

University of the Western Cape
Faculty of Community and Health Sciences

Title of thesis: A systematic review on maternal and neonatal outcomes of ingested herbal and homeopathic remedies used during pregnancy, birth and breastfeeding.

Student Name: Haaritha Boltman

Student Number:

Type of thesis: Mini – thesis Thesis

Degree: Mini thesis as partial fulfillment for M. Cur
Advanced Midwifery and Neonatology

Department / School: School of Nursing



Supervisor: Prof. Dr. C. Nikodem

Co-supervisor: Prof. Dr. Gary Linn (Tennessee State University
(TSU))

Date: 06 May 2005

10 Key words: systematic review, maternal, neonatal, ingested, herbal remedies, homeopathic remedies, pregnancy, birth, breastfeeding, perinatal

Declaration:

I declare that, " A systematic review on maternal and neonatal outcomes of ingested herbal and homeopathic remedies used during pregnancy, birth and breastfeeding" is my own work, and that it has not been submitted before for any examination in any other university, and that all sources I have used or quoted have been indicated by complete reference.

April 2005

Haaritha Boltman

Signed:.....



Acknowledgements:

All thanks and praises to due to the Almighty. This work would not have reached completion if not for His Mercy and Blessings.

This work is dedicated to the memory of my late father.

My mother, who supported me with her emotions and very soul, thanks for being by my side in the journey of life...no words, just songs in your praise.

My eldest brother, who provides for me in every way, I respect and thank you.

My baby brother, I love you for your unconditional and instinctive understanding...and comic relief when times were tough.

My supervisor, Cheryl Nikodem...went beyond far supervisorship and put just as much sweat and tears into this as I did. I thank you.



Finally, to all my friends and other loved ones, thank you for just being there.

Abstract

Title of thesis

A systematic review on maternal and neonatal outcomes of ingested herbal and homeopathic remedies used during pregnancy, birth and breastfeeding.

Background

Herbal and homeopathic compounds have been used to aid in childbearing and pregnancy for centuries (Lee, 1999:253). Unfortunately much of this information is anecdotal and lacks scientific support, making it difficult to evaluate safety and efficacy (Olson, 2001:63). Increased public interest in alternative treatments leads to the need for a systematic review on the topic. Olson (2001:63) states, "As the public's interest in complementary and alternative medicine (CAM) continues to grow, so does the amount of money being spent on herbal and nutritional supplements". Herbal remedies are most often used to treat the most common pregnancy-related problems like nausea, stretch marks and varicose veins. In contrast to this, concerns have also been raised about the adverse effects of these remedies (Ernst, 2002:229; Mabina, Pitsoe & Moodley, 1997:1008).

Objective

The primary objective of this research project was to conduct a systematic review to assess the maternal and neonatal outcomes of ingested herbal and homeopathic remedies using during pregnancy, birth and breastfeeding.

Search strategy

Relevant literature was extracted from available electronic search engines

Selection criteria

Types of studies

All randomized controlled, quasi-randomised or clinical controlled trials that met the inclusion or exclusion criteria, reporting on the benefits or adverse effects of ingested alternative herbal or homeopathic compounds utilized during pregnancy was evaluated for inclusion.

Types of participants

Women who have been pregnant and have used an ingested herbal / homeopathic compound during pregnancy, labour and breastfeeding, compared to pregnant women who have not used any compounds as a control group.

Types of intervention

Ingestion of herbal / homeopathic compounds during pregnancy, labour and breastfeeding.

Types of outcome measures

The objective outcome measures relevant to use of herbal and homeopathic compounds, concentrating on adverse effects, efficacy, and contra-indications.

Data analysis

The methodological quality and appropriateness for inclusion of trials under consideration was evaluated. Review Manager 4.2 (Revman) software was utilized to extract, tabulate, and analyse the data.

Results

Randomised controlled, quasi-randomised or clinical controlled trials were included in this review. Sample sizes for the studies in this review were small, and only nine studies met the inclusion criteria. The overall result displays no effect, which does not favour or contra-indicate the use of herbal remedies in pregnancy. It is recommended that caution should still be exercised before these remedies are used, due to the small studies reviewed.

Key words

systematic review, maternal, neonatal, ingested, herbal, homeopathic remedies, pregnancy, birth, breastfeeding

Content page	Page
Title of thesis	i
Declaration	ii
Acknowledgements	iii
Abstract	iv
Content page	v

Chapter One

1.1	Introduction	1
1.2	Rationale	1
1.3	Research problem	2
1.4	Research Objectives	2
1.5	Research Question	2
1.6	Research Statement	2
1.7	Relevance of the study	3
1.8	Ethical statement	3
1.9	Chapter outline	3
1.10	Timeline	3
1.11	Budget	4
1.12	Definitions	4
1.13	Classification of herbs used during pregnancy, labour and the post partun period	6
1.14.1	Abortifacients	6
1.14.2	Emmenagogue	8
1.14.3	Gastrointestinal	10
1.14.4	Hepatotoxic	10
1.14.5	Hormonal	10
1.14.6	Galactagogue	11
1.14.7	Low birth weight and premature birth	11
1.14.8	Mutagenic birth defects	11
1.14.9	Uterine stimulation / oxytocic / induction of labour	11
1.15	Summary	12

Chapter Two

2.1	Introduction	13
2.2	History of herbs and homeopathy during childbearing	14
2.3	Methods and effectiveness of herbal preparations	16
2.4	Herbs and homeopathy during pregnancy	17
2.5	Herbs and homeopathy during birth	18
2.6	Herbs and homeopathy during breastfeeding and the postpartum period	20
2.7	Benefits of herbs and homeopathy during pregnancy	22
2.8	Adverse effects of herbs and homeopathy during pregnancy	23
2.9	Summary	24

Chapter Three

3.1	Introduction	25
3.2	The Review Manager (RevMan) 4.2	25
3.3	Systematic reviews	26
3.4	Rationale for systematic reviews	27
3.5	Types of systematic reviews	27
3.6	Difference between traditional and scientific reviews	28
3.7	Meta-analyses	28
3.8	Main objectives for systematic reviews	29
3.9	Benefits of systematic reviews	29
3.10	Limitations of systematic reviews	30
3.11	Criteria for selection of studies in this review	31
3.12	Limitations	33
3.13	Search strategy for identification of studies	33
3.14	Methodological quality, validity and reliability	33
3.15	Data collection	34
3.16	Data analyses	35
3.17	Summary	36

Chapter Four

4.1	Introduction	38
-----	--------------	----

4.2	Types of studies	39
4.3	Types of participants	39
4.4	Types of intervention	39
4.5	Types of outcome measures	40
4.6	Characteristics of included studies	40
4.7	Characteristics of excluded studies	48
4.8	Outcomes	55
4.9	Effects of treatment for nausea in pregnancy	56
4.9.1	Severe nausea	56
4.9.2	Vomiting episodes on day four of treatment	56
4.10	Effect of treatment for duration of gestation, induction or length of labour	57
4.10.1	Maternal nausea	57
4.10.2	Duration of gestation	58
4.10.3	Onset of labour not achieved within 24 hours	59
4.10.4	Duration of labour	60
4.10.5	Vaginal delivery not achieved within 24 hours	61
4.10.6	Caesarean section	62
4.10.7	Meconium stained liquor	63
4.10.8	Postpartum haemorrhage	64
4.10.9	Serious neonatal morbidity (Apgar 1<7, fetal distress, birth asphyxia, NICU, congenital abnormalities)	65
4.11	Effects of treatment for perineal pain, post delivery	66
4.11.1	Perineal pain	66
4.11.2	Breast pain	67
4.12	Summary results	67

Chapter Five

5.1	Introduction	69
5.2	Discussion	70
5.3	Implications for practice	72
5.4	Implications for research	73
5.5	Conclusion	74

Bibliography	75
--------------	----

Figures

Figure 4.9.1	Severe nausea	56
Figure 4.9.2	Vomiting episodes on day four of treatment	56
Figure 4.10.1	Maternal nausea	57
Figure 4.10.2	Duration of gestation	58
Figure 4.10.3	Onset of labour not achieved within 24 hours	59
Figure 4.10.4	Duration of labour	60
Figure 4.10.5	Vaginal delivery not achieved within 24 hours	61
Figure 4.10.6	Caesarean section	62
Figure 4.10.7	Meconium stained liquor	63
Figure 4.10.8	Postpartum haemorrhage	64
Figure 4.10.9	Serious neonatal morbidity (Apgar 1<7, fetal distress, birth asphyxia, NICU, congenital abnormalities)	65
Figure 4.11.1	Perineal pain	66
Figure 4.11.2	Breast pain	67

Tables

Table 2.1	Uses of herbs and homeopathy during pregnancy, birth and breastfeeding	22
Table 2.2	Adverse effects reported in women	23
Table 2.3	Adverse effects reported in the fetus and newborn	23

Chapter One: Introduction

1.1 Introduction

Herbal and homeopathic compounds have been used to aid in childbearing and pregnancy for centuries (Lee, 1999: 253). However, very few compounds have been scientifically tested for its active ingredient, its mechanism of action and adverse effects during pregnancy, birth and breastfeeding. Practicing midwives have used a variety of herbs and nutritional supplements during the labouring process. Unfortunately much of this information is anecdotal and has very little scientific support, making it difficult to evaluate safety and efficacy (Olson, 2001:64).

1.2 Rationale

Herbal remedies are most often used to treat the most common pregnancy-related problems like nausea, stretch marks and varicose veins. Chamomile, meadowsweet, spearmint, slippery elm, peppermint and Iceland moss were documented as being used to alleviate nausea (Olsen, 2001:65). Olsen (2001:65) expresses concern that these herbs have not been subjected to evaluation in any kind of clinical trial. Olson (2001:65) also states the following with reference to the Chinese remedy for venous insufficiency, "Though these remedies have primarily been used in Chinese medicine and midwifery practices, no trials have been conducted concerning safety and efficacy during pregnancy".

Public interest in the use of Complementary and Alternative Medicine (CAM) is also growing. Olsen (2001:63) reports that it was estimated that 5.1 billion dollars was spent on herbal products in the United States alone. The article does not state the amount spent specifically on pregnancy and childbirth remedies. It is common knowledge that many users of herbal products suppose that it is safe for use during pregnancy because it is 'natural', and will revert to the use of herbal products especially during pregnancy and breastfeeding when the use of most medication is contra- indicated. With the

increased public interest, and lack of scientific evidence, a systematic review on the topic would shed some light on whether it is really safe to use herbal products during the perinatal period.

1.3. Research Problem

The researcher has identified that many herbal and homeopathic compounds are used for different purposes during pregnancy, childbirth and breastfeeding. Few scientific trials have been conducted to evaluate its safety during the childbearing process, and no comprehensive systematic review has been done. A systematic meta-analysis of maternal outcomes of herbal and homeopathic remedies during pregnancy, childbirth and breastfeeding will have to be done.

1.4. Research Objectives

The primary objective of the research project evaluated the maternal and neonatal outcomes when pregnant women are exposed to herbal and homeopathic remedies by doing a systematic review.



1.5. Research Question

The research question that arises is:

Is the use of various herbal and homeopathic remedies safe during pregnancy, labour and breastfeeding?

Other research questions that could arise are:

The effect of the above-mentioned remedies on neonatal outcomes (admission to ICU, preterm/post term onset of labour, birth weight, gross anomalies etc)

1.6. Research statement

The literature searched could not reveal a systematic review on the combined effects of the use of herbal and homeopathic remedies on maternal and neonatal outcomes. Some literature presented conflicting results, and so it would be necessary to compile a comprehensive review on the effects of different compounds on various maternal and/ or neonatal outcomes.

1.7 Relevance of the study

The results of the systemic review will help health professionals and mothers to make informed and safe choices about the type of herbal or homeopathic remedies they choose to use. It will also safeguard health professional involved in childbirth from advocating the use of substances proven to be adverse by the results of the review.

1.8 Ethical statement:

Ethical clearance was sought from the University of the Western Cape Faculty of Community and Health Sciences Higher Degrees Committee and Senate. Patient consent is irrelevant in systematic review of literature. The review will also be sent to the Cochrane Group for peer review, and possible publication in the online Cochrane Library.

1.9 Chapter outline

Chapter one is an introduction to the review. Chapter two is a review of the current literature. The methodology of the review is discussed in chapter three and chapter four outlines the results. The discussion of the results, conclusions and implications for further research is included in chapter five.

1.10 Time Line

Writing of Proposal	July-September 2004
Submission of proposal to higher degree	September 2004
Approval of proposal	September 2004
Sorting out of articles	May- September 2004
Entering of data in tables	September- October 2004
Analysis of data	October- November 2004
Formatting conclusions	November- December 2004
Complete writing of thesis	January-March 2005
Submission of thesis	May 2005

1.11 Budget

The financial implication of the study is currently being supported by the reviewer.

