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## CEFOXITIN SINGLE DOSE PROPHYLAXIS AND/OR T TUBE SUCTION DRAINAGE FOR VAGINAL AND ABDOMINAL HYSTERECTOMY (Prospective randomized trial on 155 patients)

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**Summary:** Pelvic infections represent the most feared complications associated with vaginal and abdominal hysterectomy. In the present paper we show the result of a prospective randomized clinical trial carried out to study different morbidities (F.M. febrile morbidity, U.T.I. urinary tract infections, P.C. pelvic cellulitis, P.A. pelvic abscess, W.I. wound infection) in a sample of 155 patients undergoing vaginal or abdominal hysterectomy for non malignant disease, divided into three groups. 1) group C, treated with 2 g cefoxitin i.v. in the preoperative period; 2) group C+T, the same treatment with the addition of T tube suction drainage; 3) group T, with only the T tube suction drainage. A statistical analysis of the sample showed the homogeneity of each group, while the study of the morbidities showed a statistical significant difference for W.I. between the groups treated with antibiotic and the T group ( $p < .001$ ). For all the other morbidities, no statistically significant differences were found between the groups, demonstrating that all three methods are considerably efficient in reducing postoperative morbidity in hysterectomy.

The most common and serious complication after hysterectomy is postoperative pelvic infection. Its incidence varies from 30 to 40% <sup>(1)</sup> and it can reach up to 70% in cases of vaginal hysterectomy <sup>(2)</sup>. This type of infection shows up as pelvic abscesses and/or pelvic cellulitis. The most widely followed treatment among those suggested for avoiding these infec-

tions is the use of prophylactic antibiotics, particularly because of their easy administration. The treatment usually consists of three or more doses in the perioperative period; one administration before and two or more after surgery at 6 or 12 hours intervals. In recent years, only two clinical studies report data obtained using a single dose of prophylactic anti-

biotic administered before surgery (<sup>3,4</sup>). Some alternatives to prophylactic antibiotic treatment such as the T tube suction drainage proposed by Swartz and Tanare in 1975 alone or in combination with an antibiotic, have however been studied (<sup>5,6</sup>).

The T tube method reduces morbidity significantly in both abdominal and vaginal hysterectomy by removing almost 40 ml of serous hematic fluid which is formed simultaneously by lymph, blood and necrosis of the tied and cut tissues and which provides an ideal medium for the growth of many bacteria (particularly anaerobic). On the basis of microbiological studies regarding pelvic infectious disease, Osborne (<sup>7</sup>) suggest cervix sterilization through hot conization after disinfection with povidone iodine. This method dramatically reduces postoperative pelvic infections. The use of antibiotic sprayed several times during vaginal hysterectomy significantly reduces the incidence of infections (<sup>8</sup>). In the present research, we carried out a prospective randomized clinical trial to study the morbidity of three groups of patients respectively treated with: 1) cefoxitin 2 g i.v. in a single dose before surgery (group C); 2) the same treatment as in group 1 plus T tube suction drainage (group C+T); 3) T tube suction drainage alone (group T).

We chose cefoxitin for its low toxicity, its few side effects and its broad spectrum of action especially against those bacteria responsible for postoperative infections.

## MATERIALS AND METHODS

This study was carried out from June 1981 to April 1982 on a sample of 155 patients admitted to the Gynecology Department. All the patients were operated for non malignant disease, 40.7% underwent vaginal hysterectomy, while 59.3% underwent abdominal procedure, 96% of the patients had general anesthesia. All of the patients were operated on by staff members. The patients eligible for the study, having given their consent, were randomly assigned before surgery to one of the three groups: C, C+T, T. Each patient was given a vaginal

douche with povidone iodine the evening before surgery; the vagina and the abdominal skin were then disinfected at the moment of the operation with povidone iodine solution. Two grams of cefoxitin were administered within 15 minutes before incision, given i.v. in three minutes. T Bardex tube no. 16 with the arms of the T 5 cm long, having three holes per arm measuring 3 mm in diameter, was placed according to Swartz (<sup>5,6</sup>) and connected to a Redivac bottle in which a vacuum of 30 cmHg was obtained. The tube was removed after 72 hours. During surgery all patients had a no. 16 Foley catheter, which was removed after 72 hours, unless complication due to operation for urinary incontinence or bladder lesions arose. In addition to hysterectomy with or without removal of the adnexa, other procedures such as urethral suspension according to Pereyra, or the Marshall Marchetti or Burch were also carried out. All patients underwent a D&C before surgery in order to obtain a specimen of the endometrium before the hysterectomy.

