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Investigation of the incidence of use of quinine sulphate as a contraceptive in the Hillbrow-Berea area

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Science in Medicine in Pharmaceutical Affairs.

Johannesburg, 2003

Declaration

I, Nishaan Jugram, declare that this research report is my own work. It is being submitted for the degree of Master of Science in Medicine in the branch of Pharmaceutical Affairs in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.


(Signature of candidate)

8TH day of AUGUST (month), 2003

In memory of my daughter

Pooja Devi Jugram

4 November 1998

to

18 November 1998

Abstract

Quinine is a naturally occurring alkaloid found in the bark of the South American cinchona tree. It is used to treat malaria, to relieve nocturnal leg cramps and is used as an antipyretic. Anecdotal evidence, especially from community pharmacists, suggests widespread misuse of quinine sulphate. It has been taken for a range of non-indicated uses ranging from a single dose monthly contraceptive to a post coital "morning after" contraceptive.

A self-administered questionnaire, together with a confidentiality and anonymity declaration, was offered to all females requesting quinine sulphate at a pharmacy in Hillbrow, Johannesburg. After completing the questionnaire, the participants were counselled on the proper indications, as well as the consequences of misuse of quinine.

Biostatisticians at the Medical Research Council, Pretoria, statistically analyzed results of the questionnaire. The results showed that the majority of participants intended using quinine sulphate for contraceptive purposes. The dosages, quantity and the time of use in relation to the menstrual cycle varied considerably. Advice and counselling from pharmacists, in particular, has been lacking. A loophole in the scheduling status of quinine makes it easy to acquire quinine under the guise of using it to treat nocturnal leg cramps, whereas it is actually use for non-indicated purposes.

The misuse is largely limited to black South African women of different ethnic backgrounds. The results of the survey are discussed with reference to the statistical analysis and recommendations are made to limit the abuse of quinine sulphate.

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Appendix 1 Questionnaire

Appendix 2 Confidentiality and anonymity

Appendix 3 Ethics clearance certificate

Chapter 1 Introduction

1.1 Background

For over 300 years, quinine was the drug of choice for the treatment and chemosuppression of malaria.[1] By 1959, quinine as an antimalarial had been totally superceded by synthetic antimalarials. However, the appearance of chloroquine-resistant strains of *Plasmodium falciparum (P.falciparum)* has led to a resurgence in the use of quinine. Of the thirty-six alkaloids found in the bark of the South American cinchona tree (*Cinchona succirubra*), four stereoisomers: quinine; quinidine; cinchonine; and cinchonidine have significant antimalarial activity. Quinine is present in highest concentration, exceeding the other active antimalarial compounds by about ten-fold.[1]

Quinine has little effect on smooth muscle other than a slight oxytocic action on the gravid uterus, especially during the third trimester of pregnancy. Clinically, it has no effect on pregnancy until labour has started. Dangerously toxic amounts may cause abortion.[1]

Other uses of quinine include relief of leg cramps occurring during recumbence at night. In many parts of the world quinine is still used as an all-purpose antipyretic.[1]

Anecdotal reports from a number of pharmacists, from newly qualified to those in practice for many years, suggest that mainly black South Africans use quinine sulphate for contraception or termination of pregnancy (TOP). Quinine has a dual registration status in South Africa. It is schedule one for use as a muscle relaxant in nocturnal cramps, and schedule four when used to treat malaria caused by *P.falciparum.* A secondary registration is the use of quinine sulphate in the diagnosis of myasthenia gravis.[2]

1.2 Aims

1.2.1 To assess the extent of non-indicated usage of quinine sulphate amongst different population groups, but especially amongst black females in the Hillbrow-Berea area.

1.2.2 To assess the contribution of the healthcare professional in propagating the misuse of quinine sulphate.

1.2.3 Knowledge of quinine use:

1.2.3.1 To quantify the demand for quinine sulphate for use as a contraceptive, in a Hillbrow pharmacy.

1.2.3.2 To identify the source of the respondent's knowledge on the use of quinine for contraceptive purposes.

1.2.3.3 To identify any association between population group, income group, age group and use of quinine as a contraceptive.

The most important outcome measures will be:

a) Reason for quinine usage;

b) Duration of quinine use;

c) Dosages used;

d) Concurrent contraceptive use.

Chapter 2 Overview of quinine

2.1 The use of quinine as an antimalarial in pregnancy

Currently the only recommended treatment for uncomplicated, multidrug-resistant *P.falciparum* infections in pregnant women is quinine (thirty milligrams per kilogram per day) for seven days, but adverse effects are common and compliance is poor. Among the adverse effects are cinchonism, which is characterized by tinnitus and dizziness. Amongst the outcomes of pregnant mothers treated with quinine, possible complications include abortion and congenital abnormalities.[3] Quinine should not be withheld during pregnancy, despite its alleged abortifacient properties at high dosage, since it safeguards the life of the mother.[4]

2.2 The use of quinine as a contraceptive or abortifacient

Quinine is reported to have contraceptive properties. It was used in Britain before the advent of oral contraceptives.[4] In the early part of the twentieth century, in addition to being used as an abortifacient, quinine was also used as an emmenagogue or menstrual regulator.[5] A study conducted among school adolescents in Benin City, Nigeria showed that 4% of females between fourteen and twenty one years of age had reportedly used quinine as a contraceptive.[6] Dannenberg, Dorfman and Johnson (1983) completed an extensive review of the literature concerning the efficacy of quinine as an abortifacient. Their results were unclear because of a lack of controlled studies and the large number of unreported cases. Of the reported cases, the results were startling. In seventy cases in which quinine was used to attempt to abort a known or suspected pregnancy, at least eleven cases resulted in the death of the mother. Abortion was achieved without death of the mother in only three cases. At least fifty-one offspring had congenital anomalies for which quinine was the suspected etiologic agent.[7]

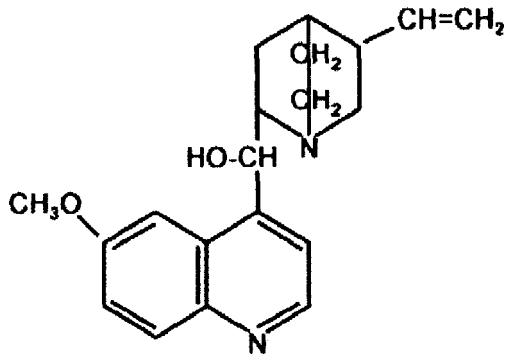
2.3 Mechanism of abortifacient action.

