3 RESULTS

3.1 Part I - Misoprostol versus Dinoprostone

Patients in the misoprostol and dinoprostone groups were similar with respect to maternal age, gravidity, parity, initial Bishop score and gestational age as listed in Table 3-1.

Demographic data	Oral misoprostol n=120	Vaginal misoprostol n=120	Dinoprostone control n=240
	median (quartiles)	median (quartiles)	median (quartiles)
Maternal age (year)	28 (23/33)	27 (23/32)	27 (23/32)
Gestational age (week)	39 (37/40)	39 (38/41)	39 (38/41)
Bishop score	3 (2/4)	4 (2/5)	3 (3/5)
Gravidity	2 (1/3)	2 (1/3)	2 (1/3)
Parity	2 (1/2)	2 (1/2)	2 (1/2)
Nulliparity	44 (36.7%)	52 (43.3%)	101 (42.1%)
No. of doses	3 (2/4)	2 (1/3)	2 (1/2)

Quartiles in brackets correspond to Q1/Q3

Table 3-1 : Demographic Data.

The portion of nulliparous patients in the groups was similar, 44/120 (36.7%) in the oral misoprostol group, 52/120 (43.3%) in the vaginal misoprostol group and 101/240 (42.1%) in the dinoprostone control group expected the first child.

The median number of misoprostol doses required was 2 in the vaginal misoprostol group as compared with 3 in the oral misoprostol group.
The median number of doses required in the dinoprostone group was 2.

The main indications for induction of labour in all three groups were pre-eclampsia and post-dates, no statistical differences were observed between the groups (cf. Table 3-2).

Indications	Oral misoprostol n=120	Vaginal misoprostol n=120	Dinoprostone control n=240
	n (%)	n (%)	n (%)
Pre-eclampsia	40 (33.3)	44 (36.7)	60 (25.0)
Hypertension	14 (11.7)	11 (9.2)	41 (17.1)
Postdates	25 (20.8)	32 (26.7)	65 (26.2)
Diabetes	13 (10.8)	15 (12.5)	18 (7.5)
Previous stillbirth	9 (7.5)	10 (8.3)	14 (5.8)
Oligohydramnios	6 (5.0)	3 (2.5)	16 (6.7)
APH	3 (2.5)	1 (0.8)	2 (0.8)
IUGR	3 (2.5)	0 (0)	8 (3.3)
other	7 (5.8)	4 (3.3)	16 (6.7)

APH= antepartum haemorrhage, IUGR= intrauterine growth restriction

Table 3-2 : Indications for induction of labour.

There was an obvious difference in the total delivery rate within 24 hours between all modes of delivery as given in Table 3-3. 109/120 (90.8%) women in the vaginal misoprostol treatment group delivered during the set time of 24 hours irrespective of the route, compared with the other groups this was highly significant (p=0.000, Fisher's exact test).

The other two groups showed a significantly lower success rate of 55.8% (67/120) in patients treated with oral misoprostol and 75.4% (181/240) in the dinoprostone control group (p=0.000, Fisher's exact test).

Success rate	Oral misoprostol n=120	Vaginal misoprostol n=120	Dinoprostone control n=240	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
Total deliveries < 24 hours	67 (55.8)	109 (90.8)	181 (75.4)	p=0.000	p=0.000	p=0.000
NVD < 24 hours	47 (39.2)	69 (57.5)	131 (54.6)	p=0.007	p=0.653	p=0.007

NVD= natural vaginal delivery, P Value ~ Fisher's exact test

Table 3-3 : Deliveries within 24 hours of the first dose.

Another primary outcome measure was the success rate of vaginal deliveries within 24 hours. 69/120 (57.5%) women in the vaginal misoprostol group achieved vaginal delivery within 24 hours compared with 131/240 (54.6%) in the dinoprostone control-group (p=0.653, Fisher's exact test).

The success rate of 39.2% (47/120) in women induced with oral misoprostol was significantly lower than either in the vaginal misoprostol group (p=0.007, Fisher's exact test) or in the dinoprostone group (p=0.007, Fisher's exact test).

The time from induction to delivery by any route was one of the main outcome measures (cf. Figure 3-1).

Women of the vaginal misoprostol group delivered within 12 h 19 min after the first application (Q1=8 h 25 min, Q3=16 h 46 min), compared with the induction interval of 14 h 49 min (Q1=9 h 52 min, Q3=23 h 56 min) in the dinoprostone group (p=0.002, Mann-Whitney-test).

The median time to delivery in the oral misoprostol group was 22 h 47 min (Q1=11 h 13 min, Q3=31 h 21 min) and thus significantly longer in comparison to the vaginal misoprostol group (p=0.000, Mann-Whitney-test) and the dinoprostone group (p=0.002, Mann-Whitney-test).

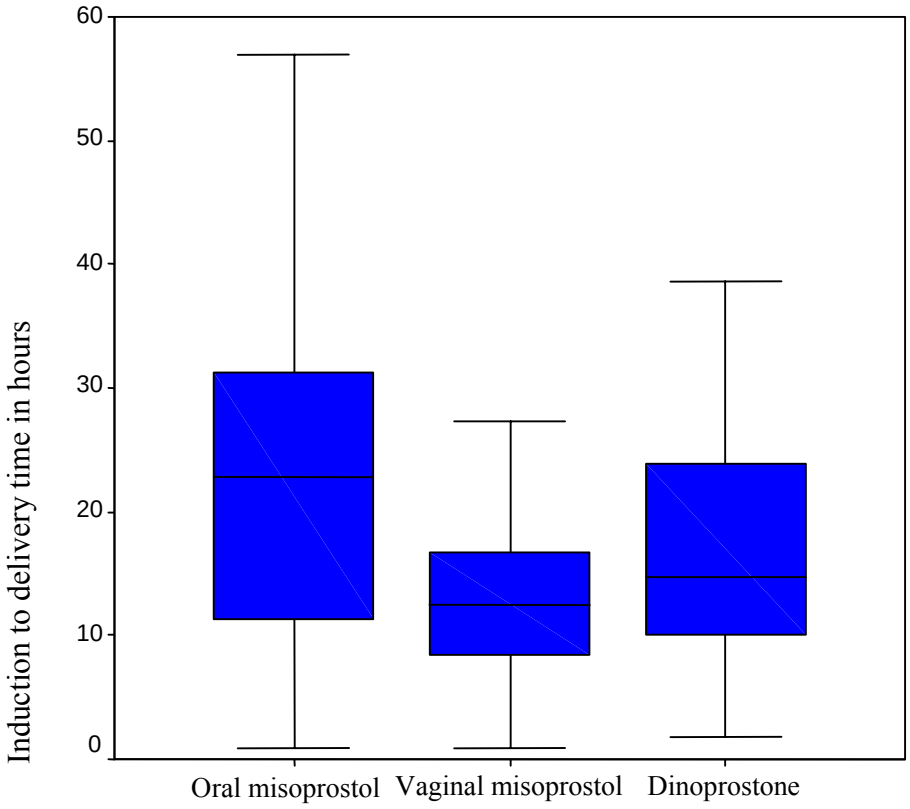

Figure 3-1 : Time from induction to delivery by any route.

The time from induction to vaginal delivery was nearly the same in the vaginal misoprostol group with 12 h 10 min (Q1=8 h 31 min, Q3=16 h 34 min) as compared with 12 h 53 min (Q1=9 h 02 min, Q3=18 h 38 min) in the dinoprostone group (p=0.489, Mann-Whitney-test). Women in

the oral misoprostol group presented with a significantly longer induction to vaginal delivery time of 22h 38 min (Q1=12 h 3 min, Q3=31 h 07 min, *p*=0.000, Mann-Whitney-test).

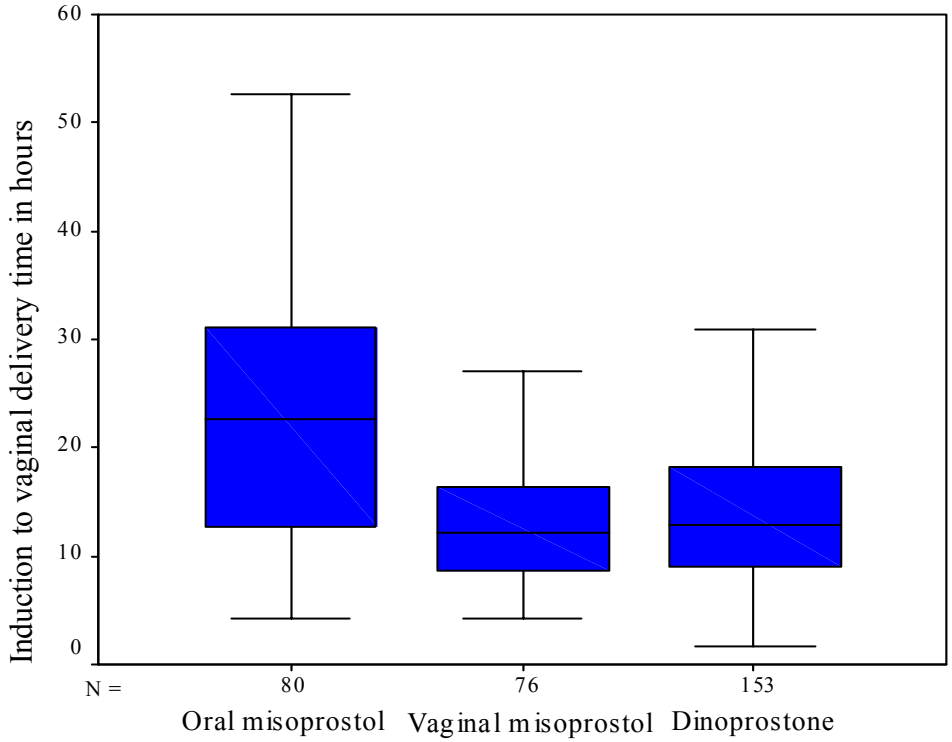

Figure 3-2 : Time from induction to vaginal delivery.

Regarding the mode of delivery, there was no difference noted between the groups as shown in Table 3-4 and Figure 3-3.

The rate of natural vaginal deliveries was about ⅔ in all three treatment groups.

Mode of delivery	**Oral misoprostol n=120**	**Vaginal misoprostol n=120**	**Dinoprostone control n=240**	**Significance χ^2**
	n (%)	**n (%)**	**n (%)**	**P Value**
NVD	80 (66.7)	76 (63.3)	153 (63.8)	*p*=0.830
Cesarean sections	39 (32.5)	42 (35.0)	82 (34.2)	*p*=0.916
Instrumental delivery	1 (0.8)	2 (1.7)	5 (2.1)	*p*=0.683

NVD= natural vaginal delivery, P Value ~ Pearson χ^2

Table 3-4 : Mode of delivery.

The overall cesarean section rate of about ⅓ did not differ between the treatment groups (p=0.916, χ2).

