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APPENDICES

APPENDIX A

Reported Adverse Events and Laboratory Test Abnormalities with Norfloxacin

Adverse Events Reported by 1162 Patients Who Received Norfloxacin (Data on File, Merck Sharp and Dohme)

Gastrointestinal (GI)		*Central nervous system*		*Dermatological*	
Abdominal pain	2	Anxiety	1	Erythema	2
Anorexia	1	Depression	1	Pruritus	2
Diarrhoea	1	Dizziness	6	Rash	3
Digestive system disorder	1	Euphoria	1		
Dyspepsia	4	Hallucinations	1	*Other*	
Dysphagia	1	Headache	4	Epiphora	1
GI cramps	1	Insomnia	2	Taste perversion	2
Nausea	13	Somnolence	1	Tinnitus	1
Tongue enlargement	1	Dry mouth	2	Vaginal swelling	1
				Tachycardia	1
				Total	57

Summary of Laboratory Test Abnormalities with Norfloxacin

Test	Deviation from normality	No. of patients with abnormal values	No. of tested incidences Patients	(%)
Liver function parameters:				
SGOT	increase	24	1208	1.99
SGPT	increase	26	1173	2.22
Alkaline phosphatase (Al-P)	increase	6	1106	0.54
Bilirubin (T-Bil)	increase	2	670	0.30
Renal function parameters:				
BUN	increase	6	1149	0.52
Serum creatinine	increase	3	1079	0.28
Hematologic parameters:				
Red blood cell	increase	1	1115	0.09
Haemoglobin	increase	1	965	0.10
Platelets	decrease	1	843	0.12
White blood cell	decrease	2	1143	0.17
Eosinophils	increase	7	697	1.00
Neutrophils	decrease	2	697	0.29
Chloride (Cl)	increase	1	330	0.30
No. of patients		51		
No. of instances		82		

APPENDIX B

Antimicrobial Therapy of Acute Bacterial Diarrhoea

Some antimicrobial therapy of acute bacterial diarrhoea are shown as follows: (69,72,73,76,79)

DIAGNOSIS	DRUG	DOSE
Shigella species (especially if fever, chills, shock ; confirm sensitivity in laboratory)	- Co-trimoxazole	TMP 160 mg + SMX 800 mg every 12 hours, 5 days
	- Ampicillin	500 mg oral 4 times/day, 5 days
	- Tetracycline	2.5 gram oral in a single dose
Salmonella (no antibiotics for uncomplicated entertis; confirm sensitivity in laboratory)	- Co-trimoxazole	TMP 160 mg + SMX 800 mg every 12 hours, 3-5 days
	- Ampicillin	1 gm every 4-6 hours, 3-5 days
	- Chloramphenicol	500 mg every 6 hours, 3-5 days
Enterotoxigenic E. coli	- Co-trimoxazole	TMP 160 mg + SMX 800 mg twice daily for 3-5 days
	- Furazolidone	100 mg 4 times/days for 5 days
Enteropathogenic E. coli	- Co-trimoxazole	As for Enterotoxigenic E. coli
V. cholerae	- Tetracycline	500 mg every 6 hours, 2-3 days
	- Co-trimoxazole	TMP 80 mg + SMX 400 mg, 1 tablet every 12 hours, 5 days
	- Nitrofurantoin	100 mg every 6 hours, 2-3 days
V. cholerae non-01	- Ampicillin (if sensitive)	100 mg/kg/day oral or IV in 4 divided doses, 7-14 days
V. parahaemolyticus (dysentery or septicemia)	- Ampicillin	100 mg/kg/day oral or IV in 4 divided doses, 5-7 days
	- Tetracycline	500 mg oral 4 times/day, 5-7 days
Campylobacter (for severe illness; eliminate pathogen and prevent relapse)	- Erythromycin	500 mg every 6 hours, 7 days
	- Tetracycline	500 mg 4 times/day, 5-7 days
	- Clindamycin	300 mg every 6 hours, 7 days

APPENDIX C

Statistics

1. The comparison of proportions from several independent samples

Suppose that m independent samples of subjects are studied, with each subject characterized by the presence or absence of some characteristic.