Quinine has a slightly oxytocic action on the gravid uterus. The pregnant uterus is stimulated to contract by quinine, but the drug is no longer used in obstetric practice. The

exact mechanism of action of quinine on the uterine muscle is unclear. Among the laity, quinine has a reputation as an abortifacient.[8]

2.4 Chemistry of quinine

Although quinine has been synthesised, the procedure is complex; quinine and the other alkaloids are, therefore, still obtained entirely from natural sources. Quinine contains a quinoline group attached through a secondary alcohol linkage to a quinuclidine ring. A methoxy side chain is attached to the quinoline ring and a vinyl to the quinuclidine.[9]



Quinine

2.5 Commercial preparations of quinine

Quinine sulphate is commercially available as a scheduled medicinal product via pharmacies, hospitals, clinics and dispensing doctors. Quinine is available as quinine dihydrochloride injection containing three hundred milligrams per millilitre (schedule four). It is also found commercially as quinine hydrochloride, which is one of six active ingredients in Ilvico tablets, a cold and flu preparation (twenty milligrams per tablet). The inclusion of quinine is probably for it's antipyretic activity, although the preparation also contains salicylamide, which is an antipyretic. Quinine sulphate is available in three hundred milligram strength tablets and is schedule one for the use as a muscle relaxant in nocturnal cramps, and schedule four when used to treat malaria caused by *P.falciparum.*[10]

Chapter 3 Methods

3.1 Setting

The survey was conducted in a pharmacy in Hillbrow, Johannesburg, Gauteng, South Africa. The pharmacy has a patronage of about between 300-350 people per day and serves consumers/patients in the greater Hillbrow and Berea areas of Johannesburg, and to a lesser degree, residents of Yeoville and Joubert Park.

3.2 Timing

The survey was conducted over a period of five months between August 2001 and December 2001 at Tower Pharmacy in Pretoria street, Hillbrow.

3.3 Study population

The study population is a working class middle- to low-income group in an urban setting. Families reside mostly in blocks of flats. The area includes Hillbrow, Berea and to a lesser degree, Joubert Park and Yeoville. Population groups present are mainly black of different ethnic South African backgrounds, as well as immigrant blacks from African countries, including Zimbabwe, Mozambique, Malawi, Democratic Republic of Congo, Nigeria, Angola, Mali and Ethiopia.

3.4 Study sample

The study sample was limited to any female requesting to purchase quinine at Tower Pharmacy in Hillbrow. A total of 100 females were surveyed.

3.5 Questionnaire

A confidential self-administered questionnaire (Appendix 1) was offered to the participants, together with a Confidentiality and Anonymity Assurance (Appendix 2). Patients were offered the opportunity to use an interpreter if they were unable to understand the questionnaire, which was in English. The questionnaire consisted of sixteen questions of a categorical nature.

3.6 Ethical considerations

The research was conducted on a female population, the majority of them of childbearing age. Participants were given the Confidentiality and Anonymity Assurance form, which also included an information sheet. Verbal consent was obtained from the participants prior to them completing the questionnaire. Following the interview, the intended use of quinine was established. The participant was then counselled on the availability of free family planning services in the area, as well as the side effects of quinine in both long- and short-term use, and of the registered indications of quinine. Any additional questions from them were answered. The protocol was submitted to the Committee for Research on Human Subjects in April 2001 and permission was granted to conduct this study. The clearance certificate number is M01-05-41 (Appendix 3).

Chapter 4 Results

4.1 Statistical analysis

All questionnaires were individually coded. A total of 100 questionnaires were completed. The response rate was 100%. The coded data was sent to the Medical Research Council in Pretoria for analysis.

4.2 Frequency tables

4.2.1 Why are you using quinine?

Reason for quinine usage

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid:				
➢ To treat/prevent malaria	10	10	10	10
➢ To treat/prevent nocturnal cramps	3	3	3	13
➢ To prevent pregnancy	67	67	67	80
➢ To abort a pregnancy	1	1	1	81
➢ To clean the womb/induce a period	17	17	17	98
➢ To treat vaginal discharge	2	2	2	100
Total	100	100	100	

4.2.2 *For how long have you been using quinine?*

Duration of quinine usage

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid:				
➢ Less than a year	61	61	61	61
➢ Between 1 and 2 years	18	18	18	79
➢ 2 – 3 years	8	8	8	87
➢ Over 3 years	13	13	13	100
Total	100	100	100	

4.2.3 Where did you buy quinine?

Source of quinine procurement

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid:				
➢ Pharmacy	97	97	97	97
➢ Doctor	2	2	2	99
➢ Clinic/Hospital	1	1	1	100
Total	100	100	100	

4.2.4 Were you ever counseled in the use of quinine?

Professional counseling

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid:				
➢ Yes	35	35	35	35
➢ No	65	65	65	100
Total	100	100	100	