### *Criteria for exclusion from the study.*

1. Hypersensitivity to antibiotics. This item, revealed through the patient's medical history, allowed for use of an allergy skin test for cefoxitin, which if negative, made the patient eligible for the study.
2. Infectious diseases.
3. Congenital immunologic deficiency.
4. Previous pregnancy less than 8 weeks before.
5. Heart disease.
6. Kidney failure and/or ureic nitrogen greater than 0.45 mg % and creatinemia more than 1.5 mg %.

### *Morbidity criteria*

1. Febrile morbidity - F.M.

We defined such morbidity on the basis of fever higher than 38 °C after 24 hours from surgery on at least two occasions with an interval of six hours from one to the other.

2. Urinary tract infection - U.T.I.

We considered cases with at least 100,000 colonies per ml, with or without clinical symptoms. The specimen was obtained by clean-catch.

3. Pelvic cellulitis - P.C.

We defined this as infection of the space between peritoneum and vaginal vault including parametria. The diagnosis was made on the basis of three symptoms: pain at the lower quadrants of the abdomen, fever and increased tension revealed through careful palpation of the lower quadrants of the abdomen.

Table 1.

Group		Vaginal hysterectomies				Abdominal hysterectomies			
		C	C+T	T	p	C	C+T	T	p
Age	mean	50.33	49.93	49.19	F n.s.	46.74	46.33	44.66	F n.s.
	standard dev.	(7.86)	(8.32)	(7.26)		(4.75)	(5.74)	(5.86)	
Menopause		40%	50%	36%	$\chi^2$ n.s.	7%	13%	10%	$\chi^2$ n.s.
Concurrent procedures		27%	25%	48%	$\chi^2$ n.s.	17%	25%	28%	$\chi^2$ n.s.
Operating time	mean	68.5	67.5	62.8	F n.s.	88.4	84.6	90.8	F n.s.
	s.d.	(29.0)	(23.7)	(22.1)		(23.2)	(29.1)	(31.5)	
Blood loss	mean	179.4	224.0	221.2	F n.s.	290.0	244.11	202.3	F n.s.
	s.d.	(108.0)	(168.0)	(159.8)		(236.0)	(169.5)	(97.8)	
Preoperative hospital stay	mean	13.5	11.8	12.36	F n.s.	11.07	11.19	13.05	F n.s.
	s.d.	(5.2)	(3.3)	(4.6)		(3.8)	(4.8)	(4.8)	
Postoperative hospital stay	mean	9.1	10.5	9.7	F n.s.	11.4	11.3	11.3	F n.s.
	s.d.	(3.3)	(3.8)	(2.8)		(4.0)	(5.5)	(4.4)	
Catheterization	mean	4.3	4.0	3.8	F n.s.	3.4	3.3	3.4	F n.s.
	s.d.	(3.8)	(2.5)	(2.1)		(1.9)	(0.9)	(1.8)	
T tube drainage	mean		49.0	48.0	F n.s.		44.1	52.7	F n.s.
	s.d.		(2.5)	(27.1)			(28.5)	(37.8)	
Patients no.		22	16	25		28	36	28	

\*  $\chi^2$  test for menopause and concurrent procedures, analysis of variance for the other parameters.

#### 4. Pelvic abscess - P.A.

Pelvic abscesses or infected hematoma is an infection in the same tissues involved in pelvic cellulitis including adnexal structures with a pelvic mass, which is palpable and/or seen by ultrasound.

#### 5. Infected surgical wound - W.I.

This is defined as a wound, draining purulent material with or without positive cultures. A positive culture draining purulent material indicates an infected wound if accompanied by redness and heat. Statistical analysis was performed by  $\chi^2$  test mod. by Yates and analysis of variance (F).

## RESULTS

Out of the 155 patients in this study 92 (59.3%) underwent abdominal hysterectomy, the other 40.7% underwent the vaginal procedure. The three groups, C, C+T, and T consisted respectively of 50, 52 and 53 patients. Table 1 shows the

characteristics of the sample in the single groups (C, C+T, T) according to the type of operation (abdominal or vaginal). There is a remarkable uniformity among groups C, C+T and T as far as both age and percentage of patients in menopause are concerned. The  $\chi^2$  test with the Yates modality does not show any significant difference among the various groups. The accessory procedures were carried out differently in each group, but the differences are not statistically significant. In the same table 1 blood losses, length of surgery (time calculated in minutes), days of hospitalization, time of catheterization are shown. All of the measurements are equally comparable without significant differences.

Table 2 shows the morbidity of all the patients considered globally in the three groups C, C+T and T. The U.T.I. are

Table 2. — *Morbidities in the three groups. Vaginal plus abdominal hysterectomies.*

Group	C	C + T	T	p
Patients no.	50	52	53	
F.M.	4 (8%)	6 (11%)	12 (22%)	n.s.
U.T.I.	33 (66%)	31 (59%)	36 (67%)	n.s.
P.C.	0	1 (1.9%)	3 (5.6%)	n.s.
P.A.	1 (2%)	1 (1.9%)	2 (3.7%)	n.s.
W.I.	0	0	8 (15%)	<0.01

F.M. febrile morbidity – U.T.I. urinary tract infections – P.C. pelvic cellulitis – P.A. pelvic abscess.

