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Original Article:

Pattern of antimicrobial agents use in hospital deliveries: A prospective comparative study

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Abstract:
Objective: Drug utilization pattern identifies the problems that arise from the drug usage in health care delivery system and highlights the current approaches to the rational use of drugs. The present study evaluates the utilization pattern of antimicrobial agents in hospital deliveries of different setups. ***Methodology:*** Two hundred hospital deliveries from a government hospital GroupI (G-I) and 100 cases each from two private hospitals Group II & Group III (G II & G III) were studied. Groups, drugs, numbers of antimicrobials used, duration with indication for their use were the criteria taken into consideration for comparison. ***Results:*** Beta-lactams, nitroimidazoles and fluoroquinolones were commonly prescribed groups of antimicrobials. The duration of prophylaxis was 6.73±1.79, 5.77±1.10 &5.14±1.53 days in three groups respectively which was significantly different ($p<0.01$). Caesarian section, episiotomy were the commonest prophylactic indications. ***Conclusion:*** The present study calls for an urgent review on rational use of antimicrobial for prophylaxis.
Key Words: Antimicrobial agents, Infection, Prophylaxis, Hospital deliveries

Introduction:
Prescription order is an important transaction between the clinician and patient.(1) It is an order for scientific medication for a person at a particular time .Now a days the prescribing pattern is changing and it has become just an indication of medicine with some instruction of doses without consideration of it's rationality.(2) Antimicrobial agents (AMA) deserve their place as one of the most powerful pillars of modern medical care.(3) AMA along with vaccines and oral rehydration salts represent potential agents in preventing mortality as well as morbidity.(4) The problem of overuse is a global phenomenon. In India, the prevalence of use of antimicrobials varies from 24-67%, where as in the Duke University Medical Centre England it accounts for 34%. Antimicrobials as a group contribute significantly to the cost of drugs and is claimed worldwide to account for 15-30% of total health budget. In India, the cost of AMA is as high as 50% of the total health budget.(5,6) In obstetrics practice, use of AMA either prophylactically or to treat infection has reduced the infectious morbidity following caesarian section and other infections associated with deliveries. Depending upon the geographical location and sensitivity pattern to AMA, the choice of these differ from one clinical setup to another. As per Kunin's criteria it was observed that 64% of total antibiotics prescribed were either not indicated or were inappropriate in terms of drug and dosage.(7) The present study was undertaken to evaluate the utilization pattern of AMA in hospital deliveries. Serial studies such as this help to evaluate the changing trend with respect to prescribing patterns.

Methodology:
This prospective study, approved by institutional ethical committee was undertaken in a government teaching hospital and two private hospitals. Four hundred cases were selected by stratified random sampling. Proportion wise samples were taken from strata (hospital), there by 200 cases from government hospital, group I (G- I), and 100 each from two private hospitals, groups II and III (G- II & G- III). Cases were selected in such a way that only those who were prescribed AMA were included in the study. The prescriptions were analyzed with respect to group, number, and indication of AMA use and duration of use. The information was collected from the case sheets and for any additional information, the doctor in charge or nursing staff were enquired. Each AMA was counted once irrespective of any change in dosage regimen. The percentage for each of the parameter was calculated. Individual comparison was done (groupwise) by Guassian test (Z) and significance was found $P< 0.05$, analysis was done using S.P.S.S.(version 12).

Results:

Beta-lactams, nitroimidazoles, fluoroquinolones and aminoglycosides were the common categories of AMA prescribed in this study (Table1).

Table 1: Categories of AMA prescribed

AMA	Group I (%)	Group II (%)	Group III (%)
Beta –lactam	202 (53.16)	62 (35.18)	122 (92.42)
Nitroimidazoles	139 (36.58)	35(19.70)	01 (0.76)
Fluoroquinolones	06 (1.58)	76 (43.50)	05 (3.79)
Aminoglycosides	21 (5.53)	01 (0.51)	02 (1.52)
Others	12 (3.15)	02 (1.11)	02 (1.13)
Total(n)	380	176	132

Single AMA was prescribed more commonly in G- II (ciprofloxacin, cephazolin) and G- III (cephotaxim); two AMA (ampicillin and metronidazole) were prescribed more commonly in G-I (Table-2).

Table 2: Number of AMA prescribed.

No. of AMA.	I (%)	II (%)	III (%)	Total (%)
1	51 (25.5)	60 (60)	76 (76)	187(46.75)
2	123 (61.5)	39 (39)	20 (20)	182(45.50)
3	21 (10.5)	1 (1)	2 (2)	24(6.00)
> 3	5 (2.5)	-	2 (2)	7(1.75)
Total (n)	200	100	100	400(100)

Prophylactic use of AMA (64, 90 and 72%) exceeded the infectious indication for AMA (36, 10 and 28%) in all the three groups; differences between the groups were significant (Table 3).