4.2.5 Did you ask any health care professional about indications of quinine?

Request for advice

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid:				
➢ Yes	41	41	41	41
➢ No	59	59	59	100
Total	100	100	100	

4.2.6 Who advised you to use quinine?

Source of advice

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid:				
➢ Family member	25	25	25	25
➢ Friend	47	47	47	72
➢ Pharmacist	7	7	7	79
➢ Nurse	9	9	9	88
➢ Doctor	12	12	12	100
Total	100	100	100	

4.2.7 Have you ever used quinine for contraceptive purposes?

Quinine as a contraceptive

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid:				
➢ Yes	62	62	62	62
➢ No	38	38	38	100
Total	100	100	100	

4.2.8 Is quinine an effective contraceptive?

Perceived efficacy

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid:				
➢ Yes	72	72	72	72
➢ No	28	28	28	100
Total	100	100	100	

4.2.9 What dosage do you use?

Dosages

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid:				
➢ 1 tablet/month at any time	34	34	34	34
➢ 1 tablet / week	7	7	7	41
➢ 2 tablets /week	1	1	1	42
➢ 2 tablets 3x daily for 7 days	5	5	5	47
➢ 1 tablet after sexual intercourse	4	4	4	51
➢ 2 tablets after sexual intercourse	6	6	6	57
➢ 1 or 2 tablets when necessary for nocturnal cramps	3	3	3	60
➢ 1 tablet /month on the day that period is due	15	15	15	75
➢ 4 tablets at once to induce abortion	1	1	1	76
➢ 2 tablets when necessary to prevent pregnancy	4	4	4	80
➢ 1 tablet/month on the same day of the month	3	3	3	83
➢ 2 tablets daily during a stay in a malaria area	1	1	1	84
➢ 3 tablets/month on 1st, 15th and 30th	1	1	1	85
➢ 1 tablet daily for 4 days	1	1	1	86
➢ 1 tablet/month between 14th and 16th day of menstrual cycle	5	5	5	91
➢ 2 tablets/month on 15th and 28th days of menstrual cycle	2	2	2	93
➢ 1 tablet daily for 5 days after period stops	1	1	1	94
➢ 2-3 tablets/month during last week of menstrual cycle	3	3	3	97
➢ 2-4 tablets on any day of menstrual cycle	2	2	2	99
➢ 1 tablet daily from 14th –20th day of menstrual cycle	1	1	1	100
Total	100	100	100	

4.2.10 What is your preferred method of contraception?

Personal preference

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid:				
➢ Quinine	57	57	57	57
➢ Condom	9	9	9	66
➢ Hormonal contraceptive pill	20	20	20	86
➢ Injection	11	11	11	97
➢ None	3	3	3	100
Total	100	100	100	

4.2.11 *What is your population group?*

Ethnic group / Nationality	Frequency	Percent	Valid Percent	Cumulative Percent
Zulu	38	38	38	38
Sotho	16	16	16	54
Tswana	4	4	4	58
Xhosa	13	13	13	71
Ndebele	2	2	2	73
Mswathi	1	1	1	74
DRC	4	4	4	78
Zimbabwe	16	16	16	94
Nigeria	2	2	2	96
Malawi	2	2	2	98
White/Coloured	2	2	2	100
Total	100	100	100	

4.3 Cross tabulations

4.3.1 Reason for quinine usage *vs.* gross monthly income

			Gross monthly income					
			Unemployed	Less than R1000	R1000 – R1999	R2000-R2999	Over R3000	Total
Reason for quinine usage	Treat/prevent malaria	Count	2	4	1	1	2	10
		Percent	20.0	40.0	10.0	10.0	20.0	100.0
	Prevent/treat nocturnal cramps	Count			1		2	3
		Percent			33.3		66.7	100.0
	Prevent pregnancy	Count	27	19	15	2	4	67
		Percent	40.3	28.3	22.4	3.0	6.0	100.0
	Abort a pregnancy	Count	1					1
		Percent	100.0					100.0
	Clean the womb/induce a period	Count	4	9	4			17
		Percent	23.5	52.9	23.6			100.0
	Treat vaginal discharge	Count	1				1	2
		Percent	50.0				50.0	100.0
Total count			35	32	21	3	9	100
Percent			35.0	32.0	21.0	3.0	9.0	100.0

4.3.2 Reason for quinine usage * coded age

			Coded age (years)						Total
			16-20	20-25	25-30	30-35	35-40	Over 40	
Reason for quinine usage	To treat /prevent malaria	Count		2	1	4	2	1	10
		Percent		10	10	40	20	10	100
	To treat /prevent nocturnal cramps	Count			1			2	3
		Percent			33.3			66.7	100.0
	To prevent pregnancy	Count	3	23	26	8	5	2	67
		Percent	4.5	34.3	38.8	11.9	7.5	3.0	100.0
	To abort a pregnancy	Count		1					1
		Percent		100.0					100.0
	To clean the womb/ induce a period	Count	1	7	2	2	3	2	17
		Percent	5.9	41.1	11.8	11.8	17.6	11.8	100.0
	To treat a vaginal discharge	Count			2				2
		Percent			100.0				100.0
Total		Count	4	33	32	14	10	7	100
		Percent	4.0	33.0	32.0	14.0	10.0	7.0	100.0

4.3.3 Reason for quinine use * ethnic group

			Ethnic group										
			Zulu	Sotho	Tswana	Xhosa	Ndebele	DRC	Zimbabwe	Nigeria	Malawi	Mswathi	N %
Reason for quinine	To treat/ prevent malaria	Count Percent	2 20	1 10				4 40	1 10	2 20			10 100.0
	To treat/ prevent nocturnal cramps	Count Percent	1 100										1 100.0
	To prevent pregnancy	Count Percent	27 40.3	11 16.4	3 4.5	10 14.9	2 3.0		13 19.4			1 1.5	67 100.0
	To abort a pregnancy	Count Percent	1 100										1 100.0
	To clean the womb/ induce a period	Count Percent	6 35.3	3 17.6	1 5.9	3 17.6			2 11.8		2 11.8		17 100.0
	To treat a vaginal discharge	Count Percent	1 50	1 50									2 100.0
	Count Percent	(n) (%)	38 38.8	16 16.3	4 4.1	13 13.3	2 2	4 4.1	16 16.3	2 2	2 2	1 1	98 99.9

Note: White and coloured subjects are not included in the above table as they do not represent an ethnic group but a race group.