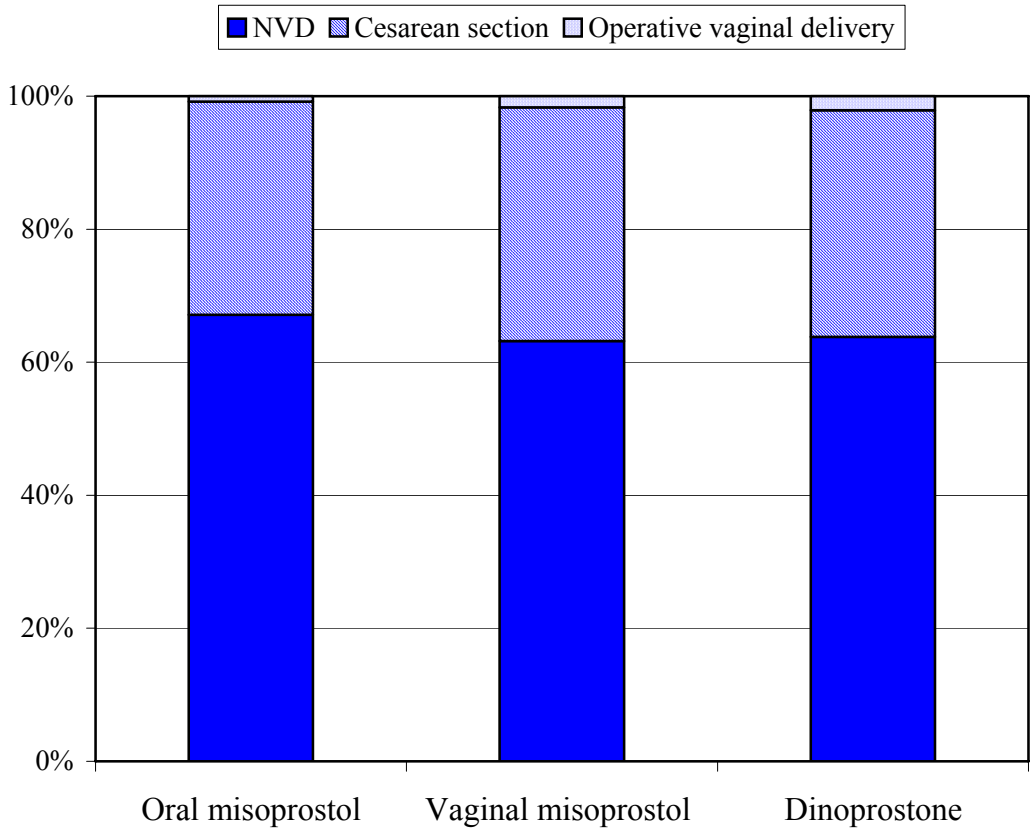

Figure 3-3 : Mode of delivery.
NVD= natural vaginal delivery

There was no difference in the cesarean section rate between Groote Schuur Hospital (tertiary level care) and Mowbray Maternity Hospital (secondary level care). The cesarean section rate was 33% and 34%, respectively.

The indications for cesarean sections are given in Table 3-5 and Figure 3-4.

Indication for C/S	**Oral misoprostol n=120**	**Vaginal misoprostol n=120**	**Dinoprostone control n=240**	**Oral misoprostol vs. control**	**Vaginal misoprostol vs. control**	**Oral vs. vaginal misoprostol**
	n (%)	**n (%)**	**n (%)**	**P Value**	**P Value**	**P Value**
Fetal distress	20 (16.7)	33 (27.5)	33 (13.8)	*p*=0.528	*p*=0.002	*p*=0.061
FIOL < 24 hrs	3 (2.5)	2 (1.7)	6 (2.5)	NS	NS	NS
FIOL > 24 hrs	8 (6.7)	1 (0.8)	22 (9.2)	*p*=0.545	*p*=0.001	*p*=0.036
CPD / SP	7 (5.8)	4 (3.3)	19 (7.9)	NS	NS	NS

C/S= cesarean section, FIOL= failed induction of labour, CPD= cephalo-pelvic disproportion, SP= slow progress,
P Value ~ Fisher's exact test, NS= not significant
Table 3-5 : Indications for cesarean section.

The main indication for cesarean section in the vaginal misoprostol group was fetal distress with 33/120 (27.5%). Only 20/120 (16.7%) women in the oral misoprostol group and 33/240 (13.8%) in the dinoprostone control group had surgical intervention for fetal distress, this showed a significant difference between the vaginal misoprostol and the dinoprostone control group (p=0.002, Fisher's exact test).

On the other hand, significantly more patients in the oral misoprostol and the dinoprostone groups had a cesarean section for failed induction after 24 hours as compared with the vaginal misoprostol group (p=0.036 and p=0.001, respectively, Fisher's exact test).

The other possible indications for surgical delivery did not show significant differences.

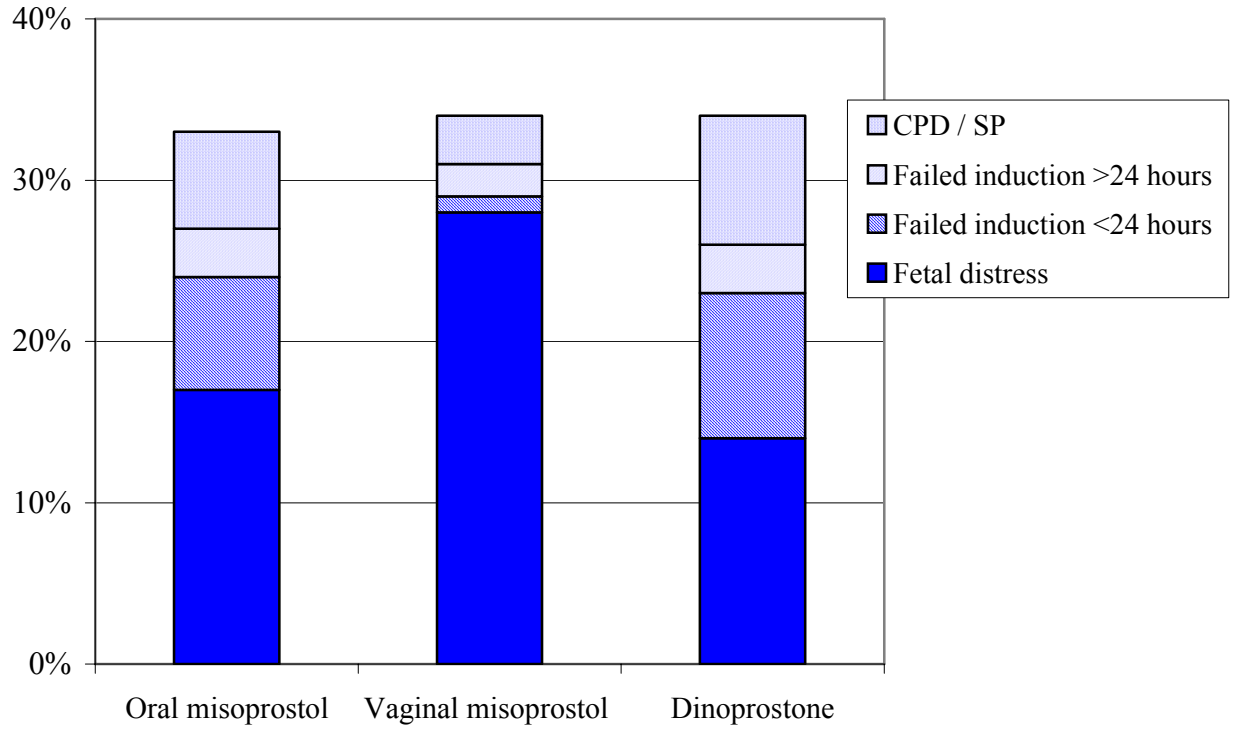

Figure 3-4 : Indications for cesarean section.
CPD= cephalo-pelvic disproportion, SP= slow progress

Augmentation with oxytocin was mainly used in women with oral misoprostol and dinoprostone treatment as shown in Table 3-6, this reached significance in comparison to the vaginal misoprostol group (p=0.039 and p=0.012, respectively, Fisher's exact test).

Significantly fewer patients in the vaginal misoprostol group had artificial rupture of membranes as compared with the dinoprostone group (p=0.001, Fisher's exact test). Artificial rupture of membranes was performed in 40/120 (33.3%) of the women in the oral misoprostol group.

Oxytocin AROM	Oral misoprostol n=120	Vaginal misoprostol n=120	Dinoprostone control group n=240	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
Oxytocin	20 (16.6)	8 (6.6)	39 (16.2)	*p*=1.00	*p*=0.012	*p*=0.039
AROM	40 (33.3)	28 (23.3)	97 (40.4)	*p*=0.207	*p*=0.001	*p*=0.115

AROM= artificial rupture of membranes, P Value ~ Fisher's exact test

Table 3-6: Use of oxytocin and artificial rupture of membranes.

The use of analgesia such as epidural anaesthesia, morphine and Entonox was similar for the groups (cf. Table 3-7).

Analgesia	Oral misoprostol n=120	Vaginal misoprostol n=120	Dinoprostone control n=240	Significance
	n (%)	n (%)	n (%)	P Value
Epidural	2 (1.7)	0	4 (1.7)	*p*=0.363
Morphine	52 (43.3)	52 (43.3)	112 (46.7)	*p*=0.764
Entonox	3 (2.5)	1 (0.8)	1 (0.4)	*p*=0.179

P Value ~ Pearson χ^2

Table 3-7: Analgesia.

The overall rate of maternal side effects in the groups was low and did not differ significantly. There was a slightly higher incidence of low pyrexia (*p*=0.49, Pearson $\chi 2$) and vomiting noted after vaginal misoprostol as compared with the other two groups (cf. Table 3-8).

Side effects	Oral misoprostol n=120	Vaginal misoprostol n=120	Dinoprostone control n=240	Significance
	n (%)	n (%)	n (%)	P Value
Low pyrexia < 38°C	0	2 (1.7)	0	p=0.49
High pyrexia ≥ 38°C	1 (0.8)	0	0	p=0.222
Shivering	1 (0.8)	1 (0.8)	0	p=0.366
Vomiting	1 (0.8)	4 (3.3)	3 (1.3)	p=0.247
Nausea	0	2 (1.7)	2 (0.8)	p=0.365
Diarrhoea	0	0	0	NS

P Value ~ Pearson χ^2 , NS= not significant

Table 3-8: Maternal side effects.

The intrapartum fetal and maternal complications and the neonatal outcome are shown in Table 3-9.

The incidence of tachysystole after vaginal misoprostol was significantly higher as compared with dinoprostone treatment. In 7/120 (5.8%) of the women in the vaginal misoprostol group and 2/240 (0.8%) in the dinoprostone group, tachysystole was noted (p=0.008, Fisher's exact test). The incidence of tachysystole in the oral misoprostol group did not reach significance as compared with the vaginal misoprostol group and the dinoprostone group (p=0.066 and p=1.00, respectively, Fisher's exact test).

There was one case of hyperstimulation syndrome in a woman who received vaginal misoprostol.

Complications and fetal outcome	**Oral misoprostol n=120**	**Vaginal misoprostol n=120**	**Dinoprostone control n=240**	**Significance χ^2**
	n (%)	**n (%)**	**n (%)**	**P Value**
Tachysystole	1 (0.8)	7 (5.8)	2 (0.8)	p=0.004
Hyperstimulation	0	1 (1)	0	p=0.222
Abruption	1 (0.8)	4 (3.3)	6 (2.5)	p=0.413
Uterine rupture	0	0	0	
Thick meconium	4 (3.3)	4 (3.3)	4 (1.7)	p=0.505
Low Apgar scores	2 (1.7)	3 (2.5)	2 (0.8)	p=0.451
Admission to NICU	2 (1.7)	6 (5.0)	8 (3.3)	p=0.355
HIE	0	1 (0.8)	0	p=0.222

NICU= neonatal intensive care unit, HIE= hypoxic ischemic encephalopathy,
P Value ~ Pearson χ2, NS= not significant

Table 3-9: Intrapartum fetal, maternal complications and neonatal outcome.

There were no significant differences in the incidence of thick meconium, maternal complications, neonatal outcomes such as Apgar scores below 7 after 5 minutes, admission to neonatal intensive care units or hypoxic ischemic encephalopathy between the groups. Abruptio placentae was diagnosed in 4/120 (3.3%) of the patients in the vaginal misoprostol group, 6/240 (2.5%) of the dinoprostone group, and one woman in the oral misoprostol group. This did not reach significance (p=0.413, Pearson χ2).

3.2 Subgroup Analysis of Part I

The four treatment groups were divided into eight subgroups, comparing outcomes based on parity and the initial Bishop score.

Regarding parity, women were classified into nulliparous and multiparous patients.

A Bishop score of less than 4 is considered to be an unfavourable cervix, 4 or more a favourable cervix.

3.2.1 A Comparison of Nulliparous and Multiparous Patients

The distribution of nulliparous and multiparous patients did not differ between the groups as shown in Table 3-10 (p=0.518, Pearson $\chi 2$).

Distribution of parity	Oral misoprostol n=120	Vaginal misoprostol n=120	Dinoprostone control group n=240
	n (%)	n (%)	n (%)
Multiparous	76 (63.3)	68 (56.7)	139 (57.9)
Nulliparous	44 (36.7)	52 (43.3)	101 (42.1)

Table 3-10: Distribution of parity.

