drugs in pregnancy is an unusual risk-benefit situation. Drugs that are of benefit or even life-saving to the mother can be harmful to the fetus, Safety in animal studies may also be reassuring but species differences demand caution in this interpretation.[2]

With advances in artificial reproductive techniques and better guidelines for management of pregnancies with pre-existing chronic medical and surgical illnesses, more patients are able to conceive with a good take home baby rate. With rising pregnancy rates in this group there is rising use of medications which may be teratogenic to the fetus. As these patients usually have a bad obstetric history and anticipated increased maternal and fetal morbidity, empirical use of drugs is increased in this group. Since our hospital is a referral centre, the study was designed to analyse use and abuse of drugs in pregnancy in this subgroup of patients with high risk pregnancy.

It has been reported that about 8% of pregnant women need drug treatment due to various chronic diseases and pregnancy related complications.[6] In our study 24.4% patients presented with chronic diseases and complications related to pregnancy.

We analysed 1000 patients regarding drug prescription and their rationale. The pattern of prescription of drugs in pregnancy was studied in 1000 pregnant women in France and they found that average number of drugs prescribed to pregnant women were 5.2, 7.1 and 6.6 in the first, second and third trimesters of pregnancy respectively[3]. A study on 105 pregnant women in Oman revealed that the average number of drugs prescribed per patient per prescription during the period of pregnancy was 2.33 ± 1.43.[8] Similar study by Uchenna *et al* in 1200 pregnant women attending 3 antenatal clinics in Nigeria showed that average number of drugs prescribed per pregnant patient was 3.[4] Sharma *et al* studied drug prescription in 395 North Indian pregnant women and showed that an average of 1.73, 2.89 and 2.49 drugs per pregnant women, were used during first, second and third trimester of pregnancy respectively.[6] Another study by Anjan Adhikari *et al* in 656 pregnant women from Central India reported that average number of drugs prescribed to each pregnant women was 2.66[7]. In our study, the average number of drugs prescribed to each patient is 3.927 which is similar to the drug prescription in Nigerian population. It is higher than those reported previously

from Indian studies possibly because women referred to our department belong to high risk pregnancy group.

The drugs prescribed in the French population were iron (74.9%), gastrointestinal drugs (69.4%), dermatological drugs (63%) and analgesics (62.3%).[2] The study by Uchenna *et al* in the Nigerian population showed that folic acid (35.4%) was the most frequently prescribed drug. Other minerals and vitamins prescribed included ferrous sulphate in 34%, vitamin C in 8.0% and calcium lactate in 1.0% pregnant women. Paracetamol (87.9%) was the most frequently prescribed analgesic.[4] In the present study the most commonly prescribed drugs were iron (88.4%), hormonal supplements which included estrogen, progesterone and HCG (69.7%), minerals including calcium (62.4%) followed by folic acid (46.2%).

In our study an average of 2 drugs were prescribed to patients without any proven beneficial effect. As the average number of drugs prescribed per prescription increased, the tendency to prescribe one or more drugs without definite indication also increased. High number of empirically prescribed drugs not only increase the risk of teratogenicity and adverse drug interactions but also pose an increased financial burden on the patients. Irrational use of antibiotics will lead to antimicrobial resistance which is a matter of great concern. No other study reviewed the prescription of empirical drug during pregnancy.

The most common drug prescription was FDA category A in the study in French population while 59.3 % women received category D drug prescription; common ones being high doses of aspirin and other non- steroidal anti-inflammatory drugs and angiotensin converting enzyme (ACE) inhibitors. 1.6 % women received a category X drug prescription.[2] The study from Nigerian population reported 48.1%, 25.7%, 17.2% and 5.0% drugs prescribed belonged to FDA category A, B, C and D respectively.[4] Study in South Indian population on 606 pregnant women also showed that the most common drug prescribed in antenatal period was a category B drug[5]. Sharma *et al* showed that majority of the drugs used in antenatal period were category A drugs followed by category B and category D. In their study, category C and X drugs constituted 2.90% and 5.71% of drugs prescribed during the third trimester and first trimester respectively.[6] A retrospective study during the period 1996 to 2000 including 152,531 deliveries revealed that 98,182 women (50.0%) received a drug from category B; 57,604 women (37.8%) received a drug from category C; 7333 women (4.8%) received a drug from category D, and 6976 women (4.6%) received a drug from category X of the USFDA classification. In our study also the most commonly prescribed drugs were USFDA category A and this is similar to the observations of most of the aforementioned studies. This highlights the policy of routine anaemia prophylaxis in India owing to the high prevalence of anaemia.

In our study 14.2% patients received category X drug of which Inj HCG was given to 9.5%% of patients. Chorionic gonadotropin may cause fetal harm when administered to a pregnant woman. Defects of forelimbs and central nervous system and alterations in sex ratio have been reported in mice receiving combined gonadotropin and chorionic gonadotropin therapy in dosages to induce superovulation. No human studies are available in published literature. This calls for more studies on patients receiving HCG in pregnancy.

This study aims to highlight the current status of drug prescription in pregnancy in a developing country like India and the authors wish to bring forth a change in attitude and practices while prescribing drugs to pregnant women. To the best of our knowledge this is the first study which analyses the bane of prescribing various FDA category drugs empirically in pregnancy specifically during the period of maximum teratogenicity.

CONCLUSION

Drug prescription in pregnancy is a challenging task for the clinician because of limited information on drug safety profile in pregnancy and current knowledge being largely based on extrapolation from animal studies. Average number of drugs prescribed to a pregnant patient is 3.927. Most of the patients receive USFDA category A drug but the proportion of patients receiving category X drugs is alarmingly high. Caution should be exercised while prescribing drugs to a pregnant woman more so before 16 weeks period of gestation which is the period of maximum teratogenesis. Empirical use of drugs leads to increased financial burden on the pregnant women while exposing both mother and foetus to deleterious effects of these drugs.

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