The Role of Prophylactic Antibiotics in Caesarean Section — A Randomised Trial

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Summary

A prospective randomised controlled study was conducted over a 6 month period on the value of administering prophylactic antibiotics in patients undergoing emergency caesarean section at the Ipoh General Hospital. A total of 222 patients were randomised to receive 24 hours of ampicillin (500 mg per dose), cefoperazone (1 gm per dose) or no antibiotics.

In all parameters of patient morbidity, the group receiving cefoperazone showed significantly better results as compared to the group not receiving antibiotics. The ampicillin group also had favourable results but generally not achieving statistical significance. Prophylactic antibiotics appear to be beneficial and consideration should be given to make it a routine in all emergency caesarean sections.

Key words: Caesarean section, antibiotic prophylaxis, Cefoperazone

Introduction

Bacterial contamination, either endogenous from vaginal and cervical flora or exogenous are 2 key factors contributing to infection after caesarean section. Moir-Bussy[1] estimated that in England and Wales, at least 6% of women who had caesarean section developed wound infection. Wound infection after caesarean section not only results in increased morbidity but has far reaching implications by way of pelvic organ disease, disturbance of the bonding process between mother and baby in the puerperium and a longer hospital stay with its inherent problems. There is strong evidence that the risk of infection after caesarean section can be reduced by prophylactic antibiotics[2].

Administration of prophylactic antibiotics would, however, add considerably to pharmacy costs. To justify the introduction of this as a policy, a prospective randomised controlled study was done at the Ipoh General Hospital. A preliminary pilot study was conducted during which we found a very low rate (1.2%) of post-operative infection in clean wounds, i.e., in elective caesarean sections. The study proper was thus limited to patients with singleton pregnancies undergoing emergency surgery.

Patients and Methods

A total of 262 patients underwent emergency caesarean section between March and August, 1991, at the Ipoh General Hospital. These patients were screened for suitability for inclusion into the study. Exclusion criteria for the study included known hypersensitivity to either antibiotic, the presence of infection or fever before the operation, patients already on antibiotics for any reason and patients with multiple pregnancies. The remaining 222 patients were then randomised to receive either cefoperazone (3 doses of 1 gram at 12 hourly intervals), ampicillin (4 doses of 500 mg at 6 hourly intervals) or no antibiotics. The first dose was

given at induction of anaesthesia and the total number of doses of antibiotics given was calculated to give coverage for the first 24 hours after surgery. Two patients were excluded from the study; 1 each from the cefoperazone group and the group not given antibiotics. These patients had antibiotics prescribed immediately following the operation because of an intraoperative problem.

Wound infection was defined as the presence of inflammation over the wound associated with a serous or purulent discharge with or without surrounding cellulitis. Assessment of the wound was made by the medical officer in charge of the postnatal ward.

Data was compiled and analysed statistically utilising Epi Info Version 5 (USD Incorporated, Stone Mountain, Georgia). Statistics on parametric data were derived using the Student's t-test, non-parametric data on the Mann-Whitney test and qualitative data on Chi squared with Fisher exact test when appropriate. A p value of less than 0.05 was taken to denote statistical significance.

Results

There were 76 patients in the cefoperazone group, 74 patients in the ampicillin group and 70 patients in the group without antibiotics.

Table I shows the demographic details of the patient groups. There was no significant difference in the age, race, parity or gestational age at delivery among the 3 study groups.

The indications for caesarean section were similar in the groups and there was similar incidence of pre-operative medical conditions (Tables II, III).