The success rate of deliveries within 24 hours irrespective of the mode of delivery is shown in Table 3-11 and Figure 3-5.

The success rate of deliveries within 24 hours after the first dose showed that more multiparous than nulliparous women delivered in the same period of time. This reached significance in the dinoprostone control group (p=0.034, Fisher's exact test).

Deliveries within 24 hours	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
Multiparous	44/76 (57.9)	62/68 (91.2)	112/139 (80.6)	p=0.001	p=0.068	p=0.000
Nulliparous	22/44 (50)	47/52 (90.4)	69/101 (68.3)	p=0.041	p=0.003	p=0.000
P Value	p=0.449	p=1.00	p=0.034			

P Value ~ Fisher's exact test

Table 3-11: Deliveries within 24 hours, irrespective of the route, in nulliparous and multiparous women.

Significantly more multiparous and nulliparous women delivered within 24 hours by any route after vaginal misoprostol as compared with oral misoprostol (p=0.000 and p=0.000, Fisher's

exact test) and dinoprostone (p=0.068 and p=0.003, respectively, Fisher's exact test). There was a higher success rate in women of the dinoprostone group than in those of the oral misoprostol group (p=0.001 and p=0.041, Fisher's exact test).

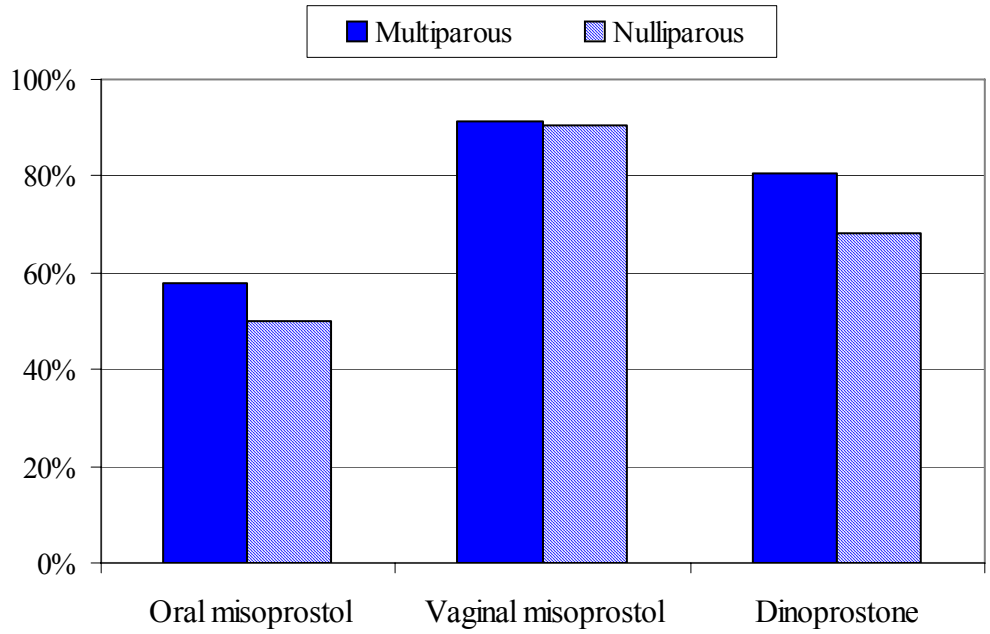

Figure 3-5: Deliveries within 24 hours from start of induction in multiparous and nulliparous patients, irrespective of the route of delivery.

Regarding the success rate of vaginal deliveries within 24 hours, the analysis showed some significant differences amongst the groups (cf. Table 3-12 and Figure 3-6).

NVD in 24 hours	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
Multiparous	**33/76 (43.4)**	**46/68 (67.6)**	**93/139 (66.9)**	**p=0.001**	**p =1.00**	**p =0.004**
Nulliparous	**14/44 (31.8)**	**23/52 (44.2)**	**38/101 (37.6)**	**p =0.574**	**p =0.487**	**p =0.293**
P Value	**p =0.247**	**p =0.015**	**p =0.000**			

NVD=natural vaginal deliveries, P Value ~ Fisher's exact test

Table 3-12: Success rate of vaginal deliveries within 24 hours of the start of induction in nulliparous and multiparous women.

After administration of oral misoprostol, 33/76 (43.4%) of the multiparous patients delivered within 24 hours as compared with 14/44 (31.8%) of the patients delivering for the first time, this did not reach statistical significance.

Vaginal misoprostol had a significantly higher effect on multiparous than on nulliparous patients regarding vaginal deliveries within 24 hours (p=0.015, Fisher's exact test). This effect was

comparable to that of dinoprostone which also showed a significantly higher delivery rate within 24 hours of induction in multiparous women (p=0.000, Fisher's exact test).

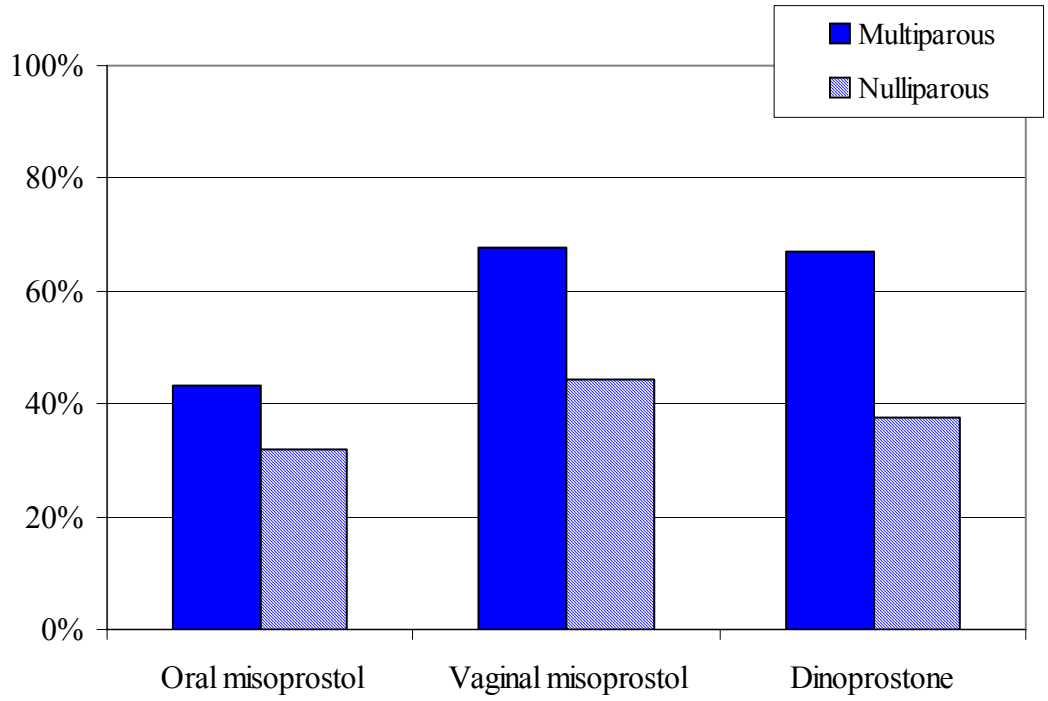

Figure 3-6: Vaginal deliveries within 24 hours from start of induction in multiparous and nulliparous patients.

A significantly higher success rate was achieved in multiparous patients after administration of dinoprostone as compared with those treated with oral misoprostol (p=0.001, Fisher's exact test). The way of administration of misoprostol seemed to make a difference in women with previous deliveries. Vaginal misoprostol showed a significantly greater effect in those women than the oral application (p=0.004, Fisher's exact test).

Manifestly the shortest induction to delivery interval occurred after administration of vaginal misoprostol with 11 h 42 min (8 h 20 min/17 h) in multiparous, and 13 h 30 min (8 h 45 min/16 h 38 min) in nulliparous women (p=0.462, Mann-Whitney-test).
Oral misoprostol showed the longest time interval to delivery in both groups of women (p=0.462, Mann-Whitney-test).
Nulliparous women delivered significantly faster with vaginal misoprostol than with oral misoprostol (p=0.000, Mann-Whitney-test) or dinoprostone (p=0.002, Mann-Whitney-test). In multiparous women, vaginal misoprostol and dinoprostone showed a similar result, whereas oral

misoprostol resulted in a significantly longer induction to delivery time interval as compared with both other groups (cf. Table 3-13 and Figure 3-7).

IDT (t=hh:mm)	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	median (quartiles)	median (quartiles)	median (quartiles)	P Value	P Value	P Value
Multiparous	20:57 (10:11 / 30:24)	11:42 (08:20 / 17:00)	13:50 (09:03 / 20:45)	*p*=0.005	*p*=0.102	*p*=0.000
Nulliparous	23:52 (13:45 / 34:43)	13:30 (08:45 / 16:38)	16:15 (12:03 / 31:53)	*p*=0.122	*p*=0.002	*p*=0.000
P Value	*p*=0.204	*p*=0.462	*p*=0.004			

IDT=induction to delivery time, t= time, h= hours, m= minutes, Quartiles in brackets correspond to Q1/Q3,
P Value ~ Mann-Whitney-test

Table 3-13: Induction to delivery interval in multiparous and nulliparous women, irrespective of the mode of delivery.

Multiparous women of the dinoprostone group delivered significantly faster than the nulliparous patients of the same group (*p*=0.004, Mann-Whitney-test).

Within both misoprostol groups parity did not influence the induction to delivery intervals significantly.

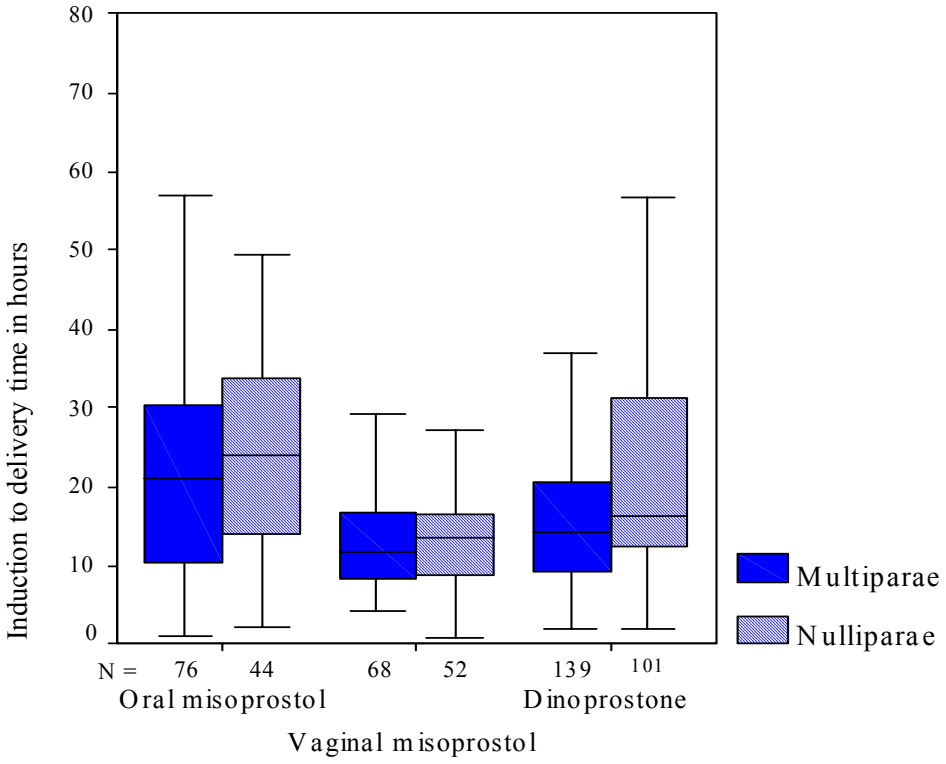

Figure 3-7: Induction to delivery interval in multiparous and nulliparous women, irrespective of the mode of delivery.

Table 3-14 and Figure 3-8 show the induction to natural vaginal delivery interval.

The induction to vaginal delivery interval with vaginal misoprostol was similar to that with dinoprostone in multiparous (p=0.544, Mann-Whitney-test) as well as in nulliparous women (p=0.656, Mann-Whitney-test).