Table 3: Rationale for prescription of AMA

Rational	Group I (%)	Group II (%)	Group III (%)	Total (%)
Prophylactic	128 (64)*	90 (90) **	72 (72)***	290 (72.5%)
Infectious	72 (36) *	10 (10) **	28 (28) ***	110 (27.5%)
Total (n)	200	100	100	400
*G-I Vs G-II (prophylactic and infectious), P<0.001; **GII Vs G-III (prophylactic and infectious), P<0.01; ***G- III Vs G-I , prophylaxis P<0.05 , infectious P<0.001.				

The duration of prophylaxis in G- I, II and III was 6.72±1.79, 5.77±1.10 and 5.14±1.53 days respectively which was statistically significant (p<0.01). Duration of antimicrobial agents use in two categories, infectious and prophylactic indications are given (Tables 4, 5 and 6).

Table 4: Duration of AMA use in prophylaxis and infections.

Duration of AMA use in days	Group I(cases)		Group II(cases)		Group III(cases)		Total	
	Prophylaxis	Infections	Prophylaxis	Infections	Prophylaxis	Infections	Prophylaxis	Infections
1	02	-	-		-		02	68
2-4	03	-	01	-	08	-	13	28
5-7	74	38	86	10	58	20	218	14
8-10	49	25	03	-	05	03	57	110
> 10	-	09	-	10	-	05	-	-
Total(n)	128	72	90	20	72	28	290	110
Mean ±SD(days)	6.72± 1.79*	7.52±2.52	5.77± 1.10**	6.01±1.05	5.14±1.53***	7.5±3.22	5.53 ± 1.24	6.94±1.35
*G-I Vs G-II (prophylaxis) P<0.001; **GII Vs G-III (prophylaxis) P<0.01; ***G- III Vs G-I (prophylaxis) P<0.010								

Table 5: Showing infectious indications for antimicrobial use.

Indication	Group I (%)	GroupII (%)	Group III (%)	Total (%)
U.T.I & associated condition	35 (48.60)	4 (40)	13 (46.42)	52 (47.23)
Wound Infection	25 (34.71)	2 (20)	8 (28.57)	35 (31.82)
Puerperal Sepsis	08 (11.11)	2 (20)	5 (17.85)	15 (13.63)
Worm infestation	2 (2.77)	-	-	2 (1.8)
U.R.T.I.	2 (2.77)	2 (20)	2 (7.14)	6 (5.45)
(n)	72	10	28	110

Table 6: Depicting the various indications for antimicrobial prophylaxis.

Indication	Group I	Group II	Group III	Total
R.M.L.E.	27 (21.09)	42 (46.67)	35 (48.61)	104 (35.86)
Surgery (LSCS+ PPS)	71 (55.46)	35 (38.89)	22(30.56)	128 (44.22)
Meconium stained liquor	13 (10.15)	8 (8.89)	8 (11.11)	29 (10)
Perineal tear	8 (6.25)	5 (5.55)	5 (6.94)	18 (6.20)
P.R.O.M.	9 (7.05)	-	2 (2.78)	11 (3.72)
(n)	128	90	72	290
RMLE - Right medio lateral episiotomy, LSCS - Lower segment caesarian section; PROM - Pre mature rupture of membrane.				

In this study, inclusive of all three groups there was a total of 14 cases where AMA administration in prophylaxis was a failure; G- I 9/128 (6.7%) and G- III 5/72 (7%).

Discussion:

Prescription by a clinician may be taken as a reflection of his attitude to the disease and role of the drug in its treatment.(8) It brings into focus the diagnostic acumen and therapeutic proficiency of the clinician with instruction for palliation or restoration of patient's health.(3) AMA use varies from geographic area and with the health care system. The data obtained from this study is unique, as the pattern of AMA utilization was assessed in hospital deliveries which has not been studied in India in the recent past. The findings in this study may explain that despite the promiscuous availability of AMA and their use in hospital deliveries, the incidence of puerperial sepsis has not declined;12.6% in 1993,16.1% in 2003.This has partly attributed to the rise in maternal mortality rate in India. The microbial flora of female genitourinary tract consists of a wide variety of organisms demanding the use of either a single AMA that covers the entire spectrum or combination of two or more AMA for prophylaxis or treatment of infection.(9) Preference is to prescribe a single AMA with wide spectrum of activity and not a combination of drugs so as to avoid possible adverse reactions, suprainfections and decreased patient compliance. In this study one AMA was used in 46.75% (187/400) cases. This was significantly higher than a similar study where single AMA use was 17.77%.(10) The increasing trend towards the use of one AMA is an indication of improved prescribing skills on the part of the clinicians and the availability of effective AMA with wide spectrum of activity. The higher percentage of single AMA used in Gs II 60% of cases (ciprofloxacin, cephazolin) and III 76% of cases (cefotaxim) is related to the affordability by patients in private hospitals. In contrast, two AMA (ampicillin and metronidazole) was prescribed maximally in 61.5 % of cases of G-I in a government teaching hospital.