RevMan workshop	R 210-00
Photocopying	R 1000-00
Stationery	R 500-00
Consumables	R 1000-00

1.12 Definitions

Some definitions of terms used throughout the thesis are defined below:

Abortifacient: that which causes abortion (Reader's Digest Universal Dictionary, 1988:16b)

Adverse effect: opposite or antagonistic effect, a negative effect (Reader's Digest Universal Dictionary, 1988:32b).



Birth: the act of coming into existence, the act of being born (Reader's Digest Universal Dictionary, 1988:168b).

Breastfeeding: giving an infant mothers milk via the breast, suckling an infant (Reader's Digest Universal Dictionary, 1988:202b).

Complementary and Alternative Medicine (CAM): therapeutic practices and medications which are allied to the biomedical model of medicine for example reflexology, acupuncture, homeopathy, herbology and iridology (Reader's Digest Universal Dictionary, 1988:326c).

Contra-indication: opposite to what is necessary, for example solid food is *contra-indicated* for babies under three months old (Reader's Digest Universal Dictionary, 1988:344d).

Efficacy: capacity to achieve results (Reader's Digest Universal Dictionary, 1988:493d).

Emmenagogue: a medication that produces or hastens the flow of the menses (Reader's Digest Universal Dictionary, 1988:505b).

Galactagogue: A substance that induces or encourages the flow of breast milk (Reader's Digest Universal Dictionary, 1988:624a).

Gravida / gravid : a pregnancy, pregnant (Reader's Digest Universal Dictionary, 1988:671a, Merriam-Websters Medical Desk Dictionary, 2003).

Hepatotoxic: poisonous to the liver (Reader's Digest Universal Dictionary, 1988:719b).

Herb: any plant, often of the aromatic variety used in medicine or seasoning (Reader's Digest Universal Dictionary, 1988:720b).



Herbal: of, relating to herbs (Reader's Digest Universal Dictionary, 1988:720b).

Homeopathic: a system of therapeutic practices that involve the use of small amounts of medication that in large quantities produce the same effects as the disease being treated (Reader's Digest Universal Dictionary, 1988:737d).

Ingestion: to take in, swallow (Reader's Digest Universal Dictionary, 1988:791b).

Labour: the physical effort involved in the birthing process (Reader's Digest Universal Dictionary, 1988:857d).

Maternal: involving or referring to mothers, motherhood (Reader's Digest Universal Dictionary, 1988:950d).

Midwifery: the science of assisting women through childbirth (Reader's Digest Universal Dictionary, 1988:978a).

Neonatal: a newborn, from time of birth up to seven days (Reader's Digest Universal Dictionary, 1988:1034c).

Obstetrics: the science of caring for women during and after pregnancy (Reader's Digest Universal Dictionary, 1988:1068c).

Oedema: accumulation of fluid in the tissues due to inadequate lymphatic drainage (Reader's Digest Universal Dictionary, 1988:1073c).

Perinatal: pertaining to pregnancy, birth and the post natal period (Reader's Digest Universal Dictionary, 1988:1150c).



Pregnancy: the period during which a woman carries a developing foetus in her uterus (Reader's Digest Universal Dictionary, 1988:1216b).

1.13 Classification of herbs used during pregnancy, labour and the post partum period

The generic and botanical name of herbs, categorized under either the primary usage or the purported adverse effect is defined below:

1.14.1 Abortifacient effects

Aloe vera	Aloe vera
Ashwagandha	Withamia somnifera
Basil	Ocimum basilicum
Bitter lemon	Momordica charantia
Boneset	Eupatorium perfoliatum
Buckthorn	Rhamnus catharticus

Calendula	Calendula officinalis
Cascara sagrada	Rhamnus purshinana
Cassia cinnamon	Cinnamonum aromaticum
Castor bean	Ricinus communis
Catnip	Nepeta cataria
Celery	Apium graveolens
Chamomile(Roman)	Chamaemelum nobile
Chicory	Cichorium intybus
Cinchona	Cinchona
Coltsfoot	Tussilago farara
Ginger	Zingiber officiale
Hemp agrimony	Eupatorium cannibinum
Horehound	Marrubium vulgare
Horseradish	Armoracia rusticana
Hyssop	Hyssopus officinalis
Joe-pye weed	Eupatorium purpureum
Juniper	Juniperus communis
Knot grass	Polygonum aviculare
Madagascar periwinkle	Vinca Rosa
Male fern	Oryopteris filix-mas
Marsh tea	Ledum palustre
Mugwort	Artemisia vulgaris
Myrrh	Commiphora myrrha
Nutmeg	Myristica fragrans
Papain	Carica papaya
Pareira	Chondodendron tomentosum
Parsley	Petroselinium sativum
Peach pit	Prunus persica
Pine	Pinus
Queen Anne's lace	Dancus carota
Rosemary	Rosmarinus officinalis
Rue	Ruta graveolus
Safflower	Carthamus tinctorius
Saffron	Crocus sativus

Sage	<i>Salvia officinalis</i>
Sandalwood	<i>Santalum album</i>
Savin	<i>Juniperus Sabina</i>
Scotch broom	<i>Cytisus scoparius</i>
Shepherd's purse	<i>Capsella bursa-pastoris</i>
St John's Wort	<i>Hypericum perforatum</i>
Stinging nettle	<i>Urtica</i>
Tansy	<i>Tanacetum vulgare</i>
Tumeric	<i>Curcuma longa</i>
Watercress	<i>Nasturtium officinale</i>
Wild ginger	<i>Asarum canadense</i>
Wild marjoram	<i>Origanum vulgare</i>
Worm seed	<i>Chenopodium ambrosioides</i>
Wormwood	<i>Artemisia absinthium</i>
Yellow cedar	<i>Thuja occidentalis</i>

(Ernst, 2002:231-233)



1.14.2 Emmenagogue

Angelica	Angelica
Asafoetida	<i>Ferula asafoetida</i>
Basil	<i>Ocimum basilicum</i>
Bitter lemon	<i>Momordica charantia</i>
Blood root	<i>Sanguinaria Canadensis</i>
Butterbur	<i>Petasites hybridus</i>
Calamus	<i>Acorus calamus</i>
Calendula	<i>Calendula officinalis</i>
Camphor	<i>Cinnamomum camphora</i>
Cassia cinnamon	<i>Cinnamomum aromaticum</i>
Castor bean	<i>Ricinus communis</i>
Catnip	<i>Nepeta cataria</i>
Celery	<i>Apium graveolens</i>
Chamomile(Roman)	<i>Chamaemelum nobile</i>
Chaste tree	<i>Vitex agnus castus</i>
Chicory	<i>Cichorium intybus</i>

Cinnamon	Cinnamomum verum
Fennel	Foeniculum vulgare
Flax	Linum usitatissimum
Garlic	Allium sativum
Ginger	Zingiber officiale
Gotu kola	Centella asiatica
Hemp agrimony	Eupatorium cannabinum
Hibiscus	Hibiscus rosa sinensis
Horehound	Marrubium vulgare
Hyssop	Hyssopus officinalis
Khella	Ammivisnaga
Lavender	Lavendula officinalis
Licorice	Glycyrrhiza glabra
Life root	Senecio aureus
Lovage	Levisticum officinale
Madder	Rubia tinctorum
Marjoram	Origanum marjorana
Masterwood	Heracleum lanatum
Motherwort	Leonurus cardiaca
Mugwort	Artemisia vulgaris
Myrrh	Commiphora myrrha
Papain	Carica papaya
Pareira	Chondrodendron tomentosum
Parsley	Petroselinum sativum
Peach pit	Prunus persica
Peony	Paeonia officinalis
Peppermint	Mentha piperita
Pomegranate	Punica granatum
Prickly ash	Zanthoxylum americanum
Queen Anne's lace	Daucus carota
Rosemary	Rosmarinus officinalis
Rue	Ruta graveolus
Safflower	Carthamus tinctorius
Saffron	Crocus sativus

Sage	<i>Salvia officinalis</i>
Sassafras	<i>Sassafras albidum</i>
Senega	<i>Polygala senega</i>
Shepherd's purse	<i>Capsella bursa-pastoris</i>
St John's Wort	<i>Hypericum perforatum</i>
Stinging nettle	<i>Urtica</i>
Tansy	<i>Tanacetum vulgare</i>
Thyme	<i>Thymus</i>
Tumeric	<i>Curcuma longa</i>
Watercress	<i>Nasturtium officinale</i>
Wild ginger	<i>Asarum canadense</i>
Wild marjoram	<i>Origanum vulgare</i>
Wood sorrel	<i>Oxalis acetosella</i>
Worm seed	<i>Chenopodium ambrosioides</i>
Wormwood	<i>Artemisia absinthium</i>
Yellow cedar	<i>Thuja occidentalis</i>



(Ernst, 2002:231-233)

1.14.3 Gastrointestinal

Blue cohosh	<i>Caulophyllum thalictroides</i>
	(Ernst, 2002:231-233)

1.14.4 Hepatotoxic

Butterbur	<i>Petasites hybridus</i>
Coltsfoot	<i>Tussilago farara</i>
Comfrey	<i>Symphytum officinale</i>
Pennyroyal	<i>Hedeoma pulegioides/ Mentha pulegium</i>
Skullcap	<i>Scutellaria laterifolia</i>
	(Ernst, 2002:231-233)

1.14.5 Hormonal

Black cohosh	<i>Cimicifuga racemosa</i>
Bugleweed	<i>Lycopus virginicus</i>

(Ernst, 2002:231-233)

1.14.6 Galactagogue

Blessed thistle	<i>Carbenia benedicta</i>
Fenugreek	<i>Trogonella fenum-gaecum</i>
Hops	<i>Humulus lupulus</i>
Milk thistle	<i>Silybum marianum</i>

(Ayers, 2000:54; Edmunds, 2003)

1.14.7 Low birth weight and premature birth

Cola	<i>Cola nitida</i>
Guarana	<i>Paullina cupana</i>
Mate	<i>Ilex paraguayensis</i>

(Ernst, 2002:231-233)

1.14.8 Mutagenic birth defects

Basil	<i>Ocimum basilicum</i>
Borage	<i>Borago officinalis</i>
Buckthorn	<i>Rhamnus catharticus</i>
Cascara sagrada	<i>Rhamnus purshinana</i>
Frangula	<i>Rhamnus frangula</i>
Ginger	<i>Zingiber officiale</i>
Nutmeg	<i>Myristica fragrans</i>
Rhubarb	<i>Rheum palmatum</i>
Senna	<i>Cassia</i>

(Ernst, 2002:231-233)

1.14.9 Uterine stimulant / Oxytotic/ Induction of labour

Alfalfa	<i>Medicago sativa</i>
Barberry	<i>Berberis vulgaris</i>
Blood root	<i>Sanguinaria Canadensis</i>
Blue cohosh	<i>Caulophyllum thalictroides</i>
Borage	<i>Borago officinalis</i>
Broom	<i>Cystisus scoparius</i>

Burdock

Rhamnus catharticus

(Ernst, 2002:231-233)

1.15 Summary

In chapter one a brief introduction to the topic of the review, and definitions of some terms used throughout the thesis is presented. The main objective of the review is to evaluate whether there is a beneficial or adverse effect to utilizing herbs and homeopathic remedies during the perinatal period.



Chapter Two: Literature Review

2.1 Introduction

Herbal and homeopathic compounds have been used to aid in childbearing and pregnancy for centuries (Lee, 1999:253). However, very few compounds have been scientifically tested for its active ingredient, [possible benefits], its mechanism of action and adverse effects during pregnancy, birth and breastfeeding. Practicing midwives have used a variety of herbs and nutritional supplements during the birthing process. Unfortunately much of this information is anecdotal and has very little scientific support, making it difficult to evaluate its safety and efficacy (Olson, 2001:63).

Olson (2001:63) states, “As the public's interest in complementary and alternative medicine (CAM) continues to grow, so does the amount of money being spent on herbal and nutritional supplements. According to one recent estimate, consumers spend about \$3.3 billion a year on high-dose vitamins and about \$5.1 billion on herbal products.”



Herbal remedies are most often used to treat the most common pregnancy-related problems like nausea, stretch marks and varicose veins. CAM has also been advocated to shorten or where appropriate increase the duration of the gestational period, augment or induce labour, decrease the duration of the birthing process, relieve perineal pain after birth, alleviate pain associated with cracked nipples and engorged breasts and increase breast milk production (Olsen, 2001:63-75; Ernst, 2002:228-230).

In contrast to this, concerns have also been raised about the adverse effects of these remedies. Some adverse effects for the pregnant woman include: increase meconium staining of amniotic fluid, increase rate of caesarean section and the possibility of acute renal failure. Side effects have also been reported in the neonate: ascites of various degrees and hepatomegaly, mental retardation, cardiac complications and enlarged genitalia (Ernst, 2002:228-230; Mabina et al., 1997:1008).