Nulliparous and multiparous women in the oral misoprostol group needed a significantly longer time to vaginal delivery as compared with patients in the other two study groups.

IVDT (t=hh:mm)	**Oral misoprostol**	**Vaginal misoprostol**	**Dinoprostone control group**	**Oral misoprostol vs. control**	**Vaginal misoprostol vs. control**	**Oral vs. vaginal misoprostol**
	median (quartiles)	**median (quartiles)**	**median (quartiles)**	**P Value**	**P Value**	**P Value**
Multiparous	20:00 (11:05 / 30:18)	11:32 (08:24 / 16:43)	12:15 (08:51 / 17:00)	p=0.001	p =0.544	p =0.000
Nulliparous	23:34 (17:40 / 31:58)	14:08 (09:56 / 16:26)	14:24 (10:27 / 19:24)	p =0.000	p =0.656	p =0.001
P Value	p =0.091	p =0.222	p =0.140			

IVDT= induction to vaginal delivery time, t= time, h= hours, m= minutes, Quartiles in brackets correspond to Q1/Q3, P Value ~ Mann-Whitney-test

Table 3-14: Induction to vaginal delivery interval in multiparous and nulliparous women.

The induction to vaginal delivery interval in women of different parity within the study groups was the same.

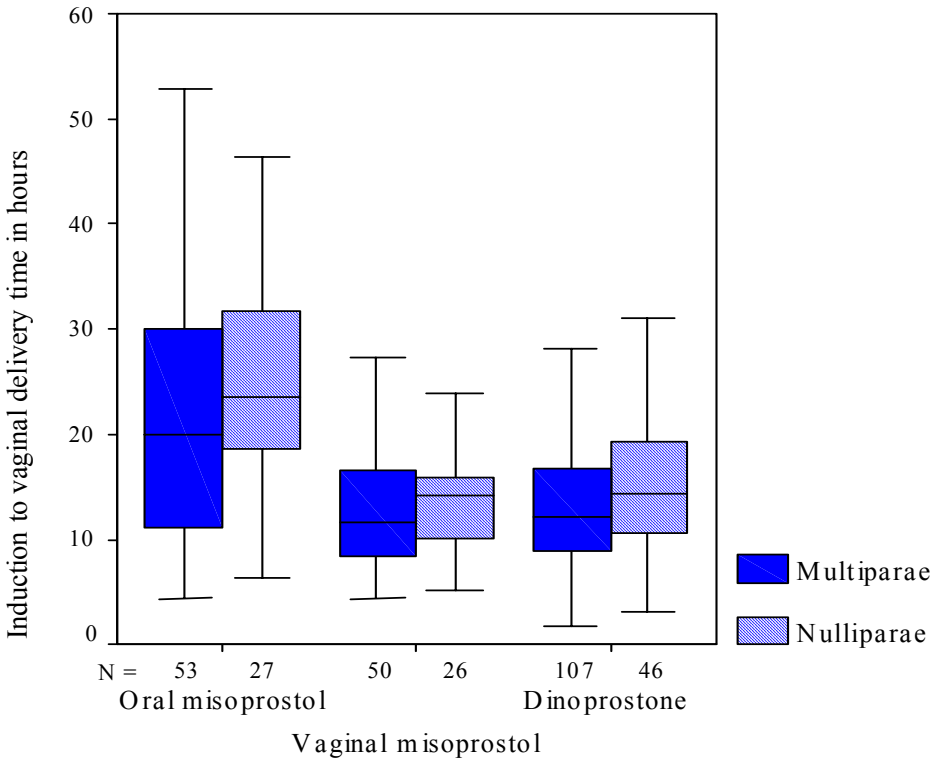

Figure 3-8: Induction to vaginal delivery interval in multiparous and nulliparous women.

The rate of vaginal delivery in multiparous patients was comparable in all three groups. Regarding the rate of natural vaginal deliveries, primiparous women had an advantage if treated with oral misoprostol; 27/44 (61.4%) of the women in the oral treatment group as compared with 26/52 (50%) in the vaginal misoprostol group and 46/101 (45.5%) in the dinoprostone control group delivered vaginally. This did not reach significance, but showed a trend towards more natural vaginal deliveries with oral misoprostol compared with the vaginal misoprostol or dinoprostone treatment in primiparous women when there is no time limit (cf. Table 3-15 and Figure 3-9).

NVD	**Oral misoprostol**	**Vaginal misoprostol**	**Dinoprostone control group**	**Oral misoprostol vs. control**	**Vaginal misoprostol vs. control**	**Oral vs. vaginal misoprostol**
	n (%)	**n (%)**	**n (%)**	**P Value**	**P Value**	**P Value**
Multiparous	53/76 (69.7)	50/68 (73.5)	107/139 (77)	*p*=0.256	*p*=0.607	*p*=0.712
Nulliparous	27/44 (61.4)	26/52 (50)	46/101 (45.5)	*p*=0.104	*p*=0.613	*p*=0.307
P Value	*p*=0.422	*p*=0.013	*p*=0.000			

NVD= natural vaginal deliveries, P Value ~ Fisher's exact test

Table 3-15: Rate of vaginal deliveries in multiparous and nulliparous patients.

Significantly more multiparous than nulliparous women delivered vaginally after vaginal misoprostol (*p*=0.007, Fisher's exact test) and dinoprostone (*p*=0.000, Fisher's exact test), in contrast to the oral misoprostol group.

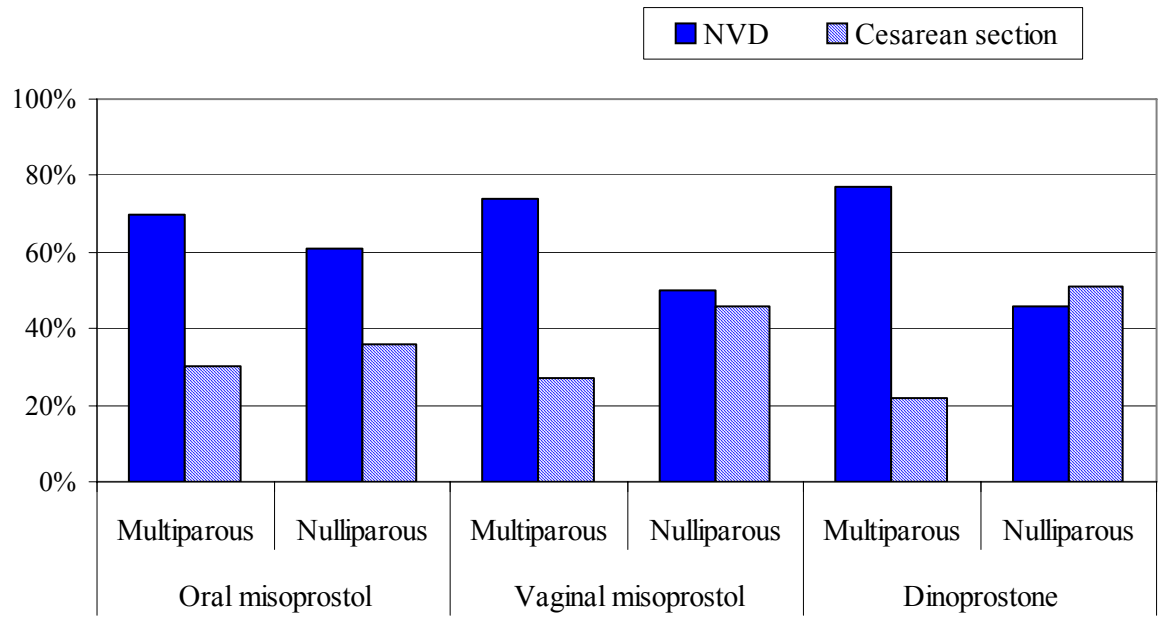

Figure 3-9: Rate of natural vaginal delivery and cesarean section in multiparous and nulliparous patients among the groups.

NVD= natural vaginal delivery

Cesarean deliveries were significantly more frequent in nulliparous as compared with multiparous patients after administration of vaginal misoprostol (p=0.034, Fisher's exact test) and also dinoprostone (p=0.000, Fisher's exact test). Vaginal misoprostol showed a similar outcome in the two subgroups as compared with dinoprostone (cf. Figure 3-9 and Table 3-16).
The difference between nulliparous and multiparous women was smallest in the oral misoprostol group, 16/44 (36.4%) and 23/76 (30.3%) of the women had surgical delivery, respectively.
The lowest cesarean section rate in nulliparous patients was observed after the administration of oral misoprostol, this showed a noteworthy trend.

C/S rate	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
Multiparous	23/76 (30.3)	18/68 (26.5)	31/139 (22.3)	p=0.249	p=0.602	p=0.712
Nulliparous	16/44 (36.4)	24/52 (46.2)	51/101 (50.5)	p=0.148	p=0.733	p=0.407
P Value	p=0.547	p=0.034	p=0.000			

C/S= cesarean section, P Value ~ Fisher's exact test
Table 3-16: Rate of cesarean sections in multiparous and nulliparous patients.

The main reasons for cesarean section were fetal distress and failed induction of labour. For the evaluation of efficacy and safety, only those two indications for cesarean sections are mentioned in the subgroup analysis. They are shown in Table 3-17, Table 3-18 and Figure 3-10.
In general, more nulliparous than multiparous women in all three groups had surgical deliveries. This reached significance in the dinoprostone control group, in 13/139 (9.4%) of the patients with previous deliveries and in 20/101 (19.8%) without previous deliveries cesarean section was performed for fetal distress (p=0.023, Fisher's exact test).

C/S for fetal distress	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
Multiparous	11/76 (14.5)	15/68 (22.1)	13/139 (9.4)	p=0.265	p=0.017	p=0.281
Nulliparous	9/44 (20.5)	18/52 (34.6)	20/101 (19.8)	p=1.00	p=0.051	p=0.172
P Value	p=0.450	p=0.151	p=0.023			

C/S= cesarean section, P Value ~ Fisher's exact test
Table 3-17: Cesarean sections for fetal distress in multiparous and nulliparous patients.

The highest percentage of cesarean sections for fetal heart rate abnormalities was noted after the application of vaginal misoprostol in 15/68 (22.1%) of the multiparous patients and in 18/52

(34.6%) of the nulliparous patients. In multiparous women this was significant in comparison to the control group (p=0.017, Fisher's exact test).

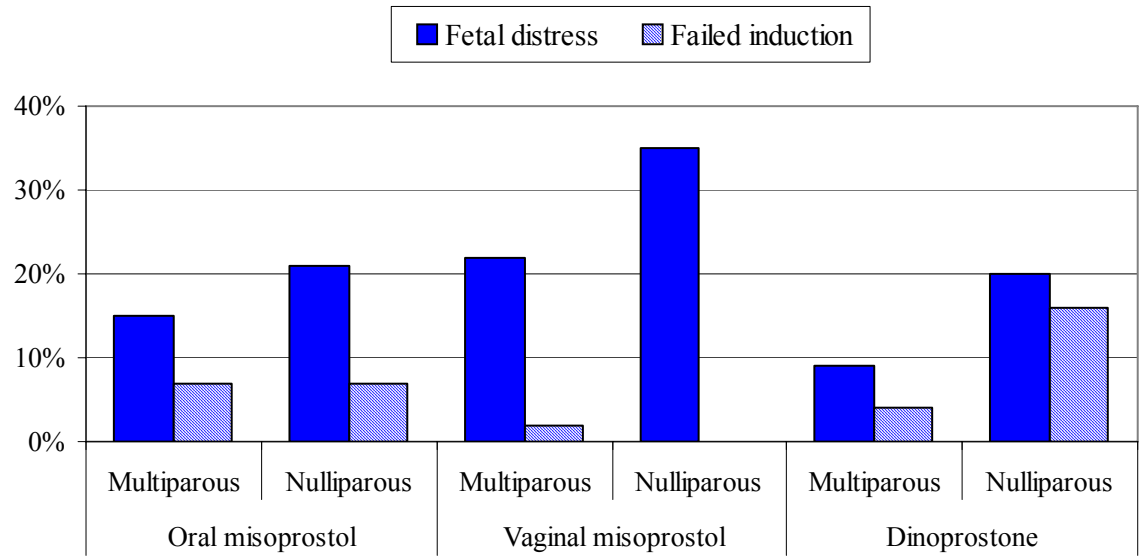

Figure 3-10: Cesarean section for fetal distress and failed induction of labour after 24 hours in multiparous and nulliparous patients.