The resulting data might be presented as follows:

Sample	Total in Sample	Number with Characteristic	Number without Characteristic	Proportion with Characteristic
1	$n_{1.}$	n_{11}	n_{12}	p_1
2	$n_{2.}$	n_{21}	n_{22}	p_2
⋮				
m	$n_{m.}$	n_{m1}	n_{m2}	p_m
Overall	$n_{..}$	$n_{.1}$	$n_{.2}$	$\bar{p}$

$$p_i = \frac{n_{il}}{n_{i.}} \qquad (1)$$

and

$$\bar{p} = \frac{n_{.1}}{n_{..}} = \frac{\sum n_{i.} p_i}{\sum n_{i.}} \qquad (2)$$

For testing the significance of the differences among the m proportions, the value of

$$\chi^2 = \sum_{i=1}^{m} \sum_{j=1}^{2} \frac{(n_{ij} - n_{i.} n_{.j}/n..)^2}{n_{i.} n_{.j}/n..} \qquad (3)$$

may be referred to tables of chi square with m-1 degrees of freedom. An equivalent and more suggestive formula for the test statistic is

$$\chi^2 = \frac{1}{\bar{p}\,\bar{q}} \sum_{i=1}^{m} n_{i.} (p_i - \bar{p})^2 \qquad (4)$$

where $\bar{q} = 1-\bar{p}$.

If χ^2 calculated $> \chi^2$ table, the proportions differ significantly.

If χ^2 calculated $< \chi^2$ table, the proportions do not differ significantly.

To identify the samples or groups of samples that contributed to the significant difference. Suppose that the m samples are partitioned into two groups, the first containing m_1 samples and the second m_2, where $m_1 + m_2 = m$. Define

$$n_{(1)} = \sum_{i=1}^{m_1} n_{i.} \qquad (5)$$

to be the total number of subjects in the first group of samples and

$$n_{(2)} = \sum_{i=m_1+1}^{m} n_{i.} \tag{6}$$

to be the total number of subjects in the second group.

Let the proportion in the first group be denoted $\bar{p}_1$, where

$$\bar{p}_1 = \frac{\sum_{i=1}^{m_1} n_{i.} p_i}{n_{(1)}} \tag{7}$$

and that in the second group be denoted $\bar{p}_2$, where

$$\bar{p}_2 = \frac{\sum_{i=m_1+1}^{m} n_{i.} p_i}{n_{(2)}} \tag{8}$$

then

$$\chi^2_{diff} = \frac{1}{\bar{p}\,\bar{q}} \frac{n_{(1)}\, n_{(2)}}{n_{..}} (\bar{p}_1 - \bar{p}_2)^2 \tag{9}$$

with 1 degree of freedom, may be used to test for the significance of the difference between $\bar{p}_1$ and $\bar{p}_2$.

$$\chi^2_{group1} = \frac{1}{\bar{p}\,\bar{q}} \sum_{i=1}^{m_1} n_{i.} (p_1 - \bar{p}_1)^2 \tag{10}$$

with $m_1 - 1$ degrees of freedom, may be used to test the significance of the differences among the m_1 proportions in the first group, and the statistic

$$\chi^2_{group2} = \frac{1}{\bar{p}\,\bar{q}} \sum_{i=m_1+1}^{m} n_{i.} (p_i - \bar{p}_2)^2 \qquad (11)$$

with $m_2 - 1$ degrees of freedom, may be used to test the significance of the differences among the m_2 proportions in the second group. It may be cheched that the three statistics given by (9)-(11) sum to the overall value of χ^2 in (4).

2. Paired Comparison (Paired t-test)

Subject No.	Before (X_1)	After (X_2)	Difference (d_i) ($X_2 - X_1$)
1	b_1	a_1	d_1
2	b_2	a_2	d_2
3	b_3	a_3	d_3
.	.	.	.
.	.	.	.
n	b_n	a_n	d_n

Let u_1, u_2 = population mean

$u_d = u_2 - u_1$

n = sample size

$\bar{d} = (\sum d_i)/n$

$s_d^2 = \dfrac{n\sum d_i^2 - (\sum d_i)^2}{n(n-1)}$

$S_d = s_d / \sqrt{n}$

The null hypothesis $H_o : u_d = 0$

The alternative hypothesis $H_a : u_d \neq 0$

The statistic t was given as $t_{(Calc)} = \dfrac{\bar{d} - u_2}{S_d}$

With degree of freedom = n-1

Comparing this $t_{(calc)}$ with $t_{(Tab)}$, obtained from the table.

If $t_{(Calc)}$ is in the acceptable region of $t_{(Tab)}$, we accept the null hypoyhesis that $u_d = 0$ and reject the alternative hypothesis.

If $t_{(Calc)}$ is not in the acceptable region of $t_{(Tab)}$, we reject the null hypoyhesis that $u_d = 0$ and accept the alternative hypothesis.

VITA

Mr. Dawlurk Raemonkorn was born in Bangkok, Thailand, on February 5, 1959. He got his degree in Bachelor of Science in Pharmacy from Faculty of Pharmacy, Mahidol University, Bangkok, Thailand, in 1981.