4.3.4 Reason for quinine use * race

			Race				Total
			Black (South African)	Black (African country)	Coloured	White	
Reason for quinine	To treat /prevent malaria	Count Percent	3 30	7 70			10 100.0
	To treat /prevent nocturnal cramps	Count Percent	1 33.3		1 33.3	1 33.3	3 99.9
	To prevent pregnancy	Count Percent	54 80.6	13 19.4			67 100.0
	To abort a pregnancy	Count Percent	1 100				1 100.0
	To clean the womb/ induce a period	Count Percent	13 76.5	4 23.5			17 100.0
	To treat a vaginal discharge	Count Percent	2 100				2 100.0
Total		Count Percent	74 74.0	24 24.0	1 1.0	1 1.0	100 100.0

4.4 Data analysis

The statistical software that has been used in the data analysis is SPSS (Stastical Product and Service Solutions), and Microsoft Excel has been used in the graphing.

P-value (or Sig. Value).

p-value < 0.05 implies significant difference, otherwise no significant difference.

Table 4.4.1 Reason for quinine use

	Frequency	Percent	Valid percent	Cumulative percent
Not to prevent pregnancy	33	33.0	33.0	33.0
To prevent pregnancy	67	67.0	67.0	100.0
Total	100	100.0	100.0	

'Not to prevent pregnancy' includes:

- to treat/prevent malaria
- to treat/prevent nocturnal cramps
- to abort a pregnancy
- to 'clean the womb'/induce a period
- to treat a vaginal discharge

Table 4.4.2 Duration of use

	Frequency	Percent	Valid percent	Cumulative percent
Less than a year	61	61.0	61.0	61.0
A year or more	39	39.0	39.0	100.00
Total	100	100.0	100.0	

Table 4.4.3 Who advised you to use quinine?

	Frequency	Percent	Valid percent	Cumulative percent
Family member	25	25.0	25.0	25.0
Friend	47	47.0	47.0	72.0
Professional person *	28	28.0	28.0	100.0
Total	100	100.0	100.0	

* Professional person refers to doctor, nurse or pharmacist.

Table 4.4.4 Race

	Frequency	Percent	Valid percent	Cumulative percent
Not a black South African	26	26.0	26.0	26.0
Black(South African)	74	74.0	74.0	100.0
Total	100	100.0	100.0	100.0

All other racial groups are listed as 'Not a black South African'

Table 4.4.5 Ethnic groupings

	Frequency	Percent	Valid percent	Cumulative percent
Nguni	54*	54.0	54.0	54.0
Sotho and Tswana	20	20.0	20.0	74.0
Others	26	26.0	26.0	100.0
Total	100	100.0	100.0	

*Nguni includes Zulu, Xhosa, Ndebele and Mswathi

Table 4.4.6 Cross tabulations (duration of use *vs* reason for quinine use)

			How long have you been using quinine		Total
			Less than a year	A year or more	
Reason For quinine Use	Not to prevent pregnancy	Count	22	11	33
		Percent	66.7	33.3	100.0
	To prevent pregnancy	Count	39	28	67
		Percent	58.2	41.8	100.0
Total		Count	61	39	100
		Percent	61.0	39.0	100.0

Chi-square tests

	Value	Df	Asymp.Sig.(2 sided)
Pearson Chi-square	13.564*	2	0.001
Likelihood ratio	13.107	2	0.001
Linear-by-linear association	8.480	1	0.004
N of valid cases	100		

* No cells (0.0%) have an expected count less than 5. The minimum expected count is 8.25. There is a significant difference between the reasons for quinine use and the duration of use (p=0.001).

4.4.7 Cross-tabulation (race *vs* reason for quinine use)

			Race		Total
			Not a black (South African)	Black (South African)	
Reason for quinine use	Not to prevent pregnancy	Count	13	20	33
		Percent	39.4	60.6	100.0
	To prevent pregnancy	Count	13	54	67
		Percent	19.4	80.6	100.0
Total		Percent	26.0	74.0	100.0

Chi-Square test

	Value	Df	Asymp. sig. (2 sided)	Exact sig. (2 sided)	Exact sig. (1-sided)
Pearson Chi-square	.665**	1	.415		
Continuity correction*	.357	1	.550		
Likelihood ratio	.672	1	.412		
Fisher's exact test				.514	.277
Linear-by-linear association	.658	1	.417		
N of valid cases	100				

* Computed only for a 2x2 table

** No cells (0.0%) have expected count less than 5. The minimum expected count is 12.87.

Remark: There is no association between the reason behind the use of quinine (in particular for pregnancy prevention) and the race group using it ($p = 0.514$), and is more than 0.05. The race groups using quinine has no significant effect on the reasoning behind the use of quinine.