Regarding the rates of failed induction after 24 hours as indication for surgical intervention, women who received vaginal misoprostol presented with the lowest rate of failed induction with 1/68 (1.5%) in the multiparous subgroup. None of the nulliparous patients required surgical delivery for that reason. This was significantly less in comparison to 16/101 (15.8%) of the women in the dinoprostone control group (p=0.001, Fisher's exact test).

3/44 (6.8%) of the nulliparous patients in the oral misoprostol group were noted with failed induction after 24 hours, which made cesarean section necessary. Compared with the vaginal misoprostol and dinoprostone group, this did not reach statistical significance.

C/S for FIOL	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
Multiparous	5/76 (6.6)	1/68 (1.5)	6/139 (4.3)	p=0.524	p=0.430	p=0.213
Nulliparous	3/44 (6.8)	0/52 (0)	16/101 (15.8)	p=0.184	p=0.001	p=0.093
P Value	p=1.00	p=1.00	p=0.003			

C/S= cesarean section, FIOL= failed induction of labour, P Value ~ Fisher's exact test

Table 3-18: Cesarean section for failed induction of labour after 24 hours in multiparous and nulliparous patients.

Fetal outcomes did not show any significant differences. 2/52 (3.8%) of the nulliparous patients in the vaginal misoprostol group delivered children with low Apgar scores after 1 minute. 4/52 (7.7%) neonates of the same group of women were admitted to the neonatal intensive care unit (cf. Table 3-19 and Table 3-20).

Low Apgar score	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Significance
	n (%)	n (%)	n (%)	P Value°°
Multiparous	2/76 (2.6)	1/68 (1.5)	0/139 (0)	*p*=0.184
Nulliparous	0/44 (0)	2/52 (3.8)	2/101 (2)	*p*=0.412
P Value°	*p*=0.532	*p*=0.578	*p*=0.176	

P Value° ~ Fisher's exact test, P Value°° ~ Pearson χ^2

Table 3-19: Apgar score after 1 minute < 7 in multiparous and nulliparous patients.

NICU	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Significance
	n (%)	n (%)	n (%)	P Value°°
Multiparous	2/76 (2.6)	2/68 (2.9)	3/139 (2.2)	*p*=0.939
Nulliparous	0/44 (0)	4/52 (7.7)	5/101 (5)	*p*=0.192
P Value°	*p*=0.532	*p*=0.401	*p*=0.286	

NICU= neonatal intensive care unit, P Value° ~ Fisher's exact test, P Value°° ~ Pearson χ^2

Table 3-20: Admission to neonatal intensive care unit in multiparous and nulliparous patients.

Hypoxic ischemic encephalopathy was noted in one neonate out of 52 (2%) after application of vaginal misoprostol to a nulliparous woman.

3.2.2 A Comparison of Outcome Measures between Low and High Bishop Score

Patients with an initial Bishop score lower than 4 were compared with those with a Bishop score equal or higher than 4 in each group.

Distribution of Bishop score	Oral misoprostol n=120	Vaginal misoprostol n=120	Dinoprostone control group n=240
	n (%)	n (%)	n (%)
BS < 4	61 (50.8)	59 (49.2)	121 (50.4)
BS ≥ 4	59 (49.2)	61 (50.8)	119 (49.6)

Table 3-21: Distribution of the initial Bishop score among the treatment groups.

The distribution regarding low and high Bishop scores did not show any difference between the groups (*p*=0.963, Pearson χ2).

The success rate of deliveries within 24 hours, no matter which route, showed significant differences within the groups as shown in Table 3-22 and Figure 3-11. More women presenting with a Bishop score of 4 or more delivered within 24 hours than those with an unripe cervix, this reached significance in the vaginal misoprostol and the dinoprostone group (p=0.028 and p=0.036, respectively, Fisher's exact test).

Deliveries within 24 hours	**Oral misoprostol**	**Vaginal misoprostol**	**Dinoprostone control group**	**Oral misoprostol vs. control**	**Vaginal misoprostol vs. control**	**Oral vs. vaginal misoprostol**
	n (%)	**n (%)**	**n (%)**	**P Value**	**P Value**	**P Value**
BS < 4	30/61 (49.2)	50/59 (84.7)	84/121 (69.4)	p=0.010	p=0.030	p=0.000
BS ≥ 4	36/59 (61)	59/61 (96.7)	97/119 (81.5)	p=0.006	p=0.005	p=0.000
P Value	p=0.205	p=0.028	p=0.036			

P Value ~ Fisher's exact test

Table 3-22: Deliveries within 24 hours in women with initially favourable und unfavourable cervical scores, irrespective of the route.

Vaginal misoprostol caused the highest rate of deliveries within 24 hours in both groups of low and high Bishop scores, followed by dinoprostone and oral misoprostol.

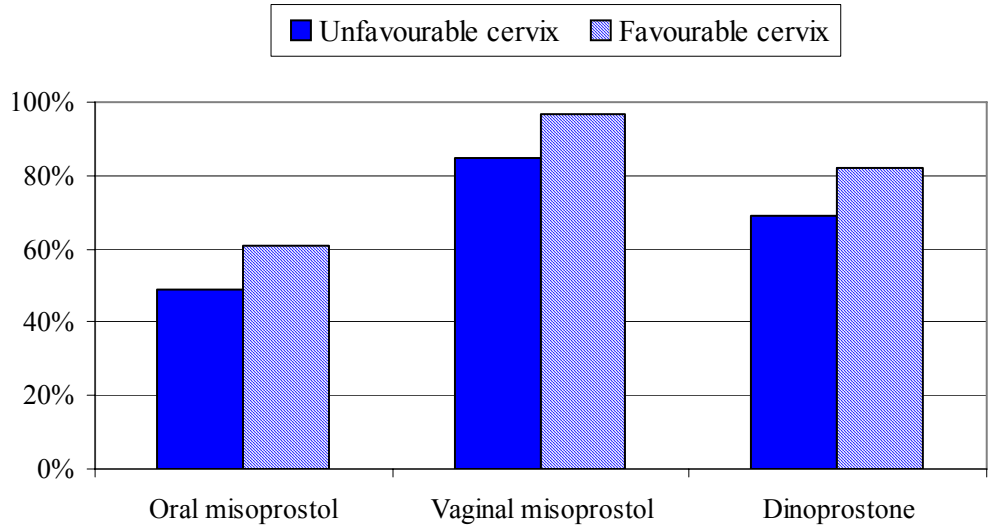

Figure 3-11: Influence of the initial Bishop scores on deliveries by any route within 24 hours after start of induction.

The data comparing the success rate of natural vaginal deliveries within the first 24 hours of induction of labour are shown in Table 3-23 and Figure 3-12. It was noted that there were more deliveries in patients after vaginal misoprostol and dinoprostone than after oral misoprostol treatment, this reached significance in women with initial unripe cervices (p=0.026 and p=0.012,

respectively, Fisher's exact test). The success rate in the vaginal misoprostol group did not differ from that in the control group with low and high cervical scores at the start of induction (p=0.875 and p=0.632, respectively, Fisher's exact test).

NVD within 24 hours	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
BS < 4	19/61 (31.1)	31/59 (52.5)	62/121 (51.2)	p=0.012	p=0.875	p=0.026
BS ≥ 4	28/59 (47.5)	38/61 (62.3)	69/119 (58)	p=0.203	p=0.632	p=0.142
P Value	p=0.092	p=0.356	p=0.303			

NVD=natural vaginal delivery, P Value ~ Fisher's exact test

Table 3-23: Natural vaginal deliveries within 24 hours after the initial dose of prostaglandin with low and high Bishop scores.

In the oral treatment group, there was a tendency towards more spontaneous deliveries when women presented with a ripe cervix.

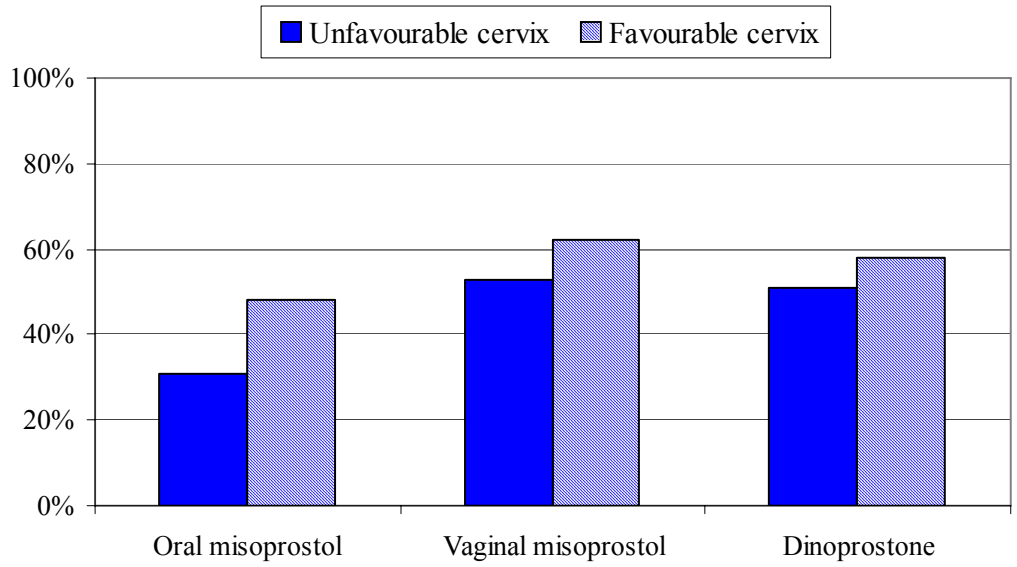

Figure 3-12: Influence of the initial Bishop scores on the success rate of natural vaginal deliveries within 24 hours after beginning of induction of labour.

The induction to delivery interval irrespective of the mode of delivery in women with an initially unfavourable cervical score was significantly shorter with vaginal misoprostol than with oral misoprostol (p=0.000, Mann-Whitney-test) and dinoprostone (p=0.023, Mann-Whitney-test); dinoprostone resulted in a shorter induction interval as compared with oral misoprostol, this did not reach significance (p=0.054, Mann-Whitney-test).

IDT (t=hh:mm)	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	median (quartiles)	median (quartiles)	median (quartiles)	P Value	P Value	P Value
BS < 4	24:10 (11:20 / 33:15)	12:55 (08:25 / 17:15)	15:50 (10:42 / 28:20)	*p*=0.054	*p*=0.023	*p*=0.000
BS ≥ 4	19:30 (11:10 / 29:50)	11:25 (07:54 / 16:00)	14:10 (09:03 / 20:00)	*p*=0.020	*p*=0.029	*p*=0.000
P Value	*p*=0.214	*p*=0.153	*p*=0.056			

IDT= induction to delivery time, t=time, h= hours, m= minutes, Quartiles in brackets correspond to Q1/Q3,
P value ~ Mann-Whitney-test

Table 3-24: Induction to delivery interval irrespective of the mode of delivery in women with initially favourable and unfavourable cervical scores.

In women with favourable cervical scores, vaginal misoprostol and dinoprostone led to a shorter induction to delivery interval than oral misoprostol (*p*=0.000 and *p*=0.020, respectively, Mann-Whitney-test).