The choice of AMA depends upon the type of infection, its severity and availability of AMA, efficacy, safety profile and cost.(11) The use of beta-lactam in this study (56%) was higher when compared two studies 39.61% and 40.4% respectively.(9,12) Among the beta-lactams used, the penicillin group (aminopenicillins-ampicillin; penicillinase resistant Penicillins - Cloxacillin) and cephalosporins (cefazolin and cefotaxim) constituted 57.73% and 42.27% respectively. In G-I ampicillin constituted 100% of beta-lactam antibiotic used, in G-II cefazolin was the commonest prescribed beta-lactam antibiotic (98.38%), in G- III ampicillin with cloxacillin and cefotaxim were prescribed almost equally.

The nitroimidazoles which are effective against B.fragilis present in the normal female genital tract was the second commonest group of AMA prescribed in this study, 25.43 %(table 1), which was higher compared to the two independent studies 11.35% and 15.36%.(10,13) Fluoroquinolones was the third commonest group of AMA used in this study (12.66%) (Table1) which was higher compared to the above mentioned studies 9.66% and 8.96%.(10,13) This is despite that fluoroquinolones are secreted in human milk and are contraindicated in pregnancy as well as in childhood. Aminoglycosides prescribed in this study was much lower (3.5%) compared to Rehan's (14.15%) and Srishyla's study (21.49%) (Table 1).The higher use of aminoglycosides in G-1 is an indication of availability in government hospital.The negligible use of aminoglycosides in G- II and G- III is related to the availability of beta-lactams, nitroimidazoles and fluoroquinolones which have a better efficacy and safety.

The prophylactic use of AMA in this study exceeded infectious indication (72.5% Vs 27.5%) and also exceeded the prophylactic use in previous studies (32% and 54.4%).(10,13) Studies have indicated that prophylaxis is justified in the dirty contaminated surgical procedures where the incidence of wound infection is high as in resection of colon, which constitutes less than 10% of the surgeries.(14) Most (75%) of total surgeries are clean surgical procedures and include the surgical interventions mentioned in this study (Table 6).The expected infection here is less than 5% and may not justify the uniformly higher use of AMA in all three groups of this study (64,90 and 72%), inspite of specific clinical indications and physician's personal benefits. The second irrationality analyzed in the prescribing pattern of this study, the importance of which outweighs the first, is the extended duration in days for which prophylaxis was given. The average duration of AMA for prophylaxis was 5.52±1.24 days in this study, which though is shorter when compared to another study(8.08 ± 0.83 days)(Table4) (10), is much longer than the common recommendation of one-three doses of AMA for prophylaxis. Prolonging the duration of AMA does not provide for an additional therapeutic benefit while the cost and the adverse effects simultaneously escalat.(9) The significantly longer duration of prophylaxis in G-1 (6.72 ±1.79 days) is an indicator of delayed admissions of patients in transit to tertiary care referral hospital with failure or complication in the previous hospital, combined with the lower nutritional status and poor hygienic condition of patients in G-1 admitted to government hospital. The average duration of antimicrobial therapy was 6.95±1.25 days without significant differences between the groups.

AMA for Treatment of Infections(Table 6): UTI was the commonest indication, followed by wound infection, puerperal sepsis and URTI in all the three groups. The higher incidence of infection in groups 1 (6.7%) and III (7%) following caesarian section may be related to inadequate aseptic precautions and delay in initiation of AMA prophylaxis (beta-lactam). In group II the incidence of infection following caesarian section and prophylaxis failure were less. This may reflect the proper timing of AMA administration, better aseptic precautions, use of effective AMA (cephalosporin, ciprofloxacin and tinidazole combination) and better adherence to treatment protocols.

Timing of AMA: In this study AMA were used in the post operative period in groups 1 and III and immediately after clamping the cord in group II. In case of artificial rupture of membrane, episiotomy and postpartal sterilization it was administered 30 minutes before in group II and after the procedure (once the patient is shifted to ward) in groups 1 and III.

Conclusions:

We conclude from our study that,

1. Duration of AMA prophylaxis should be reduced to 24 –36 hrs as against the findings in this study which was 5.58 days in all three groups. Only in presence of gross contamination, should prophylaxis be continued. Duration of prophylaxis is reducing, though still very far from the required of 1-3 days.
2. There is an increasing trend to prescribe single AMA and decrease in the trend to prescribe aminoglycosides.
3. The time of administration of AMA should be modified in GI and GIII. AMA should be administered after clamping the cord in caesarean section and not preoperatively or post operatively. In artificial rupture of membranes, episiotomy, perineal tear, post partal sterilization it should be administered 30 min before the procedure as against the finding in the study where AMA were administered after the procedures.
4. Number of antimicrobials used and class of antimicrobial used are interdependent. As for as possible use of ONE or TWO of wider spectrum were re-

commended. Since the antimicrobials with wider spectrum (cephalosporins) were not available in G-I. (Government hospital), we should convince the authority for the supply of same which will be beneficial to the patients in terms of cost & convenience of administration and also discourage the use of fluoroquinolones during hospital deliveries.

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