HISTOMORPHOLOGICAL STUDIES OF THE EFFECTS OF AMODIAQUINE ON THE OVARY IN SPRAGUE-DAWLEY RATS

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HISTOMORPHOLOGICAL STUDIES OF THE EFFECTS OF AMODIAQUINE ON THE OVARY IN SPRAGUE-DAWLEY RATS

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SEPTEMBER, 2010
DECLARATION

We hereby declare that the thesis titled “HISTOMORPHOLOGICAL STUDIES OF THE EFFECTS OF AMODIAQUINE ON THE OVARY IN SPRAGUE-DAWLEY RATS” is a record of original research work carried out by GBOTOLORUN, Stella Chinwe in the Department of Anatomy, College of Medicine of the University Of Lagos, Nigeria.

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This work is dedicated to my darling husband Olalekan, and my lovely children, Ayooluwa and Anuoluwapo who have made my life more meaningful and purposeful. God bless you all.
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What will it profit a man if he gains the whole world and loses his soul? That is the biggest question everyone must ask himself/herself one day and I want to thank God Almighty that he has helped me answer this question truthfully and also to make the right choice. I want to also thank God for life and inspiration because “in Him I live and move and have my being”.

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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>CONTENTS</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cover page</td>
<td>i</td>
</tr>
<tr>
<td>Title page</td>
<td>ii</td>
</tr>
<tr>
<td>Certification</td>
<td>iii</td>
</tr>
<tr>
<td>Declaration</td>
<td>iv</td>
</tr>
<tr>
<td>Dedication</td>
<td>v</td>
</tr>
<tr>
<td>Acknowledgement</td>
<td>vi</td>
</tr>
<tr>
<td>Table of Contents</td>
<td>vii</td>
</tr>
<tr>
<td>List of Tables</td>
<td>xii</td>
</tr>
<tr>
<td>List of Plates</td>
<td>xiv</td>
</tr>
<tr>
<td>Abstract</td>
<td>xvii</td>
</tr>
</tbody>
</table>

## CHAPTER ONE: INTRODUCTION

1.1 Background 1

1.1.1 Incidence of Malaria 1

1.1.2 History of Antimalarial Compounds 2

1.1.3 Amodiaquine (AQ) 3

1.1.4 Chemical Structure of Amodiaquine 4

1.1.5 Uses of Amodiaquine 5

1.2 Statement of the Problem 5

1.3 Overall Objective of the Study 7

1.4 Specific objectives of the Study 7

1.5 Significance of the Study 7

1.6 Operational Definitions of Terms 8
CHAPTER TWO: LITERATURE REVIEW

2.1 Metabolism of amodiaquine

2.2 Toxicity data on amodiaquine

2.3 Amodiaquine and pregnancy

2.4.0 The ovary

2.4.1 Gross anatomy of the Ovary

2.4.2 Arterial supply of the Ovaries

2.4.3 Venous and lymphatic drainage of the Ovaries

2.4.4 Innervation of the Ovaries

2.5.0 Histology of the Ovary

2.5.1 Ovarian follicles

2.5.2 Primodial follicles

2.5.3 Growing follicles

2.5.4 Mature follicles

2.5.5 Follicular atresia

2.5.6 Corpus luteum

2.6 The oestrous cycle

2.7 Pattern of FSH secretion throughout the oestrous cycle

2.8 Pattern of LH secretion throughout the oestrous cycle

2.9 Pattern of PRL secretion throughout the oestrous cycle

2.10 Folliculogenesis

2.10.1 Early folliculogenesis in humans

2.10.2 Early folliculogenesis in rodents

2.11 Follicle-stimulating hormone receptors and oocytes

2.12 Dominant selection of oocyte
2.13 Oocyte recruitment 39
2.14 Role of oocyte in primary follicular growth 41
2.15 Preantral follicle growth and differentiation 44
2.16 Gonadotropin regulation of preantral follicles 47
2.17 FSH rescue of antral follicles 49
2.18 Cyclic changes of the ovarian surface epithelium (OSE) in the rat 51
2.19 Oocyte programmed cell death 55
2.20 Gonadotropin surge-attenuating factor 58
2.21 Oxidative Stress (OS) 59
2.21.1 Oxidative stress in female reproduction 62
2.22 Anti-oxidants 65
2.23 Vitamin C 67
2.23.1 Is Vitamin C an anti-oxidant or a pro-oxidant 69
2.23.2 Human intervention studies 70
2.24 Vitamin E 76
2.25 Antimalarial drugs and the reproductive system 80

CHAPTER THREE: MATERIALS AND METHODS 87

3.1 Experimental animals 87
3.2 Experimental protocols 87
3.3 Pilot study 87
3.3.1 A study of the effect of amodiaquine on the histology of the ovary 87
3.3.2 A study of the effect of amodiaquine on ovulation 87
3.4 Main study 88
3.4.1 Experiment 1: Determination of the effects of chronic administration of amodiaquine for 28 days on the oestrous cycle and on the morphology of the ovary

3.4.2 Experiment 2: Determination of the effect of amodiaquine on ovulation

3.4.3 Experiment 3: Determination of the effect of AQ on enzymatic antioxidant status in the Ovary and co-administration with Vitamin C and Vitamin E

3.4.4 Experiment 4: Determination of the effect of AQ on reproductive hormone

3.5 Amodiaquine administration

3.6 Vitamin C administration

3.7 Vitamin E administration

3.8 Determination of oestrous cycle

3.9 Determination of ovulation

3.10 Tissue processing for light microscopy

3.11 Determination of superoxide dismutase

3.12 Determination of catase

3.13 Determination of reproductive hormones

3.13.1 Determination of FSH

3.13.2 Determination of LH

3.13.3 Determination of PRL

3.14 Statistical analysis

CHAPTER FOUR: RESULTS

4.1 Effect of Amodiaquine on Body Weight of Sprague-Dawley Rats

4.2 Effect of Amodiaquine on Oestrous Cycle

4.3 Effect of Amodiaquine on Ovulation
4.4 Effect of Amodiaquine on Serum Concentration of Prolactin

4.5 Effect of Amodiaquine on Serum Concentration of Follicle-Stimulating Hormone

4.6 Effect of Amodiaquine on Serum Concentration of Luteinizing Hormone

4.7 Effect of Amodiaquine on Superoxide Dismutase Activity in the Ovary of Sprague-Dawley Rats

4.8 Effect of Amodiaquine on Catalase Activity in the Ovary of Sprague-Dawley Rats

4.9 Effect of Amodiaquine on the Histomorphology of the Ovary in Sprague-Dawley Rats

CHAPTER FIVE: DISCUSSION

5.1 Bodyweight

5.2 Oestrous Cyclicity Studies

5.3 Ovulation and Hormonal Studies

5.4 Anti-Oxidant Studies

5.5 Histological Studies

CHAPTER SIX: SUMMARY OF FINDINGS AND CONCLUSION

6.1 Summary of Findings

6.2 Contributions to Knowledge

6.3 Conclusions

Reference
LIST OF TABLES

Table 1: The effect of oral administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on bodyweight of Sprague-Dawley rats 100

Table 2: The effect of intraperitoneal administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on bodyweight of Sprague-Dawley rats. 101

Table 3: The effect of the administration of AQ alone for 28 days, AQ + Vit C and AQ + Vit E on the length of the oestrous cycle in Sprague-Dawley rats. 102

Table 4: The effect of the oral administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on the mean number of days spent in the phases of the oestrous cycle in Sprague-Dawley rats. 103

Table 5: The effect of the intraperitoneal administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on the mean number of days spent in the phases of the oestrous cycle in Sprague-Dawley rats. 104

Table 6: The effect of the oral administration of AQ alone, AQ + Vitamin C and AQ + Vitamin E on the number of ova shed (Mean ± SD) in the oviduct in the morning of estrus in Sprague-Dawley rats 107

Table 7: The effect of the intraperitoneal administration of AQ alone, AQ + Vitamin C and AQ + Vitamin E on the number of ova shed (Mean ± SD) in the oviduct in the morning of estrus in Sprague-Dawley rats 108

Table 8: The effect of the oral and intraperitoneal administration of AQ alone, AQ + Vitamin C and AQ + Vitamin E on the concentration of Prolactin (PRL) at 6 p.m. on proestrus in Sprague-Dawley rats. 109
Table 9: The effect of the oral and intraperitoneal administration of AQ alone, AQ + Vitamin C and AQ + Vitamin E on the concentration of Follicle-stimulating hormone (FSH) at 6 p.m. on proestrus in Sprague-Dawley rats.

Table 10: The effect of the oral and intraperitoneal administration of AQ alone, AQ + Vitamin C and AQ + Vitamin E on the concentration of Luteinizing hormone (LH) at 6 p.m. on proestrus in Sprague-Dawley rats.

Table 11: The effect of the administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on enzymatic anti-oxidant activities of superoxide dismutase (SOD) in the ovary of Sprague-Dawley rats.

Table 12: The effect of the administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on enzymatic anti-oxidant activities of catalase (CAT) in the ovary of Sprague-Dawley rats.
LIST OF PLATES

Plate 1: Micrograph of cross-section of ovary of rat in control group x100 119

Plate 2: Micrograph of cross-section of ovary of rat in control group x400 120

Plate 3: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route for 28 days. x100 121

Plate 4: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route for 28 days. x400 122

Plate 5: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route and co-administration with 0.1 mg/kg bw Vitamin C for 28 days. x100 123

Plate 6: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route and co-administration with 0.1 mg/kg bw Vitamin C for 28 days. x400 124

Plate 7: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route and co-administration with 20 mg/kg bw Vitamin E for 28 days. x100 125

Plate 8: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route and co-administration with 20 mg/kg bw Vitamin E for 28 days. x400 126

Plate 9: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days. x100 127

Plate 10: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days. x400 128
Plate 11: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days and co-administration with 0.1 mg/kg bw Vitamin C. x100 129

Plate 12: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days and co-administration with 0.1 mg/kg bw Vitamin C. x400 130

Plate 13: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days and co-administration with 20 mg/kg bw Vitamin E. x100 131

Plate 14: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days and co-administration with 20 mg/kg bw Vitamin E. x400 132

Plate 15: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route for 28 days. x100 133

Plate 16: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw AQ oral route for 28 days. x400 134

Plate 17: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ oral route for 28 days and co-administration with 0.1 mg/kg bw of Vitamin C. x100 135

Plate 18: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ oral route for 28 days and co-administration with 0.1 mg/kg bw of Vitamin C. x400 136

Plate 19: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ oral route for 28 days and co-administration with 20 mg/kg bw of Vitamin E. x100 137
Plate 20: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ oral route for 28 days and co-administration with 20 mg/kg bw of Vitamin E. x400

Plate 21: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days. x100

Plate 22: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days. x400

Plate 23: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days and co-administration with 0.1 mg/kg bw of Vitamin C. x100

Plate 24: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days and co-administration with 0.1 mg/kg bw of Vitamin C. x400

Plate 25: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days and co-administration with 20 mg/kg bw of Vitamin E. x100

Plate 26: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days and co-administration with 20 mg/kg bw of Vitamin E. x400
ABSTRACT

The prevalence of female infertility ranges from 7 to 28% depending on the age of the woman. Although the origin and frequency of infertility vary about 40 to 50% of the aetiology of infertility cases is as a result of female factors. Malaria and the treatment of malaria have been a major challenge for decades. A number of antimalarial drugs have been reported to have anti-fertility actions.

Amodiaquine (AQ) is an anti-malarial drug and belongs to a class of drugs known as the 4-aminoquinolines. It was removed from the essential drug list in 1990 as a result of hepatotoxicity and agranulocytosis that occurred with long-term use. AQ is now making a comeback and is in the spotlight as a partner drug with artemisinins in the World Health Organization (WHO) recommended artemisinin based combination therapies (ACTs). In malaria-endemic regions of the world, self medication with antimalarial drugs is common and it is possible for a person to be treated several times in a year. With the frequency of treatment the risk of adverse events associated with long-term use of AQ may arise.

A number of investigators have carried out studies on the effect of AQ on pregnancy and pregnancy outcomes, however, there remains a dearth of literature on the short-term or long-term effect of AQ on the structure and function of the ovary in the non-pregnant female.

This study was carried out to investigate the histomorphological changes and responses of the ovary of Sprague-Dawley rats to AQ administration. The study was divided into 4 experimental groups. AQ was given at a dose of 6.0 and 12 mg/kg bw via oral and intraperitoneal routes for 28 days. Vitamin C was administered at a dose of 0.1 mg/kg bw 3 days in a week while Vitamin E was given at a dose of 20 mg/kg bw 5 days in a week. In each of the experiments AQ was administered alone, co-administered with
Vitamin C and co-administered with Vitamin E (AQ alone, AQ + Vitamin C and AQ + Vitamin E) according to the treatment protocol. At the end of the experiment all the animals were sacrificed by cervical dislocation.

Oestrus cycle was determined using the vaginal smear method and ovulation was determined at 10:00hr on the day of estrus. The ovary was dissected and processed for histology, assayed for superoxide dismutase and catalase activities and also assayed for reproductive hormones (follicle stimulating hormone (FSH), luteinizing hormone (LH) and prolactin (PRL).

The result of the oestrous cycle showed that AQ prolonged the length of the oestrous cycle and was statistically significant in the group that received 12 mg/kg bw via intraperitoneal route. Co-administration of AQ + Vitamin C increased the cycle length even further and was statistically significant (**p** < 0.05) except in the group that received 6 mg/kg bw intraperitoneal route. The ovulation studies showed that AQ reduced the number of ova that was shed in the morning of estrus and was statistically significant (**p** < 0.05) in the group that received 6.0 and 12 mg/kg bw oral route.

Histology of the ovary showed that AQ increased the number of atretic follicles when compared with the control. There appeared to be more atretic follicles at 12 mg/kg bw than at 6.0 mg/kg bw AQ. AQ caused reduction in the activities of superoxide dismutase and catalase in the ovary and was statistically significant (**p** < 0.05) in the groups that received AQ + Vitamin C.

The expected surge in FSH, LH and PRL between 5 to 7 p.m. on proestrus that is expected for the follicular rupture that occurs at ovulation was experienced in this study. There was no statistically significant difference in the serum concentration of these hormones when compared with the control group. The results obtained in this study shows that AQ is deleterious to the ovary.