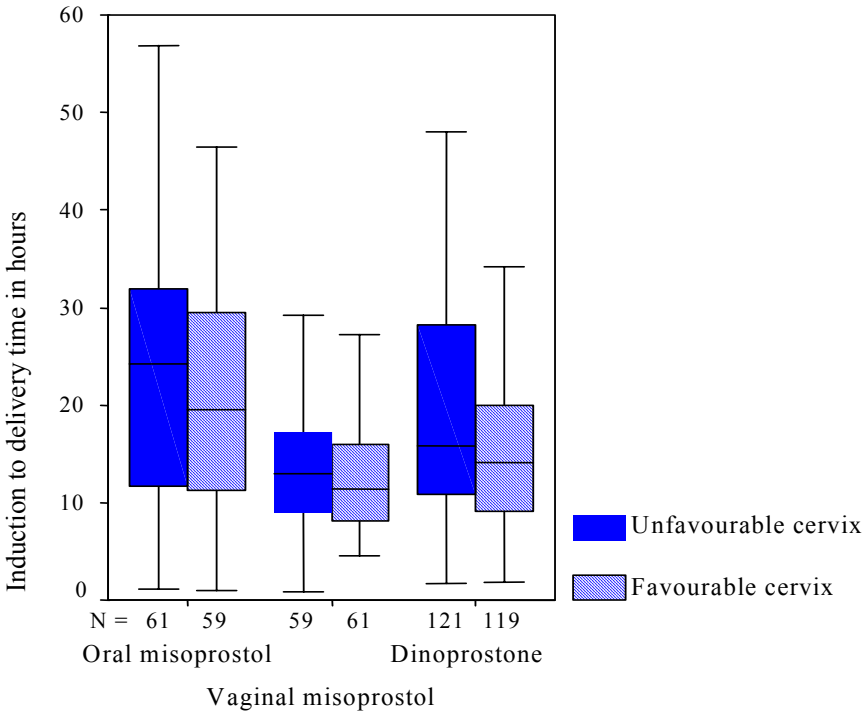

Figure 3-13: Induction to delivery interval irrespective of the mode of delivery in women with initially favourable and unfavourable cervical scores.

Vaginal misoprostol resulted in a significantly shorter induction time than dinoprostone (*p*=0.029, Mann-Whitney-test).

The induction to delivery times irrespective of the mode of delivery with initially favourable and unfavourable cervical scores did not differ significantly within the treatment groups (cf. Table 3-24 and Figure 3-13).

Table 3-25 and Figure 3-14 show the time from induction to natural vaginal delivery.

The study showed that women with an initially low Bishop score delivered significantly faster with vaginal misoprostol and dinoprostone than with oral misoprostol (p=0.001 and p=0.000, respectively, Mann-Whitney-test).

A similar effect could be noted in women with favourable cervical scores: Vaginal misoprostol and dinoprostone resulted in a shorter induction to vaginal delivery interval than oral misoprostol (p=0.000 and p=0.002, respectively, Mann-Whitney-test).

IVDT (t=hh:mm)	**Oral misoprostol**	**Vaginal misoprostol**	**Dinoprostone control group**	**Oral misoprostol vs. control**	**Vaginal misoprostol vs. control**	**Oral vs. vaginal misoprostol**
	median (quartiles)	**median (quartiles)**	**median (quartiles)**	**P Value**	**P Value**	**P Value**
BS < 4	23:13 (15:15 / 30:17)	12:55 (08:57 / 17:27)	13:33 (09:42 / 19:20)	p=0.000	p=0.939	p=0.001
BS ≥ 4	19:40 (11:20 / 31:58)	11:35 (08:25 / 16:00)	12:33 (08:16 / 16:24)	p=0.002	p=0.389	p=0.000
P Value	p=0.470	p=0.255	p=0.510			

IVDT= induction to vaginal delivery time, t= time, h= hours, m= minutes, Quartiles in brackets correspond to Q1/Q3, P Value ~ Mann-Whitney-test

Table 3-25: Induction to vaginal delivery interval in women with initially favourable and unfavourable cervical scores.

The time to delivery with vaginal misoprostol and dinoprostone was similar irrespective of the initial Bishop score.

The induction to vaginal delivery intervals with initially favourable and unfavourable cervical scores did not differ significantly between the treatment groups.

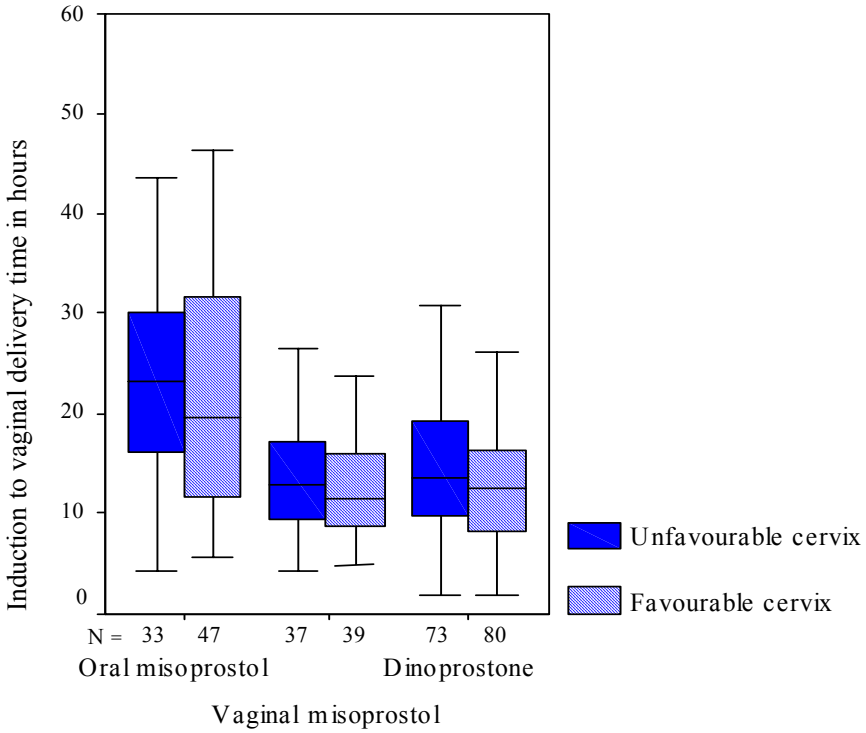

Figure 3-14: Induction to vaginal delivery interval in women with initially favourable and unfavourable cervical scores.

The success rates of natural vaginal deliveries without time limit are listed in Table 3-26.

The rate in the oral treatment group was noted to be significantly higher in women with ripe cervices as compared with women who presented with a Bishop score of less than 4 (p=0.004, Fisher's exact test). In the other two groups, the initial score did not influence the success rate of vaginal deliveries.

Rate of NVD	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
BS < 4	33/61 (54.1)	37/59 (62.7)	73/121 (60.3)	p=0.431	p=0.871	p=0.360
BS ≥ 4	47/59 (79.7)	39/61 (63.9)	80/119 (67.2)	p=0.113	p=0.740	p=0.069
P Value	p=0.004	p=1.00	p=0.285			

NVD=natural vaginal deliveries, P Value ~ Fisher's exact test

Table 3-26: Rate of vaginal deliveries with initially low and high Bishop scores.

There was a higher rate of women with ripe cervices delivering vaginally in the oral misoprostol group as shown in Figure 3-15 as compared with women in the other two groups, this did not reach significance, but showed a trend.

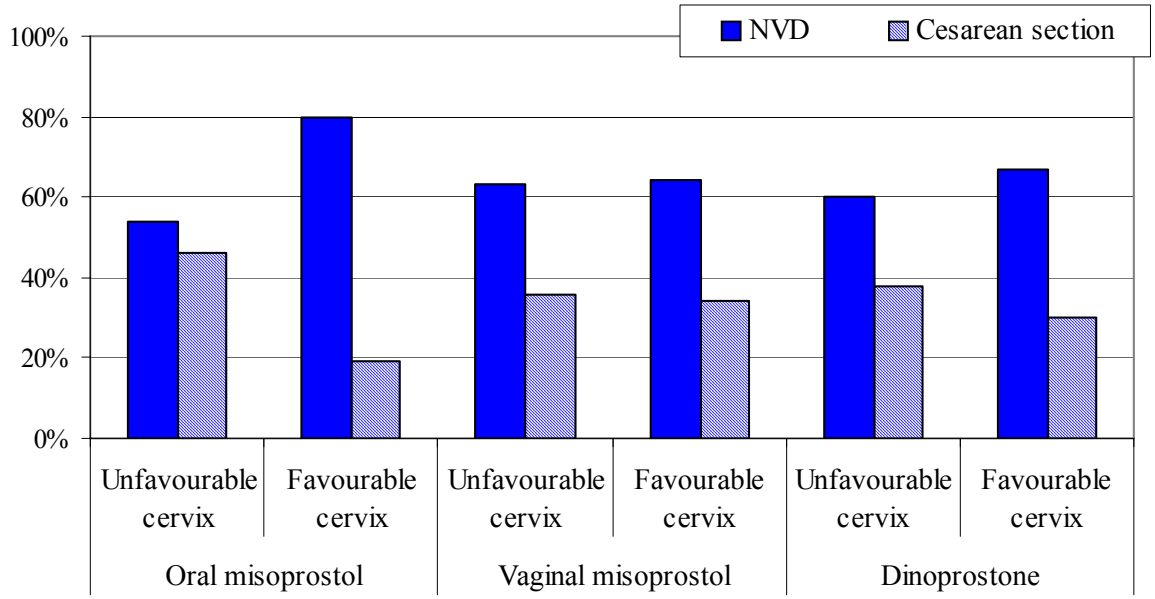

Figure 3-15: Rate of vaginal delivery and cesarean section with initial Bishop scores < 4 and ≥ 4 in the treatment groups.

NVD= natural vaginal delivery

The incidence of cesarean sections is compared in Table 3-27.

In the oral misoprostol group, cesarean deliveries in women with an initially lower Bishop score were more frequent than in those with an initially favourable cervix (p=0.002, Fisher's exact test).

There were fewer cesarean sections in women with a high Bishop score after oral misoprostol versus dinoprostone and vaginal misoprostol treatment. This did not reach significance.

C/S rate	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
BS < 4	28/61 (45.9)	21/59 (35.6)	46/121 (38)	p=0.339	p=0.870	p=0.271
BS ≥ 4	11/59 (18.6)	21/61 (34.4)	36/119 (30.3)	p=0.107	p=0.613	p=0.064
P Value	p=0.002	p=1.00	p=0.222			

C/S= cesarean section, P Value ~, Fisher's exact test

Table 3-27: Cesarean section rate in women with low and high Bishop scores.

A cesarean delivery was performed in more women of all three treatment groups presenting with unfavourable scores than in women with high cervical scores. The highest rate of cesarean sections was noted in women with unfavourable cervical scores after oral misoprostol treatment, 28/61 (45.9%) of those women delivered by cesarean section.

The indications for cesarean sections are shown in Table 3-28, Table 3-29 and Figure 3-16.

The two main indications were fetal distress and failed induction of labour after 24 hours. For better survey of the data, the comparison between the groups was carried out only on the two mentioned indications.

In the oral misoprostol group, significantly more women with a lower Bishop score had surgical delivery for fetal distress than women with a higher score (p=0.006, Fisher's exact test).

More surgical deliveries for fetal distress were performed in patients with an unfavourable cervix with oral misoprostol and vaginal misoprostol treatment than in those with dinoprostone administration (p=0.039 and p=0.011, respectively, Fisher's exact test).

In the group of women with a high Bishop score, statistically, more cesarean sections for fetal distress were performed in the vaginal misoprostol group than in the oral Misoprostol group (p=0.006, Fisher's exact test).

C/S for FD	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
BS < 4	16/61 (26.2)	17/59 (28.8)	16/121 (13.2)	p=0.039	p=0.014	p=0.839
BS ≥ 4	4/59 (6.8)	16/61 (26.2)	17/119 (14.3)	p=0.216	p=0.066	p=0.006
P Value	p=0.006	p=0.839	p=0.853			

C/S=cesarean section, FD= fetal distress, P Value ~ Fisher's exact test

Table 3-28: Cesarean sections for fetal distress in women with initially favourable and unfavourable cervical scores.

A failed induction of labour after 24 hours indicating a cesarean delivery was generally noted in more patients who presented with an unfavourable cervix.

C/S for FIOL	Oral misoprostol	Vaginal misoprostol	Dinoprostone control group	Oral misoprostol vs. control	Vaginal misoprostol vs. control	Oral vs. vaginal misoprostol
	n (%)	n (%)	n (%)	P Value	P Value	P Value
BS < 4	6/61 (9.8)	1/59 (1.7)	19/121 (15.7)	p=0.364	p=0.004	p=0.114
BS ≥ 4	2/59 (3.4)	0/61 (0)	3/119 (2.5)	p=1.00	p=0.552	p=0.240
P Value	p=0.273	p=0.492	p=0.000			

C/S=cesarean section, FIOL= failed induction of labour, P Value ~ Fisher's exact test

Table 3-29: Cesarean sections for failed induction of labour after 24 hours in women with initially favourable und unfavourable cervical scores.

The highest rate of failed induction of labour appeared to be in women with unfavourable cervical scores in the dinoprostone group with 19/121 (15.7%) patients, this reached significance in comparison with the vaginal misoprostol group (p=0.004, Fisher's exact test).

Within the dinoprostone group, more women with unfavourable cervices had a cesarean section for failed induction of labour than women with favourable cervices (p=0.000, Fisher's exact test).

The incidence of cesarean section for failed induction of labour in women with favourable cervical scores did not show significant differences.

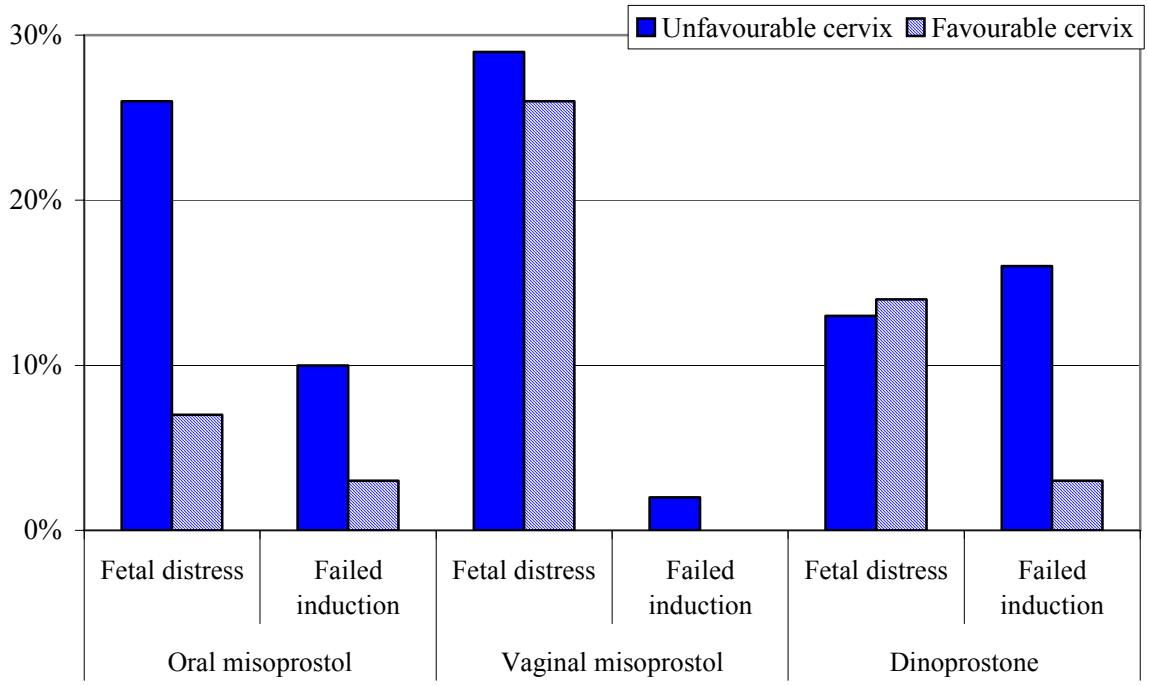

Figure 3-16: Indications for cesarean section in women with initially favourable and unfavourable cervical scores. Fetal distress and failed induction of labour.

Fetal outcomes did not show any significant differences (cf. Table 3-30 and Table 3-31).

Low Apgar score	**Oral misoprostol**	**Vaginal misoprostol**	**Dinoprostone control group**	**Significance**
	n (%)	**n (%)**	**n (%)**	**P Value°°**
BS < 4	2/61 (3.3)	2/59 (3.4)	1/121 (0.8)	p=0.393
BS ≥ 4	0/59 (0)	1/61 (1.6)	1/119 (0.8)	p=0.615
P Value°	p=0.496	p=0.616	p=1.00	

P Value° ~ Fisher's exact test, P Value°° ~ Pearson χ^2

Table 3-30: Apgar score < 7 after 1 minute.
Apgar scores of less than 7 after 1 minute were noted in very small numbers in all three groups.

In the dinoprostone control group, three newborns of women with Bishop scores of less than 4 (2.5%) and in five patients with high cervical scores (4.2%) were admitted to the neonatal intensive care unit. Four cases were noted in the vaginal misoprostol group in women with an unfavourable cervix at the start of induction (6.8%). There were no significant differences.

NICU	**Oral misoprostol**	**Vaginal misoprostol**	**Dinoprostone control group**	**Significance**
	n (%)	**n (%)**	**n (%)**	**P Value°°**
BS < 4	2/61 (3.3)	4/59 (6.8)	3/121 (2.5)	*p*=0.352
BS ≥ 4	0/59 (0)	2/61 (3.3)	5/119 (4.2)	*p*=0.289
P Value°	*p*=0.496	*p*=0.435	*p*=0.498	

NICU= neonatal intensive care unit, P Value° ~ Fisher's exact test, P Value°° ~ Pearson χ^2
Table 3-31: Admission to neonatal intensive care unit.

Hypoxic ischemic encephalopathy was noted in one neonate out of 62 (1.6%) after application of vaginal misoprostol to the mother who presented with a favourable cervix before induction of labour.

3.3 Part II – Vaginal and Oral Misoprostol versus Oral Misoprostol

Forty patients were suitable for analysis after exclusion. 20 patients were randomised to the vaginal oral misoprostol arm and 20 to the oral misoprostol arm.
All patients were nulliparous as the inclusion criteria required.

The demographic characteristics are shown in Table 3-32.

Demographic characteristics	**Vaginal oral misoprostol**	**Oral misoprostol**
	Median (quartiles)	**Median (quartiles)**
Maternal age (years)	25 (23/29)	21 (19/26)
Gestational age (week)	38 (37/40)	39 (37/41)
Bishop score	4 (3/5)	4 (2/4)
No. of doses	3 (2/3)	3 (3/3)
Fetal weight (gram)	3418 (2709/3635)	2998 (2598/3254)

Quartiles in brackets correspond to Q1/Q3
Table 3-32: Demographic characteristics – pilot study.

The main indication for induction of labour in both groups was pre-eclampsia (cf. Table 3-33). The reason for that was the fact that these inductions were carried out at Groote Schuur Hospital as a tertiary referral centre.

Indications for induction of labour	**Vaginal oral misoprostol n=20**	**Oral Misoprostol n=20**
	n (%)	**n (%)**
Pre-eclampsia	12 (60)	13 (65)
Postdates	3 (15)	4 (20)
Oligohydramnios	0	1 (5)
Gestational diabetes mellitus	2 (10)	0
IUGR	1 (5)	0
others	2 (10)	2 (10)

IUGR= Intrauterine growth restriction
Table 3-33: Indications for induction of labour - pilot study.

The success rate of deliveries within 24 hours after the first application, irrespective of the route, was higher in the combined vaginal and oral misoprostol group, this did not reach statistical

relevance as shown in Table 3-34. 16/20 (80%) of the patients delivered after combined vaginal and oral misoprostol versus 11/20 (55%) after oral treatment (p=0.176, Fisher's exact test).
The success rate of vaginal deliveries within 24 hours after the initial dose was similar: 7/20 (35%) of the women with the combined vaginal and oral and 5/20 (25%) with the oral regimen (p=0.731, Fisher's exact test).

Success rate	**Vaginal oral misoprostol**	**Oral misoprostol**	**Significance**
	n (%)	**n (%)**	**P Value**
Deliveries < 24 hours	16 (80)	11 (55)	p=0.176
NVD < 24 hours	7 (35)	5 (25)	p=0.731

NVD= natural vaginal deliveries, P Value ~ Fisher's exact test

Table 3-34: Success rate of deliveries within 24 hours after first application - pilot study.

The median time from induction to delivery irrespective of the route was about three and a half hours less after the combined vaginal and oral treatment with 18 h 08 min (Q1=9 h 8 min, Q3=23 h 56 min) as compared with 21 h 35 min (Q1=13 h 39 min, Q3=27 h 15 min) in women treated with oral misoprostol only, this difference was not significant (p=0.114, Mann-Whitney-test).

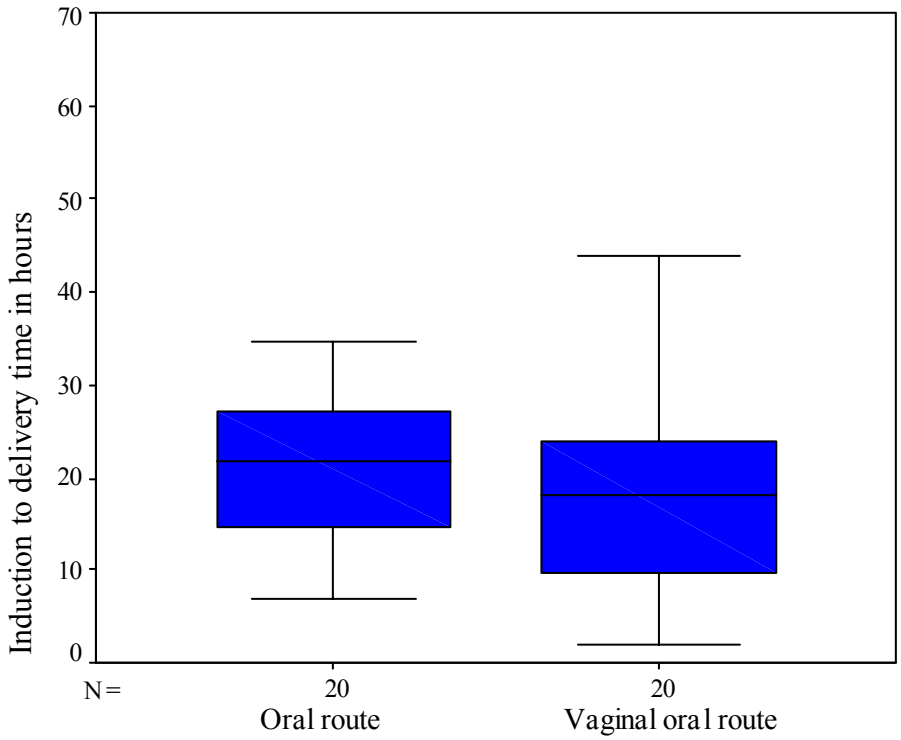

Figure 3-17: Time from induction to delivery, irrespective of the mode of delivery – pilot study.

There was a 9 h 44 min difference in the median duration from the start of induction to vaginal delivery in the combined vaginal and oral versus the oral dosing group, 20 h 29 min (Q1=10 h 29 min, Q3=22 h 49 min) versus 10 h 45 min (Q1=7 h 17 min, Q3=18 h 30 min), respectively. This was not a significant difference (p=0.101, Mann-Whitney-test), but it showed a definite trend towards faster deliveries with the combined vaginal and oral regime.

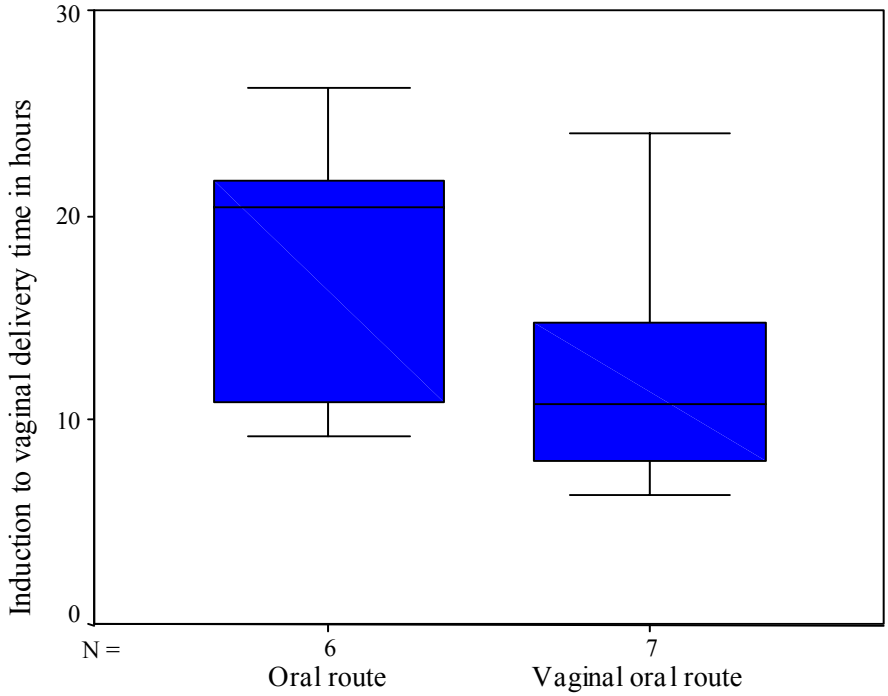

Figure 3-18: Time from induction to vaginal delivery, irrespective of the mode of delivery – pilot study.

The route of delivery was similar in the two groups (cf. Figure 3-19).

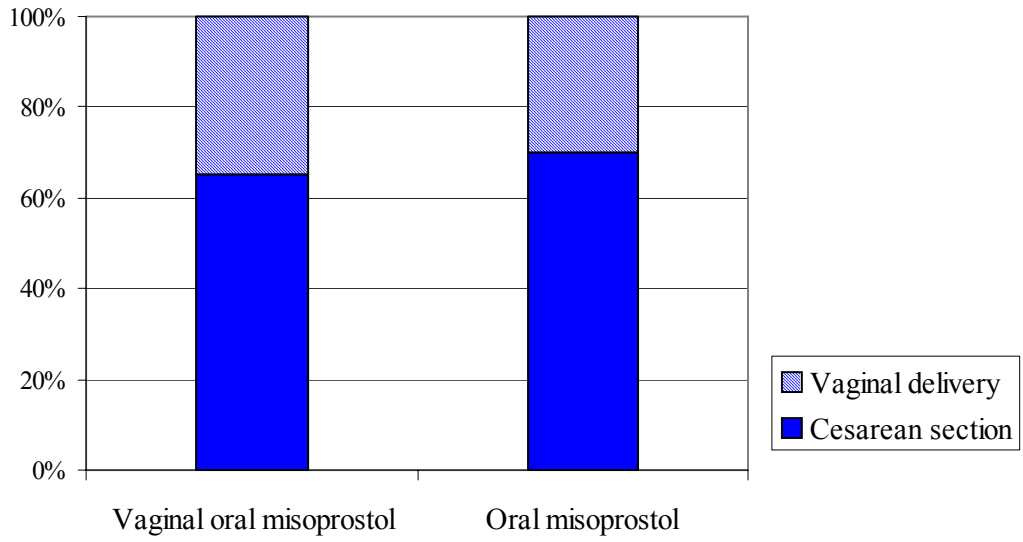

Figure 3-19: Mode of delivery - pilot study.

Both routes resulted in a fairly high cesarean section rate. 13/20 (65%) of the women in the combined vaginal and oral treatment group and 14/20 (70%) in the oral treatment group delivered by cesarean section (p=1.000, Fisher's exact test).
The remaining patients delivered vaginally (p=1.000, Fisher's exact test), as no instrumental vaginal deliveries took place in this study.

The indications for cesarean sections are shown in Table 3-35 and Figure 3-20.
The main indication for cesarean section in the combined vaginal and oral group was fetal distress, 8/13 (62%) surgical interventions were caused by distress of the foetus. After oral treatment only 3/14 (21%) women went to theatre for the same reason. This did not show a significant difference, but a trend (p=0.054, Fisher's exact test).
The main indication for the induction of labour was pre-eclampsia. 7/12 (58 %) of the pre-eclamptic patients induced with combined vaginal and oral misoprostol had a cesarean section for fetal distress and only 1/13 (8%) of the induced pre-eclamptic patients in the oral group.

The main reason for abdominal delivery with the oral misoprostol treatment was failed induction of labour after 24 hours. 6/14 (43%) of the women did not go into labour after the full oral treatment of misoprostol, whereas only 3/13 (23%) in the combined vaginal and oral group were not induced successfully (p=0.420, Fisher's exact test).

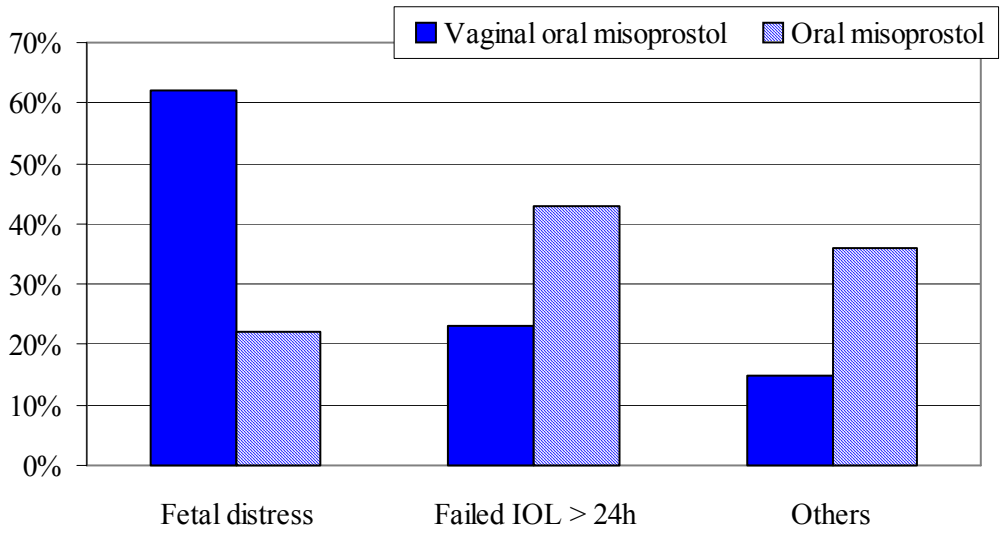

Figure 3-20: Indications for cesarean sections - pilot study.
IOL= induction of labour

Indication for cesarean sections	Vaginal oral misoprostol	Oral misoprostol	Significance
	n=13 (%)	n=14 (%)	P Value
Fetal distress	8 (62)	3 (21)	*p*=0.054
FIOL > 24 hours	3 (23)	6 (43)	*p*=0.420
Other reasons (CPD/SP)	2 (15)	5 (36)	*p*=0.385

FIOL= failed induction of labour, CPD= cephalo-pelvic disproportion, SP= slow progress,
P Value ~ Fisher exact test

Table 3-35: Indications for cesarean sections - pilot study.

Other main reasons for a cesarean section were a cephalo-pelvic disproportion and slow progress.

Analgesia requirement was not significantly different in the two groups, though there seemed to be a trend towards more need for analgesia in women induced with oral misoprostol only (cf. Table 3-36).

11 women (55%) in the combined vaginal and oral arm received analgetic treatment; all of these patients were given morphine. Only two out of 11 women (18%) asked for further analgetic treatment: one (9%) woman was given a regional neural conduction blockade and another one (9%) was offered Entonox gas.

Analgesia	Vaginal oral misoprostol	Oral misoprostol	Significance
	n (%)	n (%)	P Value
Analgesia in general	11 (55)	16 (80)	*p*=0.176
Morphine	11 (55)	15 (75)	*p*=0.320
Epidural	1 (5)	7 (35)	*p*=0.044
Entonox	1 (5)	0	*p*=1.000

P Value ~ Fisher exact test

Table 3-36: Need of analgesia - pilot study.

16 women (80%) in the oral arm needed analgetic treatment. 15 patients (75%) received morphine. 6 (40%) of these 15 patients had further pain relief and received epidural anaesthesia. One patient (5%) received epidural anaesthesia without having had morphine before.

The need for augmentation was similar in the two groups, though a tendency towards more intervention like rupturing the membranes or the use of oxytocin in the oral misoprostol group was noted (cf. Table 3-37).

Artificial rupture of membranes was performed in 7/20 (35%) of the women in the combined vaginal and oral treatment group and in 11/20 (55%) of those with oral treatment (p=0.341, Fisher's exact test).
Oxytocin augmentation was used in 7 patients of the combined vaginal and oral arm and 12 in the oral arm (p=0.205, Fisher's exact test).

Tachysystole was noted in 3 women randomised to the combined vaginal and oral group as compared with only one patient after oral treatment. This difference, however, was not statistically relevant (p=0.605, Fisher's exact test). The patient presenting with tachysystole in the oral group delivered vaginally. One of the patients in the combined vaginal and oral group delivered vaginally and two delivered by cesarean section. The indications for the cesarean sections in these cases were failed induction of labour after 24 hours and slow progress. There was no correlation between tachysystole and fetal distress leading to cesarean section.
None of the patients with tachysystole presented with a hyperstimulation syndrome on the CTG tracing.

	Vaginal oral misoprostol	**Oral misoprostol**	**Significance**
	n (%)	**n (%)**	**P Value**
AROM	7 (35)	11 (55)	p=0.341
Oxytocin	7 (35)	12 (60)	p=0.205
Tachysystole	3 (15)	1 (5)	p=0.605
Hyperstimulation syndrome	0	0	
Meconium passage	3 (15)	1 (5)	p=0.605
Abruption	0	0	

AROM= Artificial rupture of membranes, P Value ~ Fisher exact test
Table 3-37: Artificial rupture of membranes, oxytocin, tachysystole, hyperstimulation syndrome, meconium passage and abruption - pilot study.

The incidence of meconium passage was 15% and 5% in the combined vaginal and oral and in the oral treatment group, respectively (p=0.605, Fisher's exact test).
Other complications such as abruption did not occur in either group.

There were no relevant maternal side effects (cf. Table 3-38).
The main side effects were gastrointestinal side effects. Nausea was noted in 5 (25%) patients of the combined vaginal and oral group versus 4 (20%) of the oral group, vomiting in 2 (10%) after

combined vaginal and oral treatment versus 3 (15%) with only oral misoprostol. Shivering was another effect noted in 4 (20%) women in the combined vaginal and oral misoprostol arm and 2 (10%) women after application of oral misoprostol.

One patient (5%) in the combined vaginal and oral arm was reported to be pyrexic with a temperature between 37.5 and 38 °C. Two (10%) women in the oral treatment arm had a temperature of more than 38°C. Diarrhoea was not noted in either group.

Maternal side effects	Vaginal oral misoprostol	Oral misoprostol	Significance
	n (%)	n (%)	P Value
Nausea	5 (25)	4 (20)	*p*=1.00
Vomiting	2 (10)	3 (15)	*p*=1.00
Shivering	4 (20)	2 (10)	*p*=0.661
Diarrhoea	0	0	
Pyrexia ≤ 38°C	1 (5)	0	*p*=1.00
Pyrexia > 38°C	0	2 (10)	*p*=0.487

P Value ~ Fisher exact test

Table 3-38: Maternal side effects – pilot study.

The median blood loss in the third stage of labour was 360 ml (Q1=300, Q3=450) in combined vaginal and oral misoprostol treated women and 300 ml (Q1=213, Q3=388) in those with oral treatment (p=0.163, Pearson $\chi 2$).

In the oral arm, two patients were recorded with primary postpartum haemorrhage; one woman had a blood loss of 600 ml and another one 1500 ml in the first 24 hours after delivery.

Secondary postpartum haemorrhage was not reported in any case.

The data of neonatal outcome were not significantly different. All Apgar scores after 5 minutes were ≥ 7. There was no admission to the neonatal intensive care unit and no hypoxic ischemic encephalopathy (cf. Table 3-39).

Fetal outcome	Vaginal oral misoprostol	Oral misoprostol	Significance
	n (%)	n (%)	P Value
Apgar score 1 min < 7	3 (15%)	2 (10%)	*p*=0.100
Apgar score 5 min < 7	0	0	
Admission to NICU	0	0	
HIE	0	0	

NICU= neonatal intensive care unit, HIE= hypoxic ischemic encephalopathy

Table 3-39: Fetal outcome – pilot study.