\*  $\chi^2$  test for statistical significance.

uniformly distributed in the three groups. Febrile morbidity is higher in the T group, but the difference as compared with the other two groups is not significant. There are also no significant differences for P.A. and P.C. The W.I. on the contrary shows a clear predominance in the T group ( $p < .01$ ). If we analyze the items of table 3 concerning vaginal hysterectomy, a higher incidence of fever is found in the T group bordering on significance ( $p = .08$ ) while no significant difference

is found between the groups concerning U.T.I., P.A., P.C. and W.I. In table 4 the morbidity of the three groups having undergone abdominal hysterectomy is indicated. Here also the U.T.I. are uniformly distributed, while the difference in W.I. in the T group with respect to the other two is highly significant ( $p < .001$ ). If we distinguish the morbidities in two categories, tab. 5, minor and major morbidity, defining minor morbidity as that found in patients showing F.M. and/or

Table 3. — *Analysis of vaginal hysterectomy morbidities in the three groups.*

Group	C	C + T	T	p
Patients no.	22	16	25	
F.M.	2 (9%)	1 (6.2%)	8 (32%)	n.s.*
U.T.I.	15 (68%)	10 (62.5%)	16 (64%)	n.s.
P.C.	0	0	2 (8%)	n.s.
P.A.	1 (4.5%)	0	0	n.s.
W.I.	0	0	1 (4%)**	n.s.

\*  $p = 0.0800$

\*\* W.I. is the incision for Pereyra procedure.

Table 4. — *Analysis of abdominal hysterectomy morbidities in the three groups.*

Group	C	C + T	T	p
Patients no.	28	36	28	
F.M.	2 (7.1%)	5 (13%)	4 (14%)	n.s.
U.T.I.	18 (64.2%)	21 (58.3%)	20 (71%)	n.s.
P.C.	0	1 (2.7%)	1 (3%)	n.s.
P.A.	0	1 (2.7%)	2 (7%)	n.s.
W.I.	0	0	7 (25%)	<0.001

Table 5. — Morbidity in the three groups; vaginal and abdominal hysterectomy.

Group	C	C + T	T	
Major morbidity	1	0	3	
Minor morbidity	15	11	17	Vaginal hysterectomy
No morbidity	6	5	5	p<0.05 n.s. D.F.= 4

  

Group	C	C + T	T	
Major morbidity	0	0	7	
Minor morbidity	17	22	15	Abdominal hysterectomy
No morbidity	11	14	6	p<0.01 D.F.= 4

Major versus minor versus no morbidity.  
Major morbidity - P.A. - P.C. - W.I.  
Minor morbidity - F.M. - U.T.I.

U.T.I., and major morbidity as P.A. and/or P.C. and/or W.I., even with concomitant F.M. and/or U.T.I., it becomes evident that in vaginal hysterectomy there is no significant difference among the groups C, C+T, T. On the contrary, the difference between the T group and the other two groups in abdominal hysterectomy is highly significant ( $p<.01$ ). The T group has a number of patients with a major morbidity higher then the other two groups having no patient with major morbidity. In table 6 bacteria isolated from urine cultures are shown. Analysing the morbidies with respect to menopausal status or phase of the menstrual cycle, no significant result was obtained. In no case was there evidence of secondary side effect due to the use of cefoxitin administered to the patients examined. The cases of P.A. and P.C. were treated with clyndamicin 750 mg/day or metronidazol 1000 mg/day.

DISCUSSION

It is well known that vaginal hysterectomy is an operation liable to a high infectious morbidity. Having considered the principal studies carried out by comparison of a group receiving placebo and a group receiving prophylactic antibiotic

and having taken into account the high percentage of infection in the placebo group, we do not feel it is ethically acceptable today to have a placebo group versus a group with therapy <sup>(1,2,5,6,8,11,12)</sup>, especially as far as vaginal hysterectomy is concerned. For this reason we have compared three treatments (C, C + T, T), which would perspectivevely guarantee against serious morbidities. It is well known that even with use of prolonged antibiotic therapy and careful disinfection through vaginal douches it is not possible to make the vagina a germ free environment; in fact anaerobic and aerobic germs as well

Table 6. — Bacteria cultured from the urine.