Table IV lists the factors which could possibly account for differences in the results. The length of labour and duration of membrane rupture was similar in the 3 groups and there was no statistically significant difference in the number of vaginal examinations performed on the patients in each of the groups. There

Table I
Demographic data

	no antibiotics	ampicillin	cefoperazone
Age (years)	31.0±5.3	29.9±5.2	31.4±5.8
Race			
Malay	39	38	32
Indian	20	23	19
Chinese	10	11	20
Others	1	2	5
Parity	1.76±1.84	1.55±2.24	1.93±1.77
Gestational age at delivery (weeks)	39.1±2.6	39.2±1.9	38.6±2.5

No statistical differences were detected in the above parameters ($p>0.05$)

Table II
Indications for emergency caesarean section

	no antibiotics (n=76)	**ampicillin** (n=74)	**cefoperazone** (n=70)
Poor progress/cephalopelvic disproportion	24	23	25
Foetal distress	16	18	16
Placenta praevia	9	6	12
Breech presentation	5	9	3
Other abnormal presentation	7	5	5
Pre-eclampsia/eclampsia	3	6	5
2 previous caesarean sections in labour	7	3	2
Others	5	4	2

Table III
Medical conditions complicating pregnancy

	no antibiotics (n=76)	**ampicillin** (n=74)	**cefoperazone** (n=70)
Pre-eclampsia	14	18	19
Diabetes mellitus	4	3	7
Heart disease	-	1	-
Thyroid disease	-	1	-

Table IV
Details of labour

	no antibiotics (n=76)	**ampicillin** (n=74)	**cefoperazone** (n=70)
Length of labour (hours)	8.43±6.79	8.46±8.00	7.59±6.66
Period of membrane rupture (hours)	6.70±6.48	5.66±7.36	5.63±8.98
Number of vaginal examinations	3.19±2.12	3.04±2.30	2.63±1.99
Patients with previous caesarean section	15 (21%)	17 (23%)	30 (39%)
Vertical incision made	14 (11%)	13 (18%)	13 (25%)*

*P = 0.035

was no statistically significant difference in the proportion of each group having had previous caesarean sections.

In the group not receiving prophylactic antibiotics, 11% of them had vertical incisions as compared to 18% in the ampicillin group and 25% in the cefoperazone group. This reached statistical significance when comparing the cefoperazone and no antibiotic groups (p=0.035) but no such statistical difference was noted when the ampicillin group was compared with the group not receiving antibiotics. It is generally recognised that vertical incisions are more prone to infection[3] and the results showing more vertical incisions in the cefoperazone group will only further enhance the significance of our results. This is likewise in comparing the number of patients with previous caesarean sections as there is difference in the number of patients having had previous caesarean sections though not achieving statistical significance.

As for foetal outcome, the Apgar scores were similar at 1 and 5 minutes in all the study groups with no neonatal mortality. Birth weights were similarly comparable.

Table V
Febrile morbidity

	no antibiotics	ampicillin	cefoperazone
Average maximal temperature (°C)	38.07±0.62	37.94±0.40	37.85±0.42
Number of spikes>38°C	1.74±2.21	1.04±1.20	0.82±0.99*

*p=0.02

Table V shows the morbidity associated with each of the study groups. The average maximal temperature in the 3 groups was very similar and the difference did not achieve statistical significance.

In patients not given prophylactic antibiotics, there was an average of 1.74 spikes of temperature above 38°C. This compared with 1.04 spikes in the group receiving ampicillin and 0.82 spikes in the group receiving cefoperazone. Statistical significance was demonstrated in this index between the cefoperazone versus the 'no antibiotic' group (p=0.02). Spikes of temperature were determined by counting the number of episodes in which the temperature achieved or exceeded 38°C. Temperature readings were made at 4 hour intervals and consecutive readings of above 38°C were read at single spikes.