Olson (2001:64) expressed his concern regarding the use of these remedies that the herbs used by these women have not been evaluated in any clinical trial. Olson (2001:64) also states the following with reference to the Chinese remedy for venous insufficiency, "Though these remedies have primarily been used in Chinese medicine and midwifery practices, no trials have been conducted concerning safety and efficacy during pregnancy". A review of the current literature was done to provide background as well as to search for the availability of clinical trials on the topic.

Chapter two will give an overview on the history of CAM and the use of CAM in midwifery practices. Increased public interest in alternative treatments leads to the need for a systematic review on the topic

2.2 The history of herbs and homeopathy during childbearing

Egyptian medicine seems to have had the most lasting influence on the later development of medicine, through the medium of the Greeks. Price (2001:3) quoted Greek historian and traveller, Herodotus (5BC) where he commented on medical practices in Egypt; "the art of healing is with them divided up, so that each physician treats one ailment and no more. Egypt is full of physicians, some treating diseases of the eyes, others the head, others the teeth, others the stomach and others unspecified diseases". The ancient Egyptian texts of the Old Kingdom (2635-2155 BC) contain at least 50 physicians, mainly from their names on tombs. Surgery and mummification processes used by ancient Egyptians still amaze the modern experts. All major and expected diseases are known and treated, ailments are attributed to spirits, ghosts and revenge by gods and goddesses. Texts dealing with gynaecology cover fertility, sterility, pregnancy, contraception and abortion. Women were tested to decide whether they could conceive or not. However the Egyptians were behind Babylonian doctors who had gone further and designed the first pregnancy tests known in history. This test involved placing in the women's vagina a tampon impregnated with the juice of various plants in a solution of alum. This was left in position either overnight or for three days. Pregnancy or non-pregnancy was indicated by colour changes between red and green. The test used the pH value of the woman's secretions in

vagina to determine pregnancy. Rational thinking and sound medical observation were used alongside magic and sorcery (Price, 2001:3).

From earliest times, Greeks and Romans had expert familiarity with plants and their growth cycles. Agriculture dominated, alongside acute command of medicinal herbs, including production of oils and perfumes. Striking is the mélange of herbal lore and specific plants indicated for women's ailments. The Hippocratic Diseases of Women as well Soranus of Ephesus in his Gynaecology (c. AD 117) record over 300 herbal species identified and used by physicians and midwives (Scarborough, 1998:1).

Chinese herbal medicine mainly focuses on treatments involving acupuncture in combination with herbal remedies. The earliest references referred back to 1000 to 1500 BC, where inscriptions on bones and tortoise shells from the Shang dynasty mentioned the use of herbs for treatment of diseases. The first reference to gynaecology as a distinct speciality appears in the Warring States period where the famous doctor Bian Que is referred to as one who “treats diseases under the skirt belt” (Deadman, [Sa]).



The concept of homeopathy dates back to the Greek physician, Hippocrates (460-377B.C). He referred to the principle of “like can cure like”. This means that a substance that is use to treat the ailment actually produce the same symptoms as the ailment. Hippocrates is known as the “Father of Medicine” and had a personal collection of several hundred remedies. White hellebore (*Veratrum album*) is a highly poisonous root that causes excessive vomiting that leads to severe dehydration. As white hellabore produces the same symptoms as cholera, he used it to treat patients suffering from the disease. This confirms his philosophy of “like curing like”. Many years later, Hanhemann (1776), published one of the first books on Homeopathy where he explained the principle that “a drug taken in small amounts will cure the same symptoms it causes in large amounts” (Medicine, [Sa]). Hahnemann supported the essential characteristic of homoeopathy “like can cure like” with his statement of in Latin: “similia similibus curentur” (Campbell, [Sa]).

2.3 Methods and effectiveness of herbal preparations

One of the most important factors in the effectiveness of the herb quality is the freshness of the herb and the care with which it is harvested, dried and processed. Standardized extracts are chemically manipulated to isolate, measure and concentrate specific compounds that are considered to have beneficial activity. There is more potential for side effects with standardized as the synergistic effects of the plant are diminished or lost. Decoctions are used to extract the more dense parts of plants such as roots or barks and Glycerites, the sweet fraction of oil (oil minus the fatty acids) does not have the same extractive properties of alcohol. Most herbs are not effective in this preparation (Belew, 1999:232).

There are three of the main ways of preparation of herbs for ingestion are; water, oil or alcohol based or dried as an infusion or powder. Water-based preparations are commonly made from dried plants. Drying is necessary to rupture the cell wall and allow release of the constituents. A larger quantity and broader range of the nourishing properties of the plant are available in water than are in alcohol. In oil based preparations, the fresh plant is simply packed into a jar, covered with olive oil, and allowed to sit for two weeks. Essential oils are very strong and are almost never used internally. Tinctures are alcohol based preparation. Some herbs work better in tincture form, since some plant constituents are more soluble in alcohol than in water. Some plants are more effective medicinally if the fresh plant is made into tincture; in other cases, dried plant is more beneficial, and with some herbs it doesn't matter (Belew, 1999:232).

Infusions are used to prepare the leafy portion of plants. Leaves have tougher cell walls so it takes longer for the constituents to come out of the plant into solution. Cold infusions are used for a few plants, which contain valuable constituents that would be damaged by heat. Simple teas are appropriate for flowers and seeds, which open and release their contents easily, or for herbs where the volatile oils are a major constituent. Powdered, prepackaged herbs have been extensively exposed to air, causing oxidation and rapid loss of potency (Belew, 1999:234).

Other methods such as external applications of herbs in the form of poultices, compresses and fomentations, are used to accelerate healing and prevent or draw out infection. Ointments and salves can be made by adding beeswax to the herbs (Belew, 1999:235).

2.4 Herbs and homeopathy during pregnancy

Herbs are commonly used during pregnancy to alleviate some of the most common symptoms associated with childbearing like nausea, vomiting, swollen ankles and stretch marks.

Alternative remedies for nausea and vomiting during pregnancy have received the most scientific attention. A number of different herbs have been advocated to relieve the symptoms of nausea. Some of these are: chamomile, meadowsweet, spearmint, slippery elm, peppermint, iceland moss, vitamin B₆, ginger and alfalfa tablets (Olsen, 2001:64; Goldstein, 2004).

Ten to 25 mg of vitamin B₆, three times a day, and Ginger (*Ziniberis officinale*) taken as a capsule, tea, or soft drink have been shown to reduce nausea and vomiting in pregnant women (Olsen, 2001:63). Olsen (2001:63) stated that the effects of herbs may seem ineffective after some time and it may be necessary to alternate herbs or to reduce the initial usage to small amounts. Utilizing this method can reduce both tolerance and overuse. A "Pregnancy Toner Tea" made of a combination of herbs has also been documented to be served at childbirth preparation classes to reduce nausea. The recipe includes herbs such as: raspberry leaves, nettles, dandelion leaf or root, peppermint and alfalfa. In addition this tea may also relief oedema (Lee, 1999:262).

Stretch marks that develop during pregnancy may occur in over 50% of women. Olson (2001:63) states that some authors claim that herbal preparations can prevent stretch marks, but no clear evidence exists to verify these claims. Young & Jewell (2004) did a systematic review on randomised controlled trials that evaluated the effect of creams to prevent stretch marks during pregnancy. They concluded that there are no clinical trials currently available that support the use of creams to prevent stretch marks during pregnancy and state that massage in itself

may benefit women. Creams used during pregnancy to keep the abdomen soft and moisturized are: neroli, mandarin bergamot, lavender, roseweed, Vitamin E, cocoa butter, olive oil, sweet almond oil, Trofolastin (containing Centella asiatica extract, alpha tocopherol and collagen-elastin hydrolysates) and Verum (containing tocopherol, essential fatty acids, panthenol, hyaluronic acid, elastin and menthol). So far no adverse affects of above ointments have been recorded (Olson, 2001:63; Young & Jewell, 2004).

Alfalfa tablets have also been advocated to raise the vitamin K level of pregnant women and to reduce postpartum bleeding in both quantity and duration. In the neonate Alfalfa increases the vitamin K stores and reduces bleeding problems Alfalfa tablets have also been used to relieve heartburn, constipation and anemia during pregnancy (Goldstein, 2004).

Varicose veins and pedal oedema are both common during pregnancy and often increase as gestation progresses. Treatment has traditionally been aimed at relieving congestion with infusions of lime blossom and fresh ginger root, which may strengthen venous tone. Garlic and onions has been used to improve circulation. Chinese herbal medicine practitioners also believe that fresh parsley and nettles added to the diet or taken as infusions improve venous elasticity. Lotions or compresses that contain marshmallow, marigold, plantain, yarrow, hawthorne, cypress, lemongrass, lavender, and comfrey have been used to soothe aching legs. The addition of oak and witch hazel barks to any herbal lotion or compress may ease the pain of varicosities. Finally it has been reported that footbaths containing a few drops of benzoin, rose, orange, geranium, or peppermint may be beneficial (Olson, 2001:64).

2.5 Herbs and homeopathy during birth

Homeopathy is commonly used for the augmentation and induction of labour.

Castor oil is extracted from the *ricinus communis* bean. It is sometimes referred to as the hand of Christ, which means "*Palma Christi*" in Latin. Castor oil has been used since ancient times to stimulate labour. Historical records reveal that castor

bean seeds have been discovered in Egyptian tombs. It is also used for the induction of childbirth and expulsion of the placenta in China (Gabbay, 1999).

Many midwives currently use it as a traditional method to augment or induce labour. The literature on the pharmacokinetics and pharmacodynamics as well as the efficacy and safety of castor oil for induction of labour is limited. The use of castor oil for the induction of labour has been examined (Garry, Figueroa, Guillaume & Cucco, 2000:77). They have found that the initiation of labour is more successful in women who received castor oil than those who did not. They further reported that nausea was present in all the women who ingested castor oil. Kelly, Kavanagh & Thomas (2004) in their systematic review concluded that further research is needed to quantify the efficacy of castor oil as an induction agent.

Maternal side effects such as an amniotic fluid embolism (AFE) have been noted in a case report. The AFE was associated with the ingestion of castor oil, but a direct cause-effect relationship between the ingestion of the oil and the AFE was not formulated (Steingrub, Lopez, Teres, Steingart, 1988:642). An increase in meconium stained liquor and caesarean sections have been reported related to the use of *isihlambezo*, an indigenous South African herbal mixture, used to augment labour. A study sample of women presenting in early labour was randomly selected. 55% (n=126/229) had ingested *isihlambezo*. 82% (n=103/126) of the group that had ingested *isihlambezo* had meconium stained liquor (Grade II and III), and 39% (n=47/126) had caesarean sections. The control group had lower rates of both meconium stained liquor (32%:n=33/103) and caesarean sections (22%: n=23/103) (Mabina et al., 1997:1008). Neonatal adverse events such as moderate growth impairment, convulsions, cranio-facial dysmorphism, limb reductions, and vertebral defects has also been reported after women ingested castor oil (El Mauhoub, Khalifa, Jaswal & Garrah, 1983:57).

Herbal medicines that are also commonly used to induce labour are: black cohosh blue cohosh, evening primrose oil and raspberry leaf. Maternal nausea, gastric disturbances and meconium stained liquor have been reported as adverse events. These remedies also affect the neonate and complications such as: transient fetal tachycardia, fetal distress, aplastic anemia, stroke and neonatal heart failure has

been reported (McFarlin, Gibson, O'Rear, Harman, 1999:212: Stapleton, 1995:148).

A Cochrane Review on the use of blue cohosh vs placebo showed no significant differences in the proportion of women who achieved a vaginal delivery within 24 hours, duration of labour, augmentation, assisted deliveries or caesarean sections. Significantly fewer women in the cohosh group reported that they have experienced a difficult labour. The reviewers concluded though that there is insufficient evidence to recommend the use of blue cohosh as a method of induction (Smith, 2003).

Simpson, Parsons and Wade (2001:51) found that women consume the raspberry leaf herb during their pregnancies in the belief that it shortens labour and makes labour easier. They undertook a randomised, double blind, placebo controlled trial to evaluate the effectiveness of the herb. The results of the study showed that raspberry leaf tablets did not shorten labour and had no maternal and neonatal adverse effects.



2.6 Herbs and homeopathy during breastfeeding and the post partum period

Herbs work in combination with a good diet and vitamin supplementation. Plants that increase milk production (galactagogues) work by supplying nutrients, trace minerals, and alkaloids thereby enhancing the physiological processes involved with lactation (Edmunds, 2003).