Bacterium	incidence
E. Coli	42%
Proteus mirabilis	20%
Streptococcus fecalis	16%
Pseudomonas aeruginosa	14%
Streptococcus β emol. group B	5%
Klebsiella	5%
Sarcina tetragena	5%
Serratia marcescens	3%
Enterobacter areogen	2%
Enterobacter cloacae	2%
Morganella Morganii	1%
Citrobacter Freundi	1%

as negative and positive grams live in the cervical channel and enter the peritoneum at the moment of removal of specimen (<sup>7</sup>). Moreover regardless of the procedure used, tissues included in the tied up parts become necrotic and thus reduce the cellular redox potential, allowing for the growth of anaerobic germs such as *Bacteroides Fragilis* and others. The enzyme dissolution from the tied tissues determines the loss of fluid, in which we find blood, lymph and serum, so that during the post-operative days an average of 45 ml of hematoma and serous fluid gather in the retroperitoneal space; this liquid represents an optimum pabulum for germs. In the present study we have chosen a single dose of antibiotic according to Mendelson (<sup>3</sup>), who affirms that a single dose of cephadrine administered immediately before surgery has the same efficacy as a 3 g dose taken i.v. every 6 hours during the perioperative period. Prophylactic antibiotic therapy with a single dose has been also tried by other Authors (<sup>4</sup>). The choice of cefoxitin is justified by its broad spectrum of action; i.v. administration seems to be the best because the antibiotic serum concentration is the same in different patients with equal elimination and it remains high enough for at least two hours after administration (<sup>9</sup>). Some Authors experienced cefoxitin prophylactic administration as intramuscular injection, but the concentration in the plasma is not uniform and it depends on the absorption of the area of injection (<sup>10, 11</sup>).

Analyzing the tables on morbidity for vaginal and abdominal hysterectomy it becomes evident that a higher morbidity incidence in the T group especially in vaginal hysterectomy is present. Even if these differences are below statistical significance it is clear that they can be attributed to the protective effect which the antibiotic has on the other two groups. For U.T.I. the incidence varies from 58.3% to 71%. It is a very remarkable

incidence, which can be attributed to the prolonged use of transurethral catheter. Many patients have undergone procedures for urinary incontinence and had the catheter for more days. The three cases of intraoperative bladder lesion are included in the sample; in these cases the catheter was maintained for 12 days after surgery. One catheterization is enough to provoke the presence of germs in the urine in 15% of cases; after 24 hours of permanent catheter germs are present in the urine in almost 100% of cases (<sup>13</sup>). Since in our study the catheter was maintained for at least 3 days, while the antibiotic was effective only during the perioperative interval, the high percentage of urinary infections is easily explained. With a longer prophylactic treatment the incidence of U.T.I. is really lower, but as U.T.I. do not generally cause serious disease, they can also be cured at home by oral medicines and do not influence the stay in hospital, so we do not think it is necessary to use a more prolonged treatment.

The P.A. and P.C. were very rare in both type of surgery and without significant statistical differences among the various groups. An effective protection against W.I. is given by the antibiotic prophylactic treatment with cefoxitin. This item is also confirmed by new studies with the same antibiotic (<sup>14</sup>), which was also injected into the incision (<sup>15</sup>). In the present sample no W.I. was present in the two groups with abdominal hysterectomy receiving cefoxitin (C and C+T). The presence of W.I. in the T group in vaginal hysterectomy was related to one case of incision upon the pubic bone after the urethral suspension according to Pereyra procedure. It is precisely because of W.I. in abdominal hysterectomy that highest statistical significance shows up with  $p < .001$ . In our sample neither the menopause nor the phase of the cycle seemed to influence morbidity, although

the vaginal flora especially the anaerobic bacteria, vary significantly in the two phases, proliferative and secretive of the menstrual cycle, just as it varies in pregnancy and in postpartum<sup>(16)</sup>. On the basis of this study it becomes evident that all the suggested methods reduce the morbidity at a very low rate; addition of cefoxitin to the use of T tube suction drainage further reduces the already low incidence of infections, which can be obtained with the T tube alone. In abdominal hysterectomy the use of cefoxitin appears to be extremely rational because it reduces to zero the incidence of W.I. and it noticeably decreases fever within the limits of statistical significance in vaginal hysterectomy. W.I. although is not a serious complication for the life of the patient, determines a longer stay in hospital and therefore a higher cost for the hospital. In conclusion we feel that the use of cefoxitin in a single dose as prophylactic treatment is very useful. The addition of the T tube should be preferred especially for those operations in which one is forced to the wide dissections because of the uterus shape or for pathology such as endometriosis or pelvic inflammatory disease. Our data shows that T tube suction drainage is an acceptable alternative to systemic prophylactic antibiotic in vaginal hysterectomy, but it is ineffective to prevent the major cause of morbidity after abdominal hysterectomy i.e. W.I. So, on the basis of our research and through comparison of the various data offered by the literature, we may

say that, in addition to cost reduction and lower selection of resistant microorganism the single dose of cefoxitin allows us to obtain results comparable to those that can be obtained through longer treatments.

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