Table VI
Post-operative infections

	no antibiotics (n=76)	ampicillin (n=74)	p	cefoperazone (n=70)	p
Wound infection	11 (15.7%)	4 (5.4%)	0.04	0 (0%)	<0.001
Secondary suturing done	5 (7.1%)	2 (2.7%)	n.s.	0 (0%)	0.018
Microbiology performed	22 (31.0%)	11 (14.9%)	0.018	7 (9.2%)	<0.001
Antibiotics used	18 (25.7%)	12 (16.2%)	n.s.	5 (6.6%)	0.0015

*n.s.: not significant

Table VI shows that there was a 15.7% incidence of wound infection in the 'no antibiotic' group as compared to 5.4% in the ampicillin group and zero (0%) in the cefoperazone group. The difference reached statistical significance in comparing the cefoperazone and 'no antibiotic' study groups ($p<0.001$) and in comparing ampicillin to 'no antibiotics' ($p=0.04$).

A total of 7 patients underwent secondary suturing as a result of wound dehiscence; 5 in the no prophylactic antibiotic group and 2 in the ampicillin group. The difference reached statistical significance when the cefoperazone group was compared with the group not receiving antibiotics ($p=0.018$).

A total of 40 patients had specimens taken from various sites for microbiological studies based on clinical need. These were in the main wound, urine and blood cultures. As there were few positive cultures, for the purposes of statistical analysis only the frequency of sampling was analysed. Twenty-two patients in the group not receiving antibiotics had microbiological studies done compared with 11 in the group receiving ampicillin and 7 in the group given cefoperazone. There was statistical significance when the group receiving ampicillin was compared with the group not receiving antibiotics ($p=0.018$) and when the group receiving cefoperazone was similarly compared ($p<0.001$).

As for the use of other antibiotics post-operatively, 35 patients had antibiotics given for a variety of reasons, mainly for persistent fever and obvious wound infection. Of these, 18 were from the group not given antibiotics prophylactically, 12 were from the group given ampicillin and 5 were from the group administered cefoperazone. The difference reached statistical significance when cefoperazone was compared with no antibiotics ($p=0.0015$).

In comparing the average number of days the patients stayed in hospital post-operatively, the group not given antibiotics stayed an average of 6.50 days (standard deviation=3.67), the group given ampicillin stayed an average of 5.57 days (standard deviation=1.43). The differences did not reach statistical significance.

Analysing the lengths of hospital stay in more detail, there were more patients in the 'no antibiotic' group who stayed for prolonged periods in hospital. Sixteen (23%) patients in the 'no antibiotic' group stayed for 7 days or more as compared to 10 (13%) in the cefoperazone group and 12 (16%) in the ampicillin group. These differences, however, are not statistically significant. A larger series may throw more light upon this aspect, which would be of particular interest to hospital managers.

Discussion

Wound infections can constitute a significant problem in surgical procedures. In caesarean sections, this is particularly important as a wound infection may affect not just the mother but also the child and the patient's future obstetric performance. A retrospective study done recently in Kuala Lumpur[4] recorded a wound infection rate of 4.9% in their caesarean sections but no details were given as to the circumstances. This infection rate was evidently in excess of their overall hospital rate of 2.9%.

There is abundant literature on the subject of prophylactic antibiotics for caesarean sections in the West. In a recent meta-analysis of a total of 7,777 women from 58 controlled trials studying the effect of prophylactic antibiotics in caesarean sections, the results suggest a reduction in the odds of wound infection by between 56% and 72%[2]. A similar reduction in post-operative febrile morbidity was also noted.

We have, however, no such intervention studies published from Malaysia. It is particularly pertinent in government institutions to know if prophylactic antibiotics are necessary and whether they are cost

effective. Our study has attempted to address the area of the incidence of wound infections in emergency caesarean sections.

Not all indications for caesarean sections would obviously have the same risk of infection but taken as a whole, it would seem from our study that prophylactic administration of a broad-spectrum cephalosporin is useful in reducing the morbidity from emergency caesarean sections.

In our study, we found statistically significant reductions in febrile morbidity, in the rates of wound infection (15.7% versus 0%) and secondary suturing (7.1% versus 0%), the use of microbiology (31% versus 9.2%) and need for subsequent antibiotics (25.7% versus 6.6%) in comparing the group receiving no antibiotics to the group receiving cefoperazone. In the ampicillin group, we found smaller reductions in the same parameters but the improvements only achieved statistical significance in comparing the wound infection rates and the use of microbiology.