4.4.8 Cross-tabulation (who advised quinine use *vs* reason for quinine use)

			Who advised you			Total
			Family Member	Friend	Professional person	
Reason for quinine use	Not to prevent pregnancy	Count	6	10	17	33
		Percent	18.2	30.3	51.5	100.0
	To prevent pregnancy	Count	19	37	11	67
		Percent	28.4	55.2	16.4	100.0
Total		Count	25	47	28	100
		Percent	25.0	47.0	28.0	100.0

Chi-square test

	Value	Df	Asymp. sig. (2- sided)	Exact sig. (2-sided)	Exact sig. (1-sided)
Pearson Chi-square	4.593**	1	.032		
Continuity correction*	3.612	1	.057		
Likelihood ratio	4.430	1	.035		
Fisher's exact test				.051	.030
Linear-by-linear association	4.547	1	.033		
N of valid cases	100				

* Computed only for a 2x2 table

** No cells (0.0%) have expected count less than 5. The minimum expected count is 8.58.

Remark: The source of advice and the reasons for quinine use are not independent (p=0.032).

4.4.9 Cross-tabulation (ethnic group *vs* reason for quinine use)

			Coded ethnic			Total
			Nguni	Sotho & Tswana	Others	
Reason for quinine use	Not to prevent pregnancy	Count	14	6	11	31
		Percent	45.2	19.3	35.5	100.0
	To prevent pregnancy	Count	40	14	13	67
		Percent	59.7	20.9	19.4	100.0
Total		Count	54	20	24	98
		Percent	55.1	20.4	24.5	100.0

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-square	3.076*	2	0.215
Likelihood ratio	2.973	2	0.226
Linear-by-linear association	2.801	1	0.094
N of valid cases	98		

* No cells (0.0%) have expected count less than 5. The minimum expected count is 6.33.

Remark: Ethnic groups and the reason for using quinine are independent (p=0.215).

Chapter 5 Discussion

The subjects of the research were largely black South African and black immigrants from sub-Saharan countries. Language often presented a problem, in which case an interpreter was used. Some of the respondents, for example, stated that they used quinine to "*clean the womb*". Upon further questioning, some used the term to mean to clean a vaginal discharge, whereas others used the term to describe the inducing of menstruation.

The most common reason for quinine usage was to prevent pregnancy (sixty-seven percent of all respondents). Quinine has not been approved for this indication. Only thirteen percent intended to use quinine for the indicated purposes of treating malaria (ten percent), or treating/preventing nocturnal cramps (three percent). (Table 4.2.1)

The majority of quinine users (sixty-one percent) had used quinine for less than a year, while thirteen percent had been using quinine for longer than three years. (Table 4.2.2)

The majority of the subjects purchased quinine from a pharmacy. The majority of doctors in the Hillbrow/Berea area are dispensing doctors, yet only two percent of the subjects purchased quinine from a doctor. (Table 4.2.3). The doctors in this area provide a cheap, subsidised family planning service and dispense mainly hormonal oral contraceptives. Oral contraceptives sell at between R2,00 and R5,00 per month's supply at subsidised rates from contracted dispensing doctors. The retail price of one quinine tablet ranges from R3,00 to R4,50 in the different pharmacies in the area.

With regards to professional counselling, only thirty-five percent of the respondents were counselled by a healthcare professional (Table 4.2.4), whereas forty-one percent of quinine users had asked a healthcare professional about the indications and/or usage of quinine (Table 4.2.5). Pharmacists who were responsible for the sale of quinine to ninety seven percent of the respondents (Table 4.2.3) are in breach of their ethical responsibility where " A pharmacist must not give an impression to a potential purchaser that any product

associated with maintenance of health or a food supplement is efficacious when there is no evidence of efficacy"[11]

The majority of respondents did not ask the relevant healthcare professional for advice (fifty-nine percent)(Table 4.2.5). Pharmacists, however, as the main supplier of quinine, do not need to be solicited for advice, but advice should be offered and patients questioned about the intended usage of the product. As providers of schedule 1 and 2 medicines without the need for a prescription, pharmacists are ethically bound to provide advice on the safe and effective use of medicines supplied.[12]

Most of the respondents had been advised to use quinine by friends (forty-seven percent) or family members (twenty-five percent) (Table 4.2.6). In a study conducted in Nigeria, the majority of people using emergency contraceptives (53,6%) received their information from friends. Of these, ninety percent of the respondents had received incorrect information[13].

Twenty-eight percent of users were advised by healthcare professionals to use quinine (Table 4.2.6). Only thirteen percent of respondents used quinine for the manufacturer's indications as listed in the package insert (Table 4.2.1); therefore, assuming that the thirteen percent were advised to use quinine for the correct indications, then fifteen percent of the respondents were advised to use quinine for contraceptive-related purposes by a healthcare professional.

Sixty-two percent of respondents had previously used quinine for contraceptive reasons (Table 4.2.7). On further questioning, many of the respondents stated that they had suffered unpleasant side effects from oral contraceptives and hormonal implant contraceptives. In addition, the convenient dosage of one tablet per month to be taken as recommended to the users, from mainly friends and family, is easier to comply with. In some populations in the United States (e.g. unmarried black adolescents), the failure rate of oral contraceptives is eighteen percent. Other factors contribute to oral contraceptive

discontinuation. These include side effects, fears and misinformation about oral contraceptive side effects fuelled by negative media reports, and intermittent use.[14]

Seventy-two percent of respondents believed that quinine is an effective contraceptive (Table 4.2.8). The dosages varied considerably according to the indications for which it was used. Five percent had used quinine for the treatment/prevention of malaria at a dosage of two tablets three times daily for seven days. This is the correct dosage. Three percent had used quinine to treat nocturnal cramps at a dosage of one or two tablets when necessary. Thirty-four percent had used quinine as a contraceptive at a dosage of one tablet per month, but the interesting fact was that it was used at any time of the month. Fifteen percent had used quinine at a dose of one tablet per month on the day that their period was due. Ten percent of respondents had used quinine as a post-coital contraceptive, having taken one or two tablets after sexual intercourse. (Table 4.2.9).