Fenugreek, celery related seeds, hops, liquorice, fennel, anise, dill, caraway, nettles, raspberry leaf, red clover, barley and cumin has also been widely used as galactagogues. Its mechanism of action remains unknown but may be related to increased sweat production or results from its abundance of fatty acids (Ayers, 2000). Another popular herb is holy or blessed thistle. The related milk thistle is commonly used as a blood and liver purifier. Blessed thistle, likewise, is considered to have a beneficial effect on the blood, which, in turn, enriches the milk (Edmunds, 2003). Adverse effects such as shrinking of the mammary glands

and inhibition of the formation of milk production has been reported (Edmunds, 2003). Sage, shepherd's purse, walnut leaves and bark have a vasoconstriction effect on the mammary gland and are used to inhibit milk production (Edmunds, 2003).

Externally, poultices of powdered clay, distilled witch hazel, grated raw potato, carrot or cabbage leaves may be applied to contract tissue and draw out fluid. Echinacea, vitamin C, garlic, and goldenseal are also used to prevent infection (Nikodem , Danziger, Gebka, Gulmezoglu & Hofmeyr, 1993:61; Edmunds, 2003). Garlic has been shown to improve suckling, increase let down, and reduce engorgement. A report by Mennella and Beauchamp, (1991:737) found that when mothers eat garlic, their infants ingest more milk and suckle longer.

If a patient is suffering from cracking, bruising, or bleeding a fresh geranium leaf, placed furry side down, has been suggested as an aid for healing. In addition, sweet almond oil, olive oil, lanolin cream, and yarrow ointments may be of benefit in healing the cracked areas. Pure essential oils must be thoroughly removed prior to nursing (Olson, 2001:67).



St John's Wort has been used in lactating women to treat post natal depression. Although the components of the herb was found in the milk the quantities were low and no side effects have been reported (Klier, Schafer, Schmid-Siegel , Lenz & Mannel, 2002:29).

2.7 Benefits of herbs and homeopathy during pregnancy

Although very few randomized trials have been executed to prove the benefits of herbs, many authors have expressed possible usages of herbs.

Table 2.1 Uses of herbs and homeopathy during pregnancy, birth and breastfeeding

Reduction of stretch marks
Alleviation of nausea and vomiting
Relief pedal oedema
Decrease or increase duration of gestation
Augmentation and induction of labour
Relief of perineal discomfort post partum
Relief of breast engorgement
Increase milk production
Treatment of cracked nipples
Prevention and treatment of post natal depression
Reduce post partum haemorrhage, increase Vitamin K stores in infants
Prevention of birth defects

(Ernst,2002:227; Goldstein, 2004; Olson,2001:66-70)

2.8 Adverse effects of herbs and homeopathy during pregnancy

The majority of authors claim that all herbal remedies are safe but some reported case studies have refuted this statement. The following adverse effects have been reported that could possibly be associated with the use of herbal remedies.

Table 2.2 Adverse effects reported in women

Hepatotoxicity	
Meconium stained liquor	
Increased rate of assisted deliveries and caesarian section	
Abortion	
Premature labour	
Uterine hyper stimulation	
Renal failure	(Ernst, 2002:229 - 230)



Table 2.3 Adverse effects reported in the fetus and newborn

Motor and mental retardation	
Cardiac abnormalities	
Genital abnormalities due to hormonal over stimulation	
Hypertension	
Hepatomegaly	
Jaundice	
Venous occlusive disease	
Terarogenic and mutagenic birth defects	(Ernst, 2002:228)

2.10 Summary

It is clear from this literature search that there is very little scientific evidence available on the usages of herbal remedies during pregnancy, labour and the post partum period. A lot has been said in the lay literature and anecdotal reports of case studies. A systematic review is needed to do a meta analyses on the literature regarding the usage, dosage, benefits and side effects of herbs, homeopathy and other remedies during pregnancy, birth and the puerperium.



Chapter Three: Research design and methodology

3.1 Introduction

Effective research is essential to promote progress in healthcare, as well as other spheres of the environment. Appropriate research methodologies delineate findings for other researchers as well as those simply seeking information. The systematic review approach is an ideal presentation for busy health practitioners, to obtain a summary of findings without having to process large bodies of information. The systematic review method of research is used to collate studies that address the same topic, explain differences and similarities among the studies. The application of scientific strategies is used to limit bias and to amalgamate all relevant studies that address a specific clinical question. Specific statistical methods such as the meta-analysis of outcomes are used to combine and summarize the results of the primary trials. Systematic reviews may strengthen the link between effective evidence and clinical practice. It is also increasingly used to inform medical decision-making, establish clinical guidelines and to plan future research studies (Cook, Mulrow & Heynes, 1997:376).

The following chapter outlines the methodology used for this systematic review. A brief introduction on the research software, Review Manager (RevMan), an overview of meta-analysis, and a short discussion on the rationale of using a systematic review, as well as the criteria for inclusion of studies in the review is also presented in this chapter.

3.2 The Review Manager (RevMan) 4.2

Healthcare professionals, and others who have an influence on health of communities and individuals are inundated with information, which sometimes presents conflicting views on health interventions. The need for a systematic review of the information then becomes relevant. The Review Manager 4.2 (RevMan) software is a program that was designed to assist reviewers in the

preparation and maintenance of Cochrane Systematic reviews, within the Cochrane Collaboration programme. RevMan uses a specific format for entering the data and depicting the results such as the blobograms or forest plots. It further uses specific headings, such as background, objectives, references, criteria for included and excluded studies, methodological quality and characteristics of the study (RevMan, 2002:8)

3.3 Systematic reviews

A systematic review is used to collate, critically evaluate and synthesise all studies that deal with a specific clinical question in a manner that limits bias. The meta – analysis is one type of systematic review, that utilises specific statistical methods to merge and condense the results of several primary studies (Cook, Mulrow & Heynes, 1997:376).

The systematic review is a scientific investigation in itself. It subscribes to the research process in that it has a pre-planned methodology, and uses primary studies as its 'subjects'. The basic steps that are followed in a systematic review involve strategies to limit bias and random error. These steps include the collection of information by searching for all potentially relevant articles. The articles are then subjected to a series of rigorous criteria before being selected for inclusion in the review. The methodology, research design, study and participant characteristics of the primary studies are critically evaluated. Often, systematic reviews will state that primary studies were of 'poor quality'. Gaps or weaknesses in the methodology, design or characteristics lead to a primary study being labelled as 'poor quality'. After the primary studies are appraised, the relevant data is extracted and synthesised. Collected data is also subjected to rigorous process. If a statistical programme is used, data is entered twice or more to ensure reliability. Synthesised data is processed and the results obtained are interpreted and discussed (Cook, Mulrow & Heynes, 1997:378).

3.4 Rationale for systematic reviews

The explicit methods used in the RevMan program provide the rigorous framework, which ensure and enhance the validity and reliability of the analyses. A systematic review allows for large amounts of information to be collated and analyzed. The result of the meta-analyses provides the reader with a comprehensive summary of many studies on the same topic (Greenhalgh, 1997:673).

With large bodies of information available to practitioner it is sometimes difficult to reach a clinical decision based on the best evidence. Faced with such a wealth of information, it also becomes more difficult for practitioners to remain updated. In the clinical settings therefore, practitioners have come to rely on systematic reviews, especially through established review publications like the Cochrane Collaboration. Apart from the uses of reviews in clinical settings, researchers also find that scientific systematic reviews have a number of advantages. Reviews assist researchers to delineate their hypothesis, eliminate previous errors and focus their research on the areas that require attention. Reviews are time consuming, but even then, it is more cost effective than doing a new study, and may prove that a new study is not even necessary, as the conclusion of the review may be enough to provide enough evidence to reach a clinical decision (Cook, Mulrow and Heynes, 1997:379).

In summary, the rationale for a systematic review would be that is an effective and scientific manner of assisting healthcare decision makers to make informed decisions about their practice, without having to sift through large bodies of information to access facts (Cook, Mulrow and Heynes, 1997:377).

3.5 Types of systematic reviews

Systematic reviews can generally be categorised into quantitative and qualitative reviews. When the results of primary studies are summarised but the results are not subjected to any form of statistical analyses, then it is known as a qualitative review. Quantitative reviews contain results of two or more primary studies. Narrative reviews are 'overviews', and contain

summaries of research that lack clear systematic methodologies (Cook, Mulrow and Heynes, 1997:376).

Publications of review articles are adapted to suit the purpose for which it was written. Review articles can be published as systematic reviews, practice guidelines, economic evaluations or clinical decision analyses, to name a few. For example, practice guidelines are specific statements about healthcare for clinical interventions. Practice guidelines are aimed at assisting patients and healthcare practitioners to make appropriate decisions based on the available research. Evidence-based guidelines incorporate statements about healthcare and clinical interventions, but place these statements in a social context, forming a link between best practice and local circumstances and values. Economic evaluations include a comparison of the costs and consequences of diverse clinical interventions. Systematic reviews of primary studies generate the consequences that are included in an economic evaluation (Cook, Mulrow and Heynes, 1997:376).



3.6 Difference between traditional and scientific reviews

The difference between a traditional review and a scientific systematic review [according to the Cochrane Collaboration] lies in the methods of the selection of studies as well as the analyses (Cook, Mulrow and Heynes, 1997:376). Traditional reviews present the summaries of all the primary studies without statistically combining the results. A traditional review therefore is open to bias and non-scientific methods of data analyses. A scientific systematic review uses a prescribed format and protocol and statistically combines the results of primary studies using methods like meta-analysis to limit bias and random error (Cook, Mulrow and Heynes, 1997:376).

3.7 Meta – analyses

Greenhalgh (1997:672) states that a meta-analysis is, “a mathematical synthesis of the results of two or more primary studies that addressed the same hypothesis the same way”. It is thus a combination of the results from

one or more studies and it is the preferred statistical method when writing systematic reviews (Greenhalgh, 1997:672).

Meta- analyses focus on comparing a pair of interventions. A fixed or random effects model may be used when comparing and combining the outcomes of different studies. The fixed effect model can be applied when the primary outcome in the meta analyses of the included studies are mathematically compatible thus homogenous and the random effects model are mostly applied when the studies are heterogenous (Greenhalgh, 1997:674). Heterogeneity can be statistically calculated by using the chi square statistic.

One of the measurements commonly used in meta- analyses to show the effectiveness of the treatment intervention is the relative risk. The relative risk refers to the risk or the probability of the event in the experimental group divided by the risk of the event in the control group. If the relative risk equals one then there is no statistical difference between the two groups. When the risk ratio increases to above one and do not included one, then it is said that the intervention is beneficial (it reduces the risk of the disease) and when the risk ratio is below one, then the intervention is associated with an increased risk of the disease (Greenhalgh, 1997:674).

3.8 Main objectives for systematic reviews

Systematic reviews, when used appropriately, can add value to research, clinical decision making and positively influence health policy. The primary objective for considering the systematic review as a relevant research method is that it increases the possibility of identifying a real effect as statistically significant, from a collection of smaller studies, with small sample sizes. The effect that a treatment will have can be more accurately estimated when a meta-analyses is done, as there is more information, and the collation of studies provides a larger sample size (Higgins & Green, 2005: Section 4).

Primary studies usually have specific patients and interventions. Combining studies that have different characteristics but test for the same effect could

provide insight into the consistency of the effect, and allow for differences to be investigated. Systematic reviews can also provide the means to resolve contradictions in the literature, or to formulate new hypothesis. Meta-analyses of primary data allows the degree of conflict to be scientifically evaluated and quantified. The reasons for differing results can be graphically represented and explored (Higgins & Green, 2005: Section 4).

3.9 Benefits of systematic reviews

One of the primary advantages of systematic reviews is that it is an aid to clarifying contradictions in the literature. Systematic reviews obtain their data through meta-analyses of smaller primary studies. This gives greater statistical power to the compounded result, and is more economical than conducting a fresh clinical trial. The compounded results also give an indication whether further research and clinical trials are needed. The scientific findings of systematic reviews can be generalized across treatment variations, settings, and populations. The rigorous methods by which a systematic review is conducted, aims to limit bias and improve reliability and validity of results (Cook, Mulrow & Heynes, 1997: 377).

3.10 Limitations of systematic reviews

Proper use of meta-analyses as a research tool is essential in order to obtain unbiased and accurate conclusions from data. Meta-analyses is however not always the correct method to use to obtain results and is commonly criticized for combining inappropriate data. When clinically diverse studies are meta-analysed, then genuine differences in effect could be hidden due to different comparisons not being separated. In a case where there are different comparisons within the included studies, each group of comparisons would need to be considered separately to obtain a meaningful result. The same applies to outcomes that are too diverse. Outcomes that are too diverse, when combined could also obscure relevant effects or lead to misinterpretation of data (Higgins & Green, 2005: Section 4).

Reviews often conclude with the fact that there is inadequate evidence to draw a substantial conclusion. Poor quality primary studies may also influence a misleading result. If bias is present in the primary study, then meta analyses could compound this bias, and produce an inaccurate result, but lend more credibility to the inaccuracy. Repercussions of inaccurate data are serious, as systematic reviews are often used to influence patient care, economic decisions around health and service providers (Higgins & Green, 2005: Section 4).