Cefoperazone was selected as it was the most commonly prescribed cephalosporin in our hospital at the time of the study and had been used previously as empirical prophylactic therapy.

Ampicillin was also studied as it was felt that if there was a cheaper broad-spectrum antibiotic available, it would obviously be preferred. This is especially so in view of reports that the febrile morbidity in patients undergoing caesarean section was similar in groups receiving cephalosporins or the older broad-spectrum antibiotics[5,6]. From our results, the improvements in patient morbidity recorded are less than that of cefoperazone. This would suggest that ampicillin is a less satisfactory prophylactic antibiotic as compared to cefoperazone but it would be interesting to compare this with a bigger sample.

There are significant advantages in reducing the incidence of wound infection. Other than cost implications, wound infections and febrile morbidity drain both the patient and baby physically and mentally. Maternal child-bonding may be affected and breast-feeding interrupted. There is also a strong negative psychological effect on other patients in the ward as a whole (in particular with our open ward systems) when post-operative patients develop foul-smelling gaping wound infections. There must also be physical, psychological and financial implications on the family unit which we cannot quantify.

Studies from other parts of the world have shown substantial reductions in average hospital costs[5,7] when prophylactic antibiotics are given. It is not easy to itemise and determine hospital costs accurately but from a limited assessment of our results, we were able to find quite definite cost savings from prescribing prophylactic cefoperazone to cases of emergency caesarean sections.

There would be objections to the prophylactic use of antibiotics. There were no significant adverse events recorded from our series and none of the patients had to have their antibiotics ceased. There is, however, the risk of anaphylaxis associated with the administration of antibiotics. Deaths have been recorded with the use of prophylactic cephalosporins in surgical patients[8]. The risk of increasing the pool of resistant bacteria is also an important consideration[5,9]. Prophylactic use of 3 doses of cefoperazone in all our emergency caesarean sections would increase the total use of the drug in our hospital by about 9.6%. This is a significant though not an enormous increase. It is important thus that appropriate consultations be made with concerned microbiologists and infection control teams before any decision is made regarding prophylactic antibiotic use.

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References

1. Moir-Bussy BR, Hutton RM, Thompson JR. Wound infection after caesarean section. J Hosp Infect 1984;5 : 359-70.
2. Enkin M, Enkin E, Chalmers I, Hemminki I. Antibiotics and caesarean section. In: Chalmers I, Enkin M, Kierse MJNC (eds). Effective care in pregnancy and childbirth. Oxford University Press 1989;1246-69.
3. Webster J. Post-caesarean wound infection: a review of the risk factors. Aust NZ J Obstet Gynaecol 1988;28 : 201-7.
4. Yasmin Abu Hanifah. Post-operative surgical wound infection. Med J Mal 1990;45 : 293-7.
5. Mugford M, Kingston J, Chalmers I. Reducing the incidence of infection after caesarean section: implications of prophylaxis with antibiotics for hospital resources. Br Med J 1989;299 : 1003-6.
6. Louie TJ, Binns FAO, Baskett TF, Koss J. Cefotaxime, cefazolin or ampicillin prophylaxis of febrile morbidity in emergency caesarean sections. Clin Ther 1982;5 : 83-96.
7. Duff P. Prophylactic antibiotics for caesarean delivery: A simple cost-effective strategy for prevention of post-operative morbidity. Am J Obstet Gynaecol 1987;157 : 794-8.
8. Spruill FG, Minette LJ, Sturner WQ. Two surgical deaths associated with cephalothin. JAMA 1974;229 : 440-1.
9. Howie PW, Davey PG. Prophylactic antibiotics and caesarean section. Br Med J 1990;300 : 2-3.