Quinine was the most popular choice of contraceptive (fifty-seven percent) (Table 4.2.10), despite the fact that no evidence of its efficacy as a contraceptive exists. The misconception that it is effective as a once-monthly oral dose contraceptive is probably the reason for its popularity.

The majority of quinine users (thirty-five percent) were unemployed, while thirty-two percent of quinine users earned less than R1000.00 per month. Of these users, only six of the sixty-seven users had intended using quinine for indicated uses. Only nine percent of quinine users earned over R3000.00 per month and of these, two women had intended to use quinine to prevent or treat nocturnal cramps. It is possible that those earning over R3000.00 per month are of a more literate class, and also are on medical aid, so access to proper family planning services is not a problem (Table 4.3.1).

The most common age group of quinine users were 20-25 years old (thirty-three percent), whilst the next most common group was the 25-30 year old group (thirty-two percent). Sixty-nine percent of quinine users were below thirty years old. Of the study population,

34.3% of the users between 20-25 years old, and 38.8% of the users between 25-30 years old, used quinine to prevent pregnancy. (Table 4.3.2).

The population group with the highest usage of quinine are the black South African (75.5%), whilst Zimbabweans were the next most common users (16.3%). Zulu women were the most common of all users at 38.8% of the total population survey. Zulu women accounted for 40.3% of users intending to use quinine as a contraceptive, and 35.3% of users who had intended to use quinine to '*clean the womb*'. Of the total respondents, two percent of Nigerian and 4.1% of users from DRC had intended to use quinine for the treatment/prevention of malaria, an indication for which quinine has been approved. (Table 4.3.3).

Sixty-seven percent of users intended using quinine to prevent pregnancy, and seventeen percent to '*clean the womb*'. Black South African women were the largest group of quinine users (seventy-four percent of the total survey population). Only four South African women intended to use quinine for the indicated purposes of treating/preventing malaria or treating nocturnal cramps. Immigrants from other African countries accounted for twenty-four percent of total respondents, of whom seven users intended using quinine for the registered indications: (Table 4.3.4).

A Zimbabwean study on family planning knowledge showed that 0.8% of women used traditional/folk methods.[15] It is, however, not stated what these methods are, but it is possible that quinine sulphate may be used for contraceptive purposes. Of the sixteen Zimbabwean respondents, thirteen had used quinine for contraceptive purposes, which suggests that the problem is a southern African one and not necessarily a South African one.

The time taken using quinine and the reasons for using quinine are not independent ($p=0.001$) (table 4.4.6). The highly significant result indicates that there is an association between the duration of quinine use and whether it was used for contraception or not. The pattern of responses in the two periods (less than a year and more than a year) is

significantly different. The proportion of those who used it for contraception to the proportion who used it not for contraception differ significantly in the two time periods. Races of subjects and the reasons for using quinine are independent (p=0.514) (table 4.4.7). The result indicates that there is no association between race and whether it was used for contraception or not. The pattern of responses in the two racial groups (Black South African and not a Black South African) is significantly not different. The proportion of subjects who used it for contraception does not differ significantly in the two racial groups.

The source of advice and the reasons for using quinine are not independent (p=0.032) (table 4.4.8). The highly significant result indicates that there is an association between the source of advice and whether it was used for contraception or not. The pattern of responses in the three sources of advice (family member, friend or professional person) is significantly different. The proportion of those who used it for the prevention of pregnancy differs significantly in the three advice sources.

Ethnic groups and the reason for using quinine are independent (p=0.215) (table 4.4.9). The result indicates that there is no association between the ethnic groups and whether it was used for contraception or not. The pattern of responses in the three ethnic groups (Nguni, Sotho and Tswana, and other) is significantly not different. The proportion of those subjects who used quinine for contraception to the proportion who did not use it for contraception do not differ significantly in the three groups.

Chapter 6 Conclusions and recommendations

6.1 Conclusions:

The results obtained in the study refer to a population studied in the Hillbrow-Berea area of Johannesburg only.

- The most common reason for the purchase of quinine by black South African women was for the purpose of contraception.
- The majority of women who used quinine for contraception had used quinine for less than one year.
- Most users of quinine had purchased quinine from a pharmacy.
- The pharmacist did not counsel most of the users of quinine on the proper use of quinine.
- Less than half of the users had asked a healthcare professional about the proper use of quinine.
- Mostly friends were responsible for recommending quinine to be used as a contraceptive.
- The majority of black South African women believed that quinine is an effective contraceptive.
- The most common dosage of quinine for the purposes of contraception was one tablet (three hundred milligram strength) taken at any time of the month without reference to the menstrual cycle.
- Amongst all the purchasers of quinine by black South African women, the majority of women had used quinine as their preferred method of contraception.
- The majority of women who used quinine for contraception were unemployed.
- The majority of women who used quinine as a contraceptive were Zulu.
- Women between the ages of twenty and thirty years old were the most common users of quinine as a contraceptive.
- The person who gave advice made a significant difference to the reason for quinine use.
- There was no significant difference between the reason for quinine use and the duration of use.

6.2 Recommendations:

- Because of the wide dosing range used by the lay population, it is possible that overdosing may occur. The fatal oral dose of quinine for adults is about two to eight grams.[9] Pharmacists need to question and appropriately counsel patients requesting quinine on the proper indications of use. Patients also need to be educated on the dangers of inappropriate use and very possible failure of quinine to act as a contraceptive.
- The manufacturers of quinine should state on the packaging that quinine is not a proven contraceptive or abortifacient.
- The Medicines Control Council should remove the schedule 1 status, as this is clearly being used as a loophole to dispense quinine as an over-the-counter preparation for the treatment of nocturnal cramps, whereas only three percent of the users who purchase quinine as an over-the counter preparation use it for this purpose (Table 4.2.1)
- Pharmacists should provide an alternate safe, cheap and efficacious family planning service. It seems that one of the reasons for using quinine is that it is relatively cheap at approximately R4,00 per tablet, especially for the users who believe and use one tablet per month as a menstrual regulator.