3.11 Criteria for selection of studies in this review

The research question - Is the use of various ingested herbal and homeopathic remedies safe during pregnancy, labour and breastfeeding? - decided the studies that were to be included in this systematic review. The issues considered in this review include:

- Types of studies

Clinical trials comparing any ingested homeopathic or herbal remedies with placebo or another method for the prevention or treatment of ailments or interventions as listed below during pregnancy, childbirth and the post partum period.

Ailments or interventions:

Nausea and vomiting

Prevention of premature labour

Augmentation and induction of labour

Relief of perineal pain

Increase in breast milk production

- Types of participants

Women in the reproductive age (21-51years), who either were pregnant at the time of the study or had already borne children, and who had used herbal or homeopathic remedies during pregnancy, birth or breastfeeding to alleviate

common pregnancy-related illnesses. Some common ailments include, but are not limited to:

Nausea and vomiting

Prevention of premature labour

Augmentation and induction of labour

Relief of perineal pain

Increase in breast milk production

Pregnant women or women in the post partum who used herbal or homeopathic remedies during pregnancy, birth or breastfeeding for the above interventions

- Types of interventions:

Various herbal and homeopathic remedies that were commonly used by women as an intervention during pregnancy, birth and/ or breastfeeding – related ailments. A list of the interventions include:

Raspberry leaf

Castor oil

Fish oil

Ginger

Isihlambezo (a traditional African herbal concoction)

Evening primrose oil

Arnica



- Types of outcome measures

Studies were considered for inclusion in this review if they were appropriately designed to evaluate the outcome measures relevant to the use of herbal and homeopathic remedies during pregnancy, birth and breastfeeding. Some relevant outcomes include duration of pregnancy, duration of labour, induction of labour, birth weight, nausea, vomiting. Some secondary outcomes include incidence of meconium stained liquor, mode of delivery and maternal side effects. Studies that were included in the review were those that had data in an appropriate format for inclusion.

3.12 Limitations

This review differs from the RevMan systematic review as far as inclusion criteria are concerned. A hand search for possible articles was not done.

3.13 Search strategy for identification of studies

An extensive electronic search was done to ensure that all relevant literature was included in the review. The initial search was done on the major electronic biomedical databases like PubMed, EBSCO, Medline and the Cochrane Controlled Trials register. The bibliographies of articles were consulted to ensure that all the relevant trials were included in the review. Key words for the search included: herbs, pregnancy, homeopathy, breastfeeding, antenatal, intrapartum, birth, labour, post partum care, puerperium, induction of labour, alternative remedies, childbearing & traditional midwifery, randomized* (all variations), trial. The herbs (listed under 1.9) were also entered in the search. Key words were used in isolation, but also in combination with each other. Full articles were obtained online when available or ordered through the library facilities of the University of the Western Cape. The study selection was undertaken independently by the researcher and the trials were included only if they met the inclusion criteria. All studies that met the broader selection criteria were then evaluated for methodological quality. The studies were discussed with the supervisor and discrepancies for inclusion or exclusion were resolved. Only nine out of 15 articles met the eligible inclusion criteria. The excluded articles were noted and the reasons for exclusion are included in this review.

3.14 Methodological quality, validity and reliability

The validity of a systematic review to a large extent depends on the methodological quality of the primary studies that were included in the review, and the precision by which the review was designed and conducted.

Four main types of bias are associated with a systematic review: selection bias, performance bias, attrition bias and detection bias. Allocation concealment is a method of reducing selection, performance and detection

bias. Selection bias occurs when comparison groups are selected on the basis that they will accurately prove or disprove the hypothesis. Difference in care provided to the treatment or control group in a primary study is known as performance bias. Detection bias refers to differences between the comparison groups in outcome assessment (Feinstein, 1985:42). The nature of the intervention, ingested herbal or homeopathic remedies allows for adequate allocation concealment through either sequential central randomisation, sealed, opaque envelopes or coded identical containers. New and innovative methods of allocation concealment also occur, but the basic principle and objective remains the same (Higgins & Green, 2005: Section 6).

The degree to which different reviewers assess the review is referred to as the reliability of the review. The reviewer and her supervisor assessed the primary studies and resolved disagreements about outcomes and inclusion criteria through discussion. Studies were only included once consensus was reached.



The reviewer further ensured reliability and validity by double entry. The data from each primary study was extracted without concealing the authors' names, intervention, results, study sites and participant characteristics. In order to ensure correctness, the data was entered into RevMan twice, and this was checked by the supervisor.

3.15 Data collection

The data from each publication was extracted independently. Authors names, study site, intervention and trial results were not masked, and data was then entered into a special data collection sheet, one for each included study. The outcome measures of herbal use during pregnancy versus the control group, were indicated on the data collection sheet.

3.16 Data analysis

After the data was extracted from the studies and entered into the data collection sheet, it was entered into the Review Manager (RevMan) Program for analysis. Revman is a specialised program designed for calculation of statistics utilised in meta – analysis. Revman processes the data and presents the results in graphic and tabular form. Comparisons included in the systematic review, and their outcomes are displayed in the tabular summary. The program display results in tabular and graphical form.

The results can be viewed in the tabular summary. The table presents the results in five columns or sections. The first column displays the comparisons and their outcomes. The second column states the number of studies that were utilised for a specific outcome. In the third column, the total number of participants for the studies that contributed to the analysis of the outcome is displayed. In the fourth column the statistical method used to do the analyses can be found. In this review, the random effects relative risk model (RR) and 95 % confidence interval(CI) are used as the method for statistical analyses. The confidence interval and effect size (displayed as the effect estimate) that resulted from the meta – analyses is presented in the fifth, and final column.

A forest plot, which is a standard graphic chart, is used by RevMan, to display the results. Three columns are used. The study identifier is displayed in the first column. The second column includes the sample size (N) of the intervention group and the incidence of the event (n). The third column depicts the sample size and incidence of the event in the control group.

The effects estimates in RR and CI for both individual studies and meta – analysis are displayed in the graphical part of the forest plot. Each study is assigned a blobbogram. A forest plot looks like a series of horizontal lines, with different sizes of 'blocks' intersecting the line. The horizontal lines either intersect, or do not touch a solid vertical line that represents the 'null effect'. The confidence interval is depicted by the horizontal line, and the point estimate is represented by the block on the line. The size of the square block is commonly referred to as the 'size of the trial', but actually refers to the

weight of the specific study in the meta-analysis, with a larger block representing a bigger weight, and a narrower confidence interval. Smaller confidence intervals carry more weight. A diamond in the forest plot corresponds to the confidence intervals for the totals of the meta-analyses. The weight that each study (in percentage form) contributed to the overall analysis is presented in column five, and column six contains the numeric values of the RR and CI. The foot of the forest plot gives a summary of the events that occurred in each column, or event. Then the heterogeneity test is stated. (Chi^2 statistic has a value equal to its degrees of freedom (df) and P-value and the I^2 statistic, measuring the extent of inconsistency among the results). The random relative effects model was used. This is followed by the test for overall effect, Z statistic with the P-value.

The position of the RR and CI in the forest plot gives rise to the interpretation of the results. A confidence interval of 95% and random relative risk was used for this systematic review. Relative risk can be explained as follows: it is the ratio between the rate of intervention in the population exposed to a particular factor (like homeopathy) and the rate in those not yet exposed (women in the control group). The relative risk value can be interpreted in three ways.

- If the RR = one, or the confidence interval (CI) includes one, then there is no significant difference between the control group and those who received homeopathy/ herbal treatment during pregnancy.
- If the RR > one and the CI does not include one, events are significantly more likely in the herbal/ homeopathy than the control group.
- If the RR < one and CI does not include one, events are significantly less likely in the herbal/ homeopathy than the control group. (Evidence based and the Cochrane Collaboration Workshop)

3.17 Summary

The methodological quality of a systematic review is important to ensure an accurate result. Systematic reviews are used to influence policy, clinical practitioners, clients and make economic decisions, and so rigorous methods have to be applied in order to ensure that the review presents the best

available evidence. While systematic reviews may not always be the most applicable method of conducting research, it is very helpful in delineating research hypotheses and presenting a scientific summary of lots of information.



Chapter Four: Results

4.1 Introduction

Eight studies met the inclusion criteria and were meta-analysed for the purpose of this systematic review. Chapter four contains the results of the meta analyses, done using Review Manager software. The outcomes were analysed as dichotomous outcomes, with a 95% confidence interval. Outcomes that were reported on include: duration of gestation, maternal nausea, severe nausea, onset of labour not achieved within 24 hours, meconium stained liquor, vaginal delivery not achieved within 24 hours, duration of labour, caesarean section, uterine hyperstimulation, postpartum haemorrhage, perineal pain, breast pain and serious neonatal morbidity. Outcomes with no data and thus no results were not reported on. These outcomes include maternal death, serious maternal morbidity and neonatal death.



The eight studies used in this review are as follows:

- Dove and Johnson (1999)
- Garry (2000)
- Hofmeyer (1990)
- Ingram (2003)
- Mabina (1997)
- Olsen (1992)
- Simpson (2001)
- Vutyavanich (2001)

The chapter also contains a description of the studies included in the review. The results in this chapter are displayed as forest graphs for individual outcomes. Chapter three contains an explanation of the characteristics of a forest graph.

4.2 Types of studies

A total of eight studies met the inclusion criteria. Five studies were randomized control trials, reporting on the use of ingested herbal remedies and the effect of these remedies on pregnancy related outcomes. The studies were characterized into the following groups: six studies reported on the effect of the treatment of duration of gestation and labour, one study reported on perineal pain, and one on nausea and vomiting during pregnancy. The randomized controlled trials (RCT's) reported on the effect of Arnica D6 and Arnica D30 on perineal healing after episiotomy or tears during delivery, caulophyllum on duration of labour, fish oil supplementation on duration of pregnancy and birth weight, raspberry leaf on duration of labour, and the effect of ginger on nausea and vomiting. The retrospective, comparative study examined the effect of evening primrose oil on duration of gestation. The effect of castor oil as an induction agent was explored through a study following the prospective evaluation design. The trial exploring the use of *isihlambezo* utilized a quasi-randomised control design. Inclusion criteria are random control, quasi random control, prospective or retrospective studies that mention an experimental and a control group.

4.3 Types of participants

All the studies used for this review included female participants who were in their reproductive age and had used some form of ingested herbal or homeopathic remedy during their perinatal period, to alleviate common pregnancy-related illnesses. The pregnancy-related problems that occurred in the studies used include: nausea and vomiting, post maturity, premature rupture of membranes, perineal pain and premature labour.

4.4 Types of intervention

Ingested herbal or homeopathic substances used in all the trials that formed the primary studies for the review. The herbal or homeopathic substances were

ingested to relieve some form of pregnancy-related ailment. Homeopathic substances used in the trials are Arnica D6, Arnica D30, and caulophyllum. It is the same basic homeopathic substance (arnica) but used in different strengths. Herbal substances used in the trials include: raspberry leaf, castor oil, fish oil, ginger, *isihlambezo* and evening primrose oil.

4.5 Types of outcome measures

Studies that were included in this review had clinical outcomes relevant to the use of herbs and homeopathy during the perinatal period. Primary outcomes that were evaluated included: duration of gestation, maternal nausea, treatment of severe maternal nausea, onset of labour not achieved within 24 hours, duration of labour and perineal pain. Secondary outcomes include: meconium stained liquor, vaginal delivery not achieved within 24 hours, caesarean section, post partum haemorrhage, breast pain and serious neonatal morbidity. Only studies with data in an appropriate format for inclusion formed part of this review.



4.6 Characteristics of included studies

Studies are identified by the author, the year in which it was conducted and its title. The methods used to conduct the study are briefly explained, as well as the participants and the interventions at which the study was aimed evaluating. The outcomes are documented and allocation concealment methods are stated. Notes are added in the event of potential confounders.

Study Identifier: Dove & Johnson(1999). Oral evening primrose oil: its effect on length of pregnancy and selected intrapartum outcomes on low risk nulliparous women

Methods: A retrospective, comparative study comparing women who orally self administered evening primrose oil, and a control group of women who did not.

Participants: The sample was drawn from the records of all nulliparous women registered for care at a free-standing birth center in the northeastern region of the United States between January 1991 and September 1998. The treatment group consisted of 54 women who ingested evening primrose oil during their pregnancies in a standard dose regimen. The control group consisted of 54 women who did not take evening primrose oil during their pregnancy. The study sample was randomly drawn from the population of all women meeting the study's criteria who registered for care at the Center from January 1991 through September 1998.

Interventions: Women who took evening primrose oil in their pregnancies according to a standard dose regimen. The standard dose regimen or prescribed dosage of evening primrose oil was 500mg orally three times per day for 1 week beginning at 37 weeks gestation, then 500 mg orally once per day until labour began. Clients taking evening primrose oil in any other dosage or regimen were excluded from the study.



Outcomes: The primary outcome of the study was to evaluate the effect of evening primrose oil on decreasing length of gestation and labour. Also the study looked at the effect of evening primrose oil on decreasing the incidence of meconium stained liquor, postdates induction, prolonged rupture of membranes, prolonged latent and active phase labour, secondary arrest of dilatation, arrest of descent, vacuum extraction, and caesarean delivery.

Allocation concealment: A purposeful selection of the study group who took evening primrose oil compared to a random selection of women who met the selection criteria but did not ingest any evening primrose oil.

Notes: There were no losses to follow up.

Study Identifier: Garry, Figueroa, Guillaume and Cucco (2000). Use of castor oil in pregnancies at term.

Methods: The study had a prospective evaluation design, comparing women who used castor oil at 40 weeks gestation, and those who did not.

Participants: The inclusion criteria for this study was women with singleton pregnancies, intact membranes and at 40 – 42 weeks gestation. They were referred for antepartum testing from July 1992 - February 1993 at Saint Mary's Hospital in Brooklyn, New York, United States. The study group was composed of 52 women who received the castor oil after meeting study criteria, 51 women who did not receive any castor oil. Exclusion criteria for the study included : ruptured membranes, multiple gestations, oligohydramnios, abnormal fetal heart rates, intrauterine growth retardation, non-cephalic presentation, poor medical histories and those with present medical complications.

Interventions: Women who received a single oral dose of castor oil. The castor oil was administered as a 60 ml dose diluted in orange or apple juice. Castor oil was considered successful if labour began within 24 hours of dosing.

Outcomes: Castor oil as a labour induction agent. Groups were compared for onset of labour in 24 hours, method of delivery, presence of meconium stained fluid, Apgar score and birth weight.

Allocation concealment: The method used was alternate assignment either to a treatment or control group.

Notes: No losses to follow up. Small sample size.

Study Identifier: Hofmeyer, Piccioni & Blauhof (1990). Postpartum homeopathic *Arnica Montana*: a potency finding pilot study.

Methods: Double blind, randomized control trial

Participants: The study sample consisted of 37 women in the Arnica D6 treatment group and 39 in the Arnica D30 treatment group (total in treatment group=76). The placebo group consisted of 85 women. Inclusion criteria were women with episiotomy or perineal tearing that required suturing, post delivery. The trial took place at the Johannesburg Hospital, Johannesburg, South Africa.

Interventions: Lactulose tablets impregnated with Arnica D6 or Arnica D30. The dosage was spread over a five day period. Three tablets were to be consumed four hourly for two day, and then the same dosage three times daily for three days. The precise dosage and pharmacological preparation of the placebo was not described.

Outcomes: Arnica D6 and D30 in promoting perineal healing, following injury to the perineum during delivery. Specific outcomes measured were separated into two categories, the physical appearance of the perineum on day four, and the subjective replies of the women, as obtained from a questionnaire. The perineal appearance outcomes were: bruising, presence of oedema, inflammation of sutures, presence of infection, and healing. Subjective outcomes included: level of perineal pain, level of breast pain and state of emotion (happy/unhappy).

Allocation concealment: The containers with the medication were labeled with sequential numbers using random table allocation, ratio 1:1:2, and no other means of identification was used. The code was placed in a sealed envelope, and only opened once the trial was completed.

Notes: Small sample size. Precise pharmacology of placebo is not described, but it is stated that the placebo is not medicated. The results from one participant could not be obtained and so she was withdrawn from the study.

Study Identifier: Ingram (2003). The effect of caulophyllum on the length of labour.

Methods: Randomised, double blind, control trial.

Participants: The study sample consisted of a total of 35 women. Due to the random nature of the study, there were uneven numbers of women in the placebo and treatment group. Twenty four patients formed the treatment group, and 11 were in the placebo group. The study was conducted from August 2002 to March 2003 at two midwife-run units in Gauteng, South Africa.

Interventions: The ingested herbal remedy in this study consists of single caulophyllum or placebo globules. The globules were to be used sub-lingually (under the tongue). The initial dosage was to be taken as soon as contractions were five minutes apart. The dosage of four tablets sublingually was to be repeated hourly until the patient delivered.



Outcomes: The primary outcome measured was length of labour. Secondary outcomes included the mother's need for pain control, and the resuscitation scoring of the infant at one and five minutes after birth.

Allocation concealment: A double blind method was used. The researcher and the participants were both unaware whether it was the placebo or treatment being administered. Allocation was done in sealed, opaque envelopes.

Notes: Small sample size.

Study Identifier: Mabina, Pitsoe & Moodley (1997). The effect of traditional herbal medicines on pregnancy outcome: The King Edward VIII Hospital experience.

Methods: Retrospective comparative study.

Participants: The study sample consisted of a total of 229 women, presenting in early labour. 126 women formed the study group, and were selected on the basis of a positive history of herbal ingestion. 103 women (control group) had a negative history of herbal ingestion. The study was conducted from January to June 1994, at the King Edward Hospital, Kwa Zulu Natal, South Africa.

Interventions: Ingestion of a herbal product, primarily *isihlambezo*.

Outcomes: Outcomes measured were fetal distress, meconium stained liquor, poor progress, cephalopelvic disproportion, the rate of caesarean section and the rate of vaginal deliveries between the study and the control group.

Allocation concealment: A control group was used. Participants in early labour were interviewed. The allocation of the groups to a control or treatment group depended on whether participants had ingested *isihlambezo* or not.

Notes: Small sample size.

Study Identifier: Olsen (1992). Randomised controlled trial of effect of fish oil supplementation on pregnancy duration

Methods: The study was a randomized controlled trial. The study included a group of women who received a prescribed dosage of fish oil supplement in capsule form, a control group who received olive oil capsules as a placebo, and a second control group who received no treatment.

Participants: Of 868 women approached, 553 women took part in the study. The three study groups were similar at trial entry. Women were recruited at 30 weeks gestation. At a post delivery interview, 202 (78%) of women in the fish oil

group and 97 (75%) in the olive-oil group said they took the prescribed dosage of four capsules per day, 9% of each group said they took three or fewer capsules per day, and for 69% (n=402) women, the compliance was unknown. The trial was based in Aarhus, Denmark, at the main midwifery clinic in the area.

Interventions: The active treatment was four 1g gelatin capsules daily containing fish oil, one control group received four 1g capsules of olive oil daily, and the second control group received no treatment.

Outcomes: Fish oil to increase duration of gestation and birthweight.

Allocation concealment: A sealed, opaque envelope contained a randomization number that decided a woman should either receive no treatment or a particular package of oil capsules. Capsules were coloured and the capsules and the boxes looked identical for both fish oil and olive oil. As soon as an eligible woman had agreed to join the study, her name was written in a book beside the next available study number.

Study Identifier: Simpson (2001). Raspberry leaf in pregnancy: its safety and efficacy in labour.

Methods: A randomized, double blind, placebo controlled trial. The study included a group of women who took the tablet form of the raspberry leaf herb and the control group who received a placebo tablet.

Participants: 192 women took part in this study. 96 were the raspberry leaf group and 96 women formed the control group. The study was undertaken at major tertiary referral hospital in Sydney, Australia between May 1999 and February 2000. Criteria for entry to the study included nulliparity, with low risk, health pregnancies, and having a doctors approval certificate to participate.

Interventions: 1.2 g or raspberry leaf extract per raspberry leaf tablet. All participants were directed to take two tablets per day from 32 weeks of gestation, until commencement of established labour. The women were asked to ingest the tablets with food, and not to consume any additional form of raspberry leaf while participating in the study.

Outcomes: To explore the effect of the raspberry leaf herb on labor and birth outcomes

Allocation concealment: The raspberry leaf and the placebo tablets were contained in individual, dark brown bottles that were identical in appearance. The randomized bottles were administered in numerical sequential order to either the control or placebo group.

Notes: The original number of participants in the study numbered 240. 48 participants were lost due to: medical advice, complaining of side effects or other non-specific reasons. Both women who complained of side effects belonged to the placebo group.

Study Identifier: Vutyavanich, Kraissarin & Ruangsri (2001). Ginger for nausea and vomiting in pregnancy: randomized, double masked, placebo controlled trial.

Methods: During a five month period, 70 women who were eligible to participate in the trial were randomized in a double masked design to receive either oral ginger 1g daily or an identical placebo, both for four days.

Participants: The study was conducted in the Maharaj Nakorn Chiang Mai University Hospital in Chiang Mai, Thailand. Clients were included in the study if they first attended the clinic before 17 weeks gestation and had nausea of pregnancy, with or without vomiting. They were excluded if the nausea and vomiting were not pregnancy-related (due to previous medical or surgical

disorders, or associated with medication usage), if they were disadvantaged due to language barriers, unable to comply with the treatment regimen or unable/unwilling to give consent.

Interventions: One 250mg capsule of ginger three times daily after meals and one capsule before bedtime for four days. Those in the placebo group received identical capsules according to the same regimen.

Outcomes: Severity of nausea according to visual Lickert scale, number of vomiting episodes, side effects. Secondary outcome measures include adverse effects on pregnancy outcome.

Allocation concealment: Before the trial began, a research nurse who was not responsible for patient care used a table of random numbers to prepare the treatment assignment. The treatment codes were kept sequentially in a sealed opaque black envelope. As each participant entered the trial, she received an envelope that determined her treatment regimen. The list of treatment codes were kept strictly confidential by the research nurse, and was not accessible to the physicians. The physicians as well as the patients did not know the identity of the drug administered.

Notes: Three participants were lost during the study. They all belonged to the placebo group and did not show up for the follow-up visits, and so were lost from the study.

4.7 Characteristics of excluded studies

Study Identifier: Beer & Heiliger (1999). Randomised, double blind trial of Caulophyllum D4 for induction of labour after premature rupture of membranes at term.

Methods: Double blind placebo controlled trial

Participants: The study sample included forty women with premature rupture of membranes, with a gestational age of 38 – 42 weeks. These women were not in labour. The study group was composed of 20 women and the control group of 20 women. Baseline characteristics that were taken indicate that there were no differences between the age, weight, height and cervical score at trial entry and at the time that premature rupture of membranes occurred. The study was conducted in Germany.

Interventions: A 250 mg tablet of Caulophyllum trituration D4, magnesium stearate and wheat starch. The placebo contained 250 mg no active ingredients but a combination of wheat starch and magnesium stearate. The tablets were administered hourly for a period of seven hours.

Outcomes: The primary outcome of the study was to evaluate the time taken to the onset of regular uterine contractions. Labour and delivery outcomes were also assessed, as well as the incidence of maternal and neonatal infection.

Allocation concealment: The method of allocation concealment is unclear.

Notes: There were no losses to follow up. Sample size is small. No calculation of sample size was included.

Reason for exclusion: Data was not in an appropriate format for inclusion in the review.

Study Identifier: Boris, Jensen, Salvig, Secher & Olsen (2004). A randomised controlled trial of the effect of fish oil supplementation in late pregnancy and early lactation on the n-3 fatty acid content in human breast milk.

Methods: Randomised controlled trial.

Participants: 44 women participated in the study. The study was conducted in Aarhus C, Denmark. Inclusion criteria for the study were healthy, gravid women from 30 weeks gestation, who were willing to give samples of their breast milk at day four, 16 and 30 postpartum.

Interventions: The treatment group ingested 1.3 g EPA and 0.9 g DHA once daily from week 30 of gestation to delivery or 30 days post delivery. The control group was randomly assigned to either olive oil or no oil ingestion.

Outcomes: n-3 fatty acid content in samples of breast milk.

Allocation concealment: Participants were randomly allocated to a treatment or control group.

Reason for exclusion: Data was published after analyses was done for the review. Article was published in December 2004.

Study Identifier: Dorfman, Laserre and Tetau (1987). Homeopathic preparation for labour: two fold experiment comparing a less widely known therapy with a placebo.

Methods: Double blind placebo controlled trial.

Participants: A total of ninety three women participated in the trial. They were all at thirty six weeks gestation. Forty three women were randomly allocated to the study group and forty to the control group. Exclusion criteria for the trial included women with a poor obstetric history, a current history of hypertension, previous caesarean section, diabetes, or cephalo-pelvic disproportion. The trial took place in France.

Interventions: Five homeopathic remedies, caulophyllum, arnica, actea racemosa, pulsatilla and geranium. Three granules were administered twice daily, morning and evening from 36 weeks gestation. The same dosage (three granules) was continued when the woman commenced labour, but the frequency was changed to every fifteen minutes for the first two hours of labour, until the woman was comfortable. The precise dosage and pharmacological preparation of the placebo was not described.

Outcomes: The primary outcome that the trial measured was the average length of labour, and the difficulty of labour.

Allocation concealment: The method of allocation concealment is unclear.

Notes: The sample size was not calculated, and there were no losses to follow up.



Reason for exclusion: Data was not in an appropriate format for inclusion in the review.

Study Identifier: Fischer-Rasmussen, Kjaer, Dahl & Asping (1991). Ginger treatment of hyperemesis gravidarum.

Methods: Double blind randomised cross over trial.

Participants: The study was conducted at Hvidovre Hospital, Denmark. 30 women were recruited to participate in the trial. Three participants had to be withdrawn.

Interventions: 250 mg ginger four times daily in the treatment group. Lactose tablets were administered to the control group, also four times daily. Both groups took the treatment over a period of four days.

Outcomes: Severity of nausea

Allocation concealment: Participants were randomly allocated to a treatment or control group.

Reason for exclusion: Format of data. The data was not in an appropriate format for inclusion in the review.

Study Identifier: Shelton (1980). Standardised senna in the management of constipation in the puerperium: A clinical trial.

Methods: A randomised controlled clinical trial

Participants: Trial took place in South Africa. Participants were separated by race into 'white' and 'coloured' groups.



Interventions: Ingestion of standardised senna tablets, or placebo

Outcomes: Constipation in the puerperium

Allocation concealment: The method of random allocation is not adequately described.

Reason for exclusion: Data is not in an appropriate format for inclusion in the review.

Study Identifier: Sripramote & Lekhyananda (2003). A randomised comparison of ginger and vitamin B6 in the treatment of nausea and vomiting of pregnancy.

Methods: A randomised double blind controlled trial.

Participants: The study took place at Vajira Hospital in Bangkok, Thailand. Women pregnancy related nausea or vomiting at or before 16 weeks of gestation with no medical complications, were not hospitalised, and were able to attend a follow up visit after one week were included in the trial. 138 women participated in the study.

Interventions: The treatment group ingested 500 mg of ginger(one capsule) three times daily for three days. 10 mg of Vitamin B6 was administered to the control group, also one capsule, three times daily for three days. Both capsules were identical.

Outcomes: Severity of nausea and number of vomiting episodes during the three days of treatment.

Allocation concealment: Participants were randomly allocated to either a control or treatment group.



Reason for exclusion: Data is in an inappropriate format for inclusion in the review.

Study Identifier: Strandberg, Jarvenpaa, Vanhansen & McKeigue (2001). Birth outcome in relation to liquorice consumption during pregnancy.

Methods: A retrospective comparative study. Glycyrrhizin (liquorice) intake was measured through a detailed questionnaire, and data for the outcomes measured were obtained from the clients hospital records. Between March and November 1998 the questionnaires were administered at the Helsinki City Maternity Hospital in Helsinki, Finland. This hospital is the principal maternity hospital in Helsinki.

Participants: Participants with singleton, healthy births, where both parents were of Finnish origin, were encouraged to participate. A total of 1, 049 mothers completed the questionnaire to estimate their liquorice intake.

Interventions: Low, high or medium level intake of glycyrrhizin during pregnancy. Low intake was defined as <250 mg/week of glycyrrhizin, medium intake was defined as 250 – 499 mg of glycyrrhizin/week, and high intake was more than, or equal to 500 mg or glycyrrhizin/ week.

Outcomes: The effect of liquorice on birth weight and mean duration of gestation.

Allocation concealment: A retrospective comparative study of women who ingested different levels of glycyrrhizin per week.

Reason for exclusion: Format of data. The data was not in an appropriate format for inclusion in the review.



Study Identifier: Willets, Ekangaki & Eden (2003). Effect of ginger extract on pregnancy induced nausea: a randomised controlled trial.

Methods: Double blind randomised placebo controlled trial

Participants: Trial took place at the Royal Hospital for Women, Randwick, New South Wales, Australia. 120 women at less than 20 weeks gestation who presented with morning sickness daily at least for one week, and experienced no relief through dietary changes were included in trial.

Interventions: 125 mg of ginger extract or a placebo given four times daily for four days to the treatment and control group respectively.

Outcomes: Nausea, vomiting and retching

Allocation concealment: Random allocation of participants to either a treatment or control group.

Reason for exclusion: Format of data. Data is in an inappropriate format for inclusion in the review.

4.8 Outcomes

All outcomes relevant to herbal and homeopathic ingestion during the perinatal period, in the primary studies were collated. The outcomes were grouped according to the effects of treatment on pregnancy-related problems. The categories were as follows:

- Effects of treatment for nausea in pregnancy
- Effects of treatment for induction and augmentation of labour
- Effects of treatment for perineal pain, post delivery

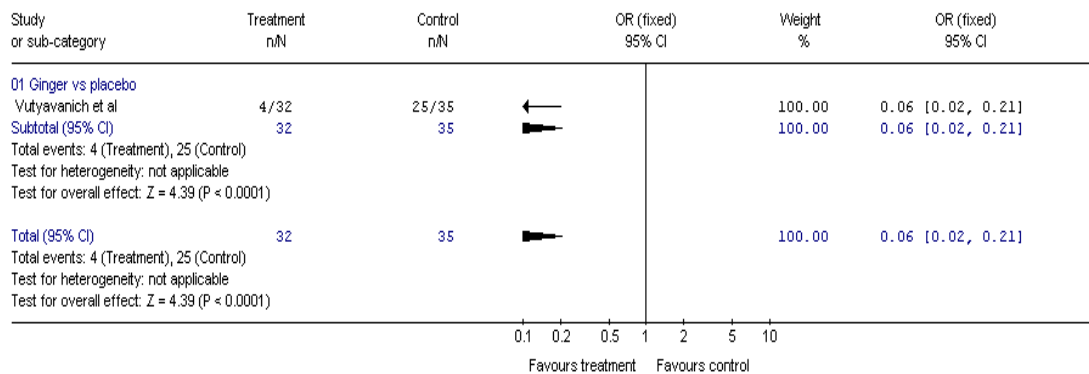


Data was processed by the RevMan programme.

4.9 Effects of treatment for nausea in pregnancy

4.9.1 Severe nausea

Review: A systematic review of ingested natural (homeopathy / herbal) remedies for use during the perinatal period
 Comparison: 01 Natural remedy versus placebo or control
 Outcome: 01 Severe nausea

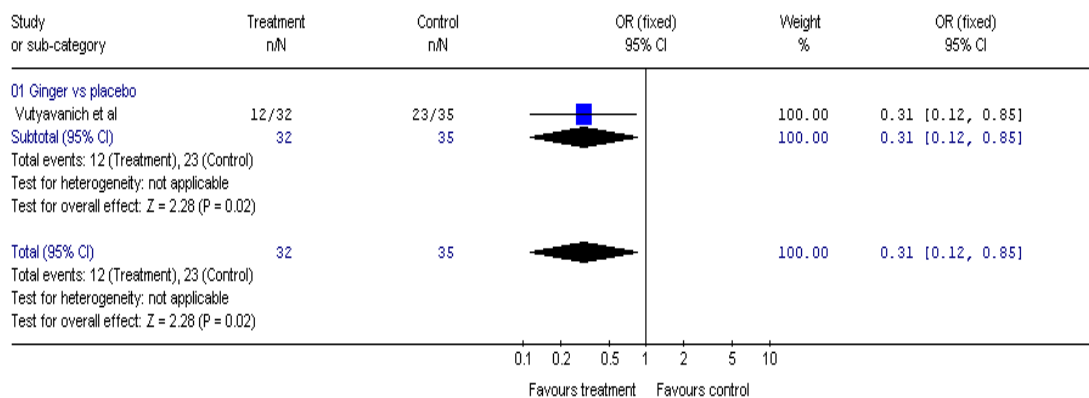


Ginger versus placebo favours the treatment group. The results of this forest plot show that ingested ginger has an overall significant effect in reducing severe nausea during pregnancy (P=0.0001).



4.9.2 Vomiting episodes on day four of treatment

Review: A systematic review of ingested natural (homeopathy / herbal) remedies for use during the perinatal period
 Comparison: 01 Natural remedy versus placebo or control
 Outcome: 02 Vomiting episodes on day 4 of treatment

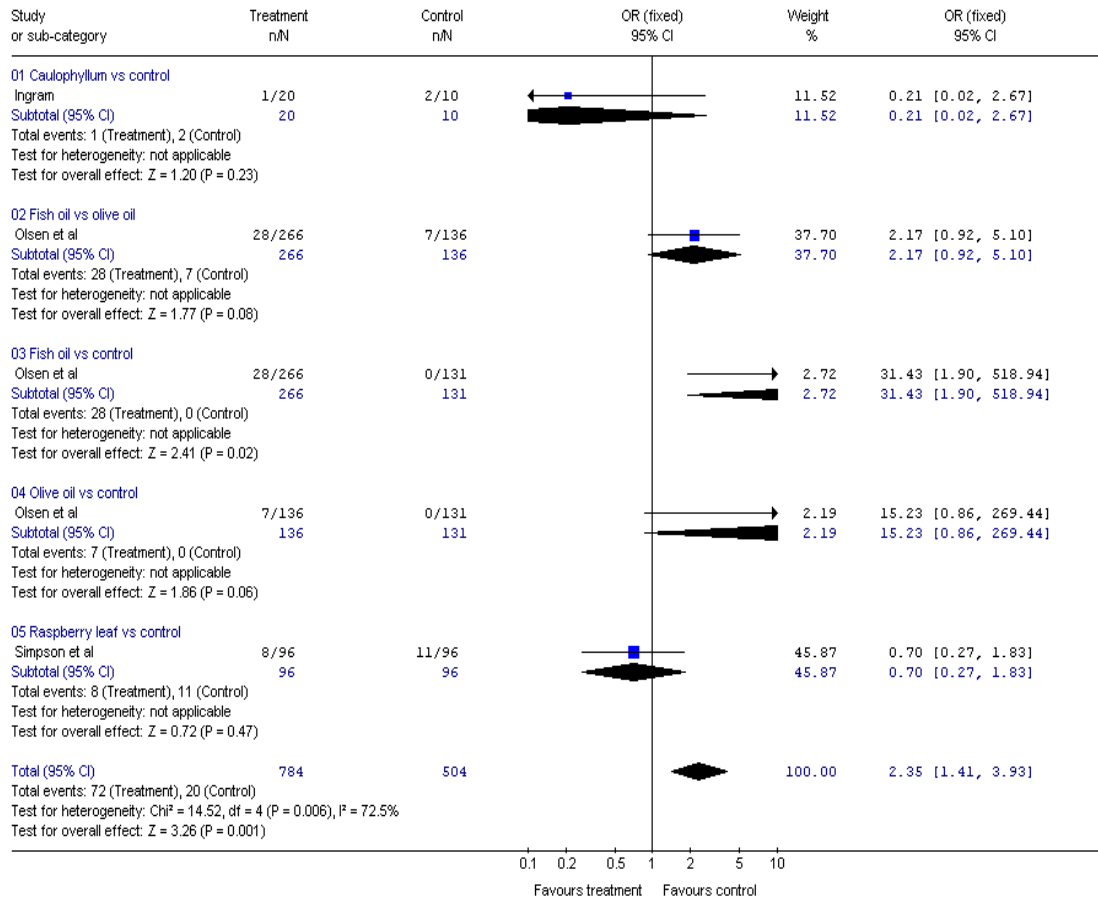


In comparing the number of vomiting episodes between the treatment and control groups, ginger versus placebo favours treatment (P=0.02).

4.10 Effect of treatment for duration of gestation, induction or length of labour

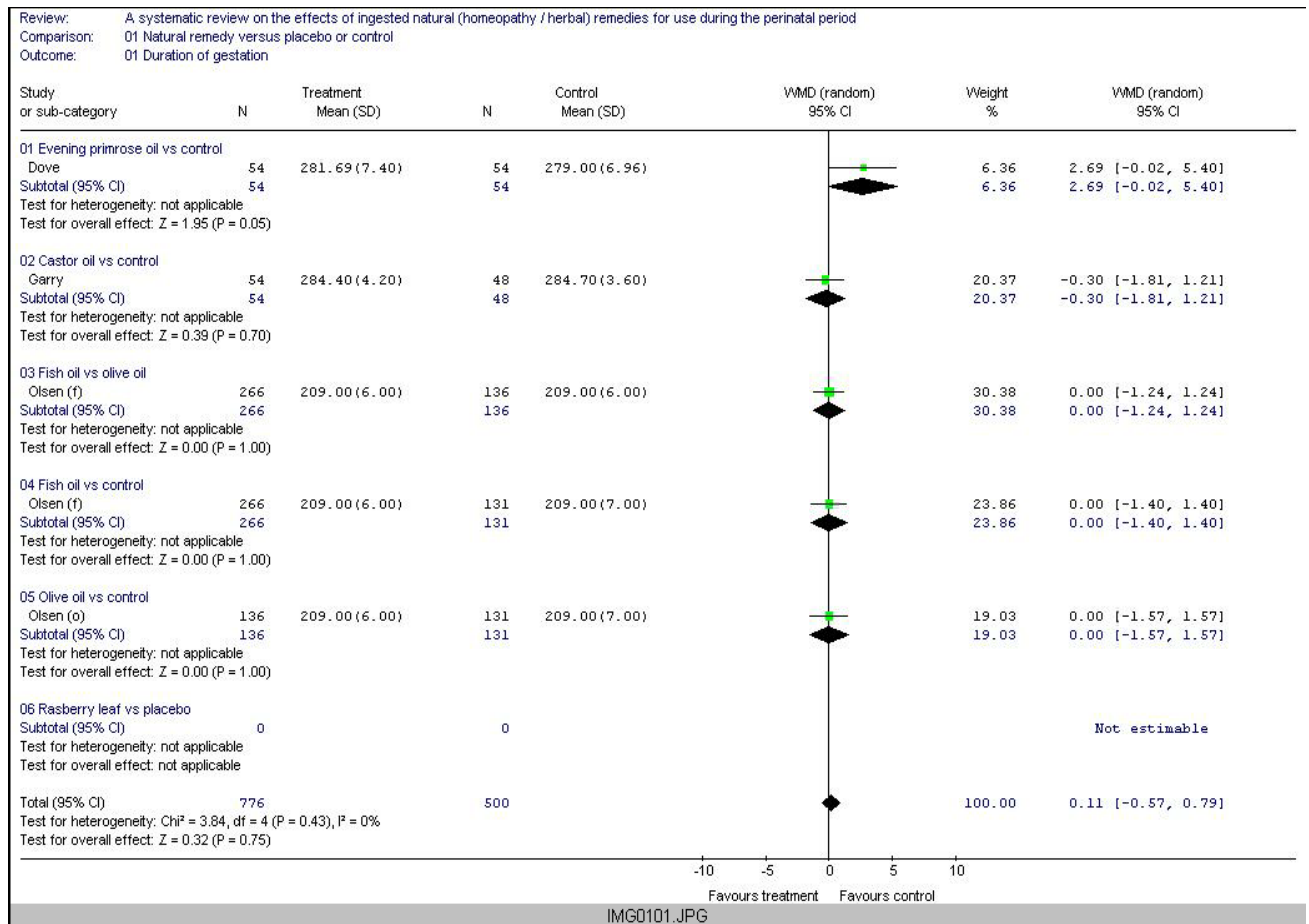
4.10.1 Maternal nausea

Review: A systematic review on the effects of ingested natural (herbal / homeopathic) remedies for use during the perinatal period
 Comparison: 01 Natural remedy versus placebo or control
 Outcome: 02 Maternal nausea



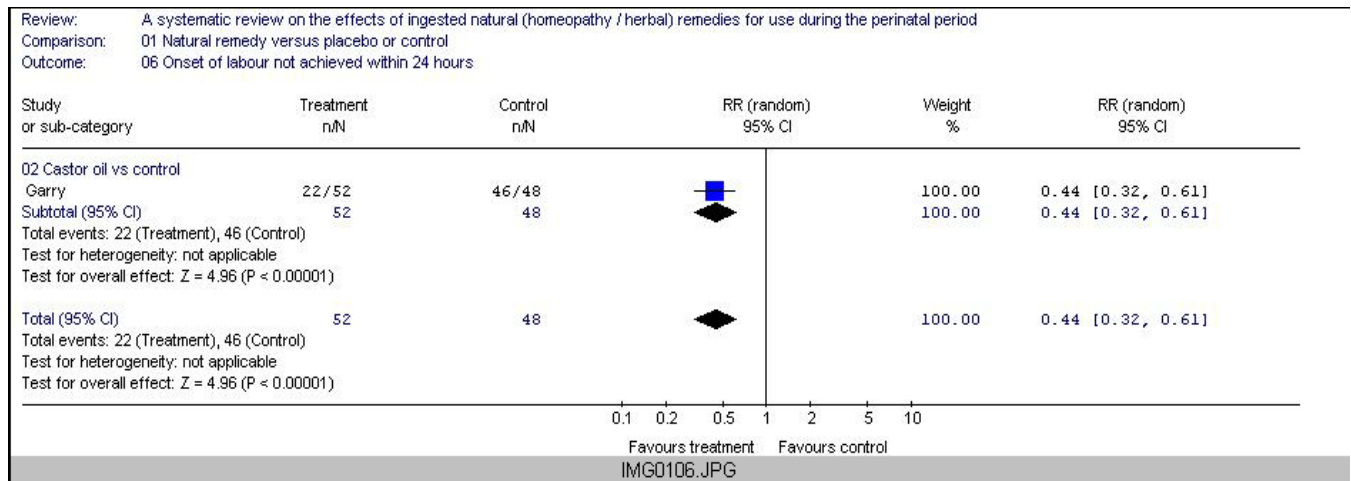
For the intervention duration of gestation, induction or length of labour, maternal nausea was reported as a side effect. Significantly fewer mothers in the control group experienced nausea as a side effect.

4.10.2 Duration of gestation



When we look at ingested herbs used for duration of gestation, induction or length of labour we found that ingested herbs had no effect on duration of gestation

4.10.3 Onset of labour not achieved within 24 hours

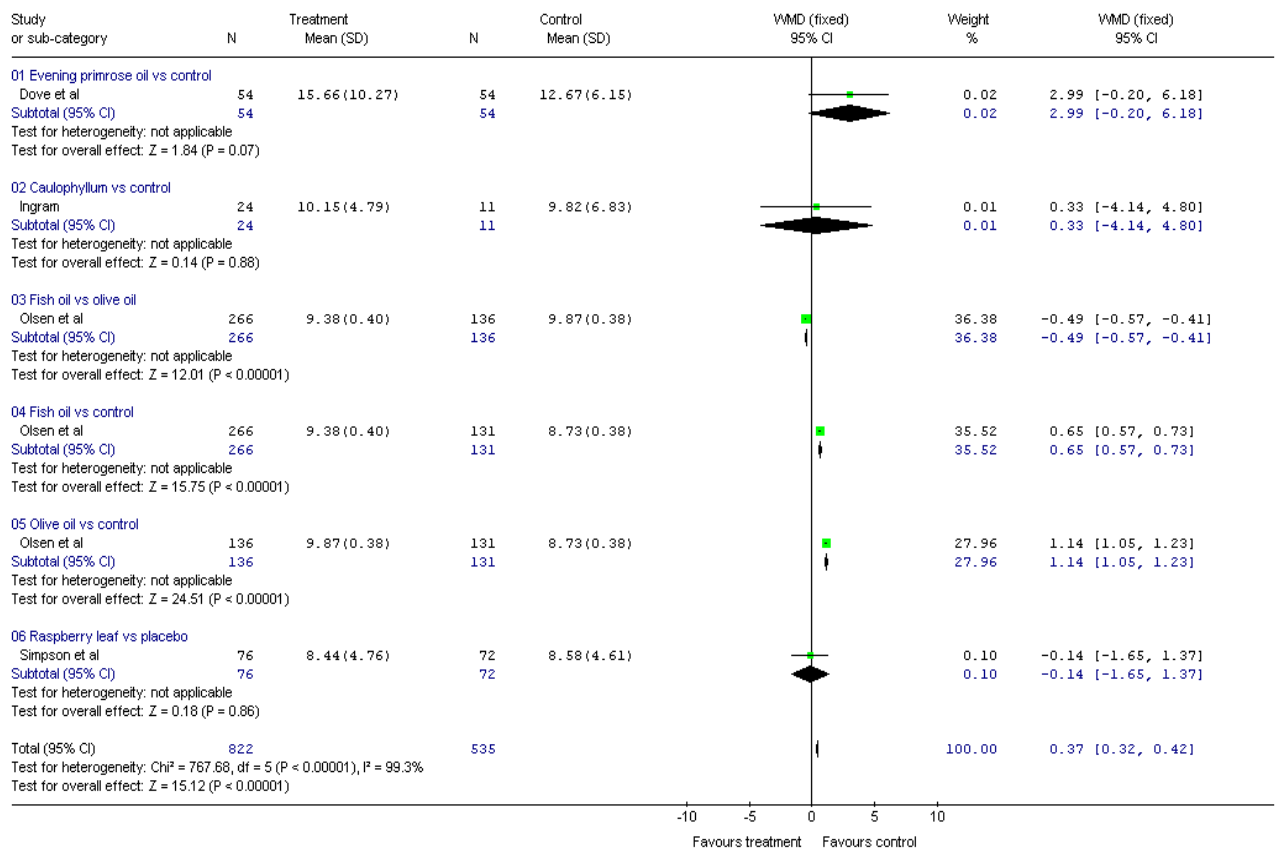


Castor oil has a significant effect when used to induce labour. More women in the control group did not achieve labour within 24 hours of ingesting the remedy.



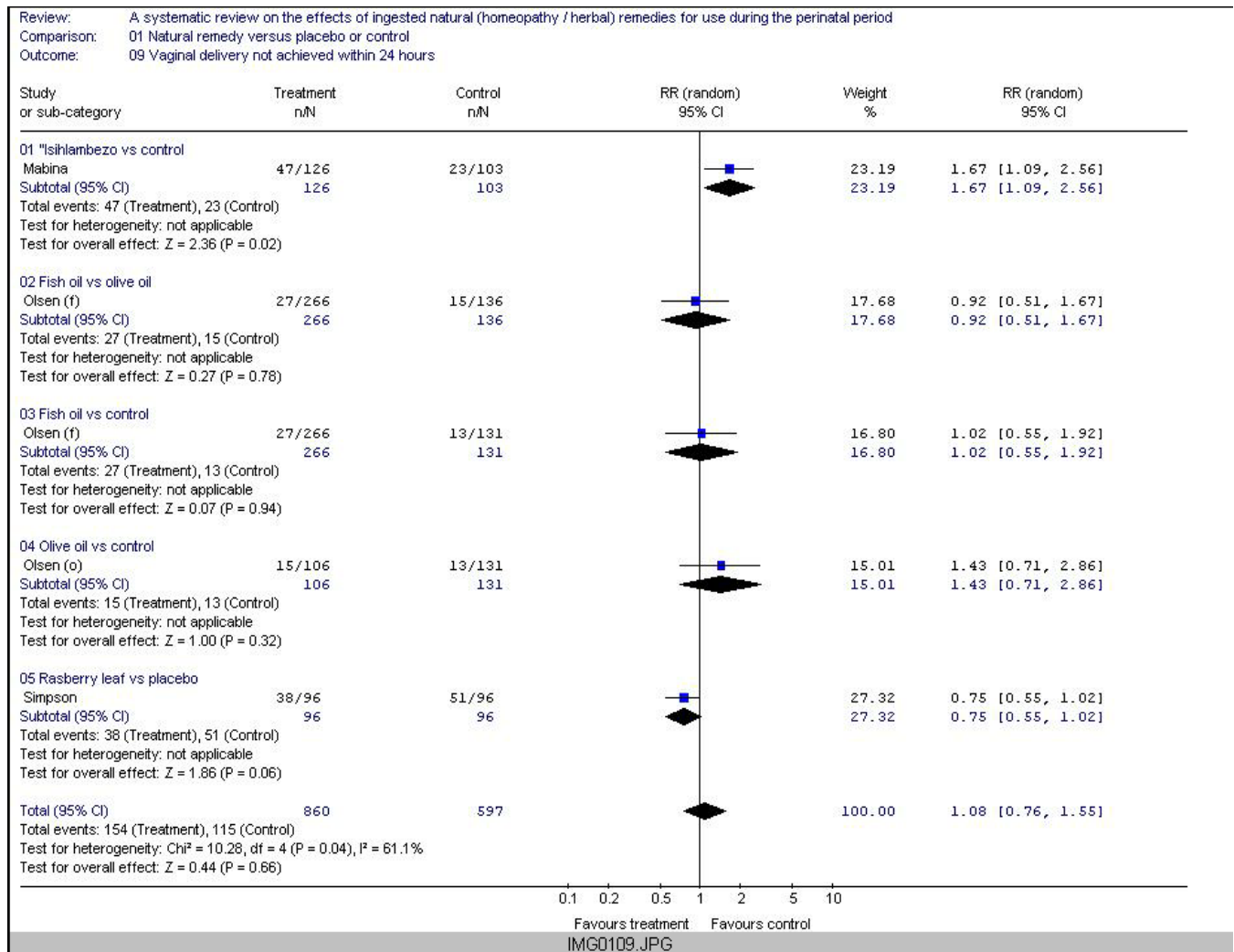
4.10.4 Duration of labour

Review: A systematic review on the effects of ingested natural (herbal / homeopathic) remedies for use during the perinatal period
 Comparison: 01 Natural remedy versus placebo or