During counselling, some users had cited side effects of the hormonal contraceptive pill and injections as reasons for wanting to change to quinine. Many respondents had taken advice from friends and relatives to use quinine as a contraceptive, but many who were purchasing quinine for the first time were unsure of the dose to be taken or the time of the menstrual cycle at which it should be taken.

Those patients who had used quinine as a post-coital contraceptive, were advised to use the Yupze regimen (E-GEN-C or Ovral) or the progestogen-only regimen (Norlevo), which appears to be better tolerated. Both of these regimens are available without prescriptions from pharmacies and are schedule 2 medicines. The recommended retail price of E-Gen-C is R64,36 and Norlevo retails at R68,90. Ovral, although recommended as a post coital contraceptive, is not registered for this indication with the Medicines Control Council. The Yupze regimen has long been recognised internationally as the preferred method for

emergency contraception.[16] Currently, post-coital methods of emergency use involve either administration of steroid hormones (oestrogens or oestrogen/progestin combinations), or less commonly, insertion of copper-releasing intra-uterine device (IUD). With the Yupze regimen, pregnancy can be prevented in up to 99.6% of cases and the risk of pregnancy is even lower with post-coital use of an IUD.[17]

After counselling about the dangers of using quinine as a contraceptive, some patients had returned to purchase quinine, but when asked about its intended use, they stated that they had intended to use it to treat nocturnal cramps. The pharmacist in such a situation is placed in a dilemma, as quinine is schedule 1 for this indication, and as such, he is not in contravention of any legislation if quinine is dispensed to a patient requesting it for this indication.

In the United States of America (USA), quinine sulphate, which is widely prescribed for nocturnal leg cramps, used to be available over the counter. However, because 157 adverse drug reactions were reported from 1969-1992, the Food and Drug Administration (FDA) concluded that quinine was not safe for treatment of this disorder. In 1994 the FDA prohibited the marketing of quinine for nocturnal leg cramps and discontinued its availability in nonprescription form.[18]

Because of a lack of data on the use of quinine as a contraceptive or abortifacient, it is entirely possible for users to unintentionally overdose. The most common signs of overdose are cinchonism (tinnitus, deafness, nausea and vomitting). Cardiac arrhythmias and myocardial depression are signs of severe poisoning. Visual disturbances may occur, including total blindness.[19]

One of the most satisfying outcomes of the research project was the appreciation of a number of people for the advice given to them on both the misuse of quinine and the availability of proper contraception at family planning clinics and affiliated general practitioners. However, in general, users who had been using quinine as a contraceptive for

over a year dismissed the counselling as time wasted, as they had not fallen pregnant during their time of using quinine, and therefore regarded it as an effective contraceptive.

References:

1. Katzung B.G and Goldsmith R.S. Antiprotozoal drugs. In: B.G.Katzung, editor. 1987. *Basic and Clinical Pharmacology.* (3rd Edition). Connecticut: Appleton and Lange; 618-624.

2. Gibbons C.J and Swanepoel C.R. 1991. *South African Medicines Formulary.* (3rd Edition); 390-391.

3. McReady R, Cho T, Hkirijaroen L, Simpson J, Chongsuphajaisiddhi T, White N.J and Nosten F. 1998. Quinine and mefloquine in the treatment of multidrug-resistant *Plasmodium falciparum* malaria in pregnancy. *Annals of Tropical Medicine and Parasitology*, **92**(6); 643-653.

4. Drugs used in parasitic diseases. 1995. *WHO Model Prescribing Information.* (2nd Edition). World Health Organization. Geneva. 38-40.

5. McFadyen M.L, Smit J.A, Kubeka M. and Majola M.P. 2001. Quinine is not a proven contraceptive although often used as such: End user survey in Durban Pharmacies. *South African Pharmaceutical Journal.* **68**(1); 15-21.

6. Otoide V.O, Oronsaye F, Okonofua F.E. 2001. Sexual behaviour and contraceptive use among secondary school adolescents in Benin City, Nigeria. *Journal of Obstetrics and Gynaecology.* **21**(3): 298-302.

7. Smith J.P. 1998. Risky choices: The dangers of teens using self-induced abortion attempts. *Journal of Paediatric Health Care.* **12**: 147-151.

8. Grossland J. 1980. The chemotherapy of protozoal disease: malaria. *Lewis's Pharmacology.* (5th Edition). Churchill Livingstone; 865-866

9. Tracy J.W and Webster L.T. (Jr). Drugs used in the chemotherapy of protozoal infections. Malaria. In: Hardman J.G, Limbird L.E and Gillman A.G, editors. 2001. *The Pharmacological Basis of Therapeutics.* (10th Edition). International edition. McGraw-Hill; 1086-1089.

10. Snyman J. 2000. Mims desk reference. **35**: 52, 839, 895.

11. Putter S. and Hattingh D. 1997. Code of Ethics. *Good Pharmacy Practice in South Africa* (1st edition); **25**.

12. Rules relating to acts or omissions in respect of which the board may take disciplinary steps. *Compendium of Laws and Regulations relating to Pharmacy.* **22**; 249(47); 1996

13. Bako A.U. 1998. Knowledge and use of emergency contraception amongst Nigerian undergraduates. *Journal of Obstetrics and Gynaecology.* **18**(2): 151-153.

14. Adams Hillard P.J. 1992. Oral contraceptive noncompliance: The extent of the problem. *Advances in Contraception.(* 8) suppl; 13-20.

15. Schwartz U, Tshimanga M. and Shodu L.K. 1999. Knowledge and practices of family planning in Zimbabwe. *Central African Journal of Medicine.* **45**(8): 204-209.

16. Coningham T. and van Schoor J. 2002. Contraception – An Update. *South African Pharmaceutical Journal.* **69**(4): 24-27.

17. Adekunle A.O, Arowojolu A.O, Adedimeji A.A. and Okunlola M.A. 2000. Emergency contraception: survey of knowledge, attitudes and practice of health care professionals in Ibadan, Nigeria. *Journal of Obstetrics and Gynaecology.* **20**(3): 284-289.

18.Mori J, Krantz M.D, Dart R.C. and Mehler P.S. 2002. Transient pulmonary infiltrates possibly induced by quinine sulphate. *Pharmacotherapy.* **22**(6): 775-777.

19. Boland M.E, Brennand Roper S.M. and Henry J.A. 1985. Complications of quinine poisoning. *The Lancet.* **8425**(1): 384-385.

Appendix 1
Questionnaire on quinine use in Hillbrow-Berea area

1. Is the quinine for your personal use?

Yes	
No	

2. Why are you using quinine?

To prevent or treat malaria	
To diagnose myasthenia gravis (muscle weakness)	
To prevent or treat nocturnal (night-time) cramps	
To prevent pregnancy	
To abort a pregnancy	
Other reasons (please state)	

3. For how long have you been using quinine for the reason as stated in question 2?

Less than 1 year	
Between 1 and 2 years	
2-3 years	
More than 3 years	

4. Previously, where did you buy quinine?

A Pharmacy	
A Medical Practitioner (Doctor)	
A Clinic or hospital	
Other (please state)	

5. Were you ever counselled on the use and/or indications of quinine sulphate?

Yes	
No	

6. Did you ask any healthcare professional (doctor, nurse, pharmacist) about the indications or dosage of quinine?

Yes	
No	

7. Who advised you to use quinine?

A Family member	
A Friend	
A Pharmacist	
A Nurse	
A Doctor	
A Traditional Healer	
Other (please state)	

8. Have you ever used quinine sulphate for contraceptive purposes?

Yes	
No	

9. Do you think quinine is an effective contraceptive?

Yes	
No	

10. What dosage of quinine do you use?

1 Tablet per month	
1 Tablet per week	
2 Tablets per week	
2 Tablets 3 times daily for 7 days	
1 Tablet after sexual intercourse	
2 Tablets after sexual intercourse	
1 or 2 Tablets when necessary for nocturnal (night-time) cramps	
Other dosage (please state the dosage you use):	

11. Are you currently taking any other contraceptive?

Yes	
No	

12. If yes, which of the following contraceptives are you using?

Condom	
Hormonal contraceptive pill	
Contraceptive injection	
Spermicidal jelly	
Other (please specify)	

13. What is your preferred method of contraception?

Quinine	
Condom	
Hormonal contraceptive pill	
Contraceptive injection	
Spermicidal jelly	
Other (please specify)	

14. Your current gross monthly income is:

Less than R1000	
R1000 – R1999	
R2000 – R2999	
Over R3000	

15. Your population group is: (kindly note this question is for statistical purposes only)

Black (South Africa)	
Black (Immigrant from African country)	
Coloured	
Indian	
White	
Other (please specify)	

16. What is your age group?

16-20 years	
20-25 years	
25-30 years	
30-35 years	
35-40 years	
Over 40 years	

Thank you for taking the time to complete this questionnaire.

The information provided is to be used for research purposes and your identity is strictly confidential and will not be revealed.

Please ensure that the pharmacist has counselled you on the proper use of quinine before you leave.

Appendix 2

Confidentiality and anonymity

Hello, my name is Nishaan Jugram. I am a qualified pharmacist currently studying at the University Of the Witwatersrand. I would like to invite you to participate in research that I am doing, by completing the attached questionnaire.

The purpose of the questionnaire is to study the reasons that people use quinine. After filling in the questionnaire, I shall talk to you about quinine, and you may feel free to ask me any questions about the use or abuse of quinine, including any questions that you may have about it's side effects and long term effects.

You are requested to answer the questions by marking the box that you feel best describes your answer. Please feel free to ask me any questions that you may have about the questionnaire, including any questions that you do not understand. I may be contacted at the telephone number below to answer any questions that you may have forgotten to ask when completing the questionnaire.

Your name is not required on the questionnaire and your answers as well as your identity shall remain confidential.

You are under absolutely no obligation to participate in the survey, and participation is totally voluntary.

Regards

Nishaan Jugram

Tel (011)642-1360 (work)

082-783-4232 (cell)

Appendix 3

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

COMMITTEE FOR RESEARCH ON HUMAN SUBJECTS (MEDICAL)
Ref: R14/49 Jugram

CLEARANCE CERTIFICATE **PROTOCOL NUMBER** M01-05-41

PROJECT Investigation of The Incidence of Use of Quinine Sulphate As A Contraceptive In The Hillbrow-Berea Area

INVESTIGATORS Mr N Jugram

DEPARTMENT School of Clinical Medicine, Private Pharmacy

DATE CONSIDERED 01-05-25

DECISION OF THE COMMITTEE *

Approved unconditionally

DATE 01-07-06 **CHAIRMAN**.....(Professor P E Cleaton-Jones)

* Guidelines for written "informed consent" attached where applicable.

c c Supervisor: Dr G Lowndes
Dept of School of Clinical Medicine, Wits Medical School

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DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10001, 10th Floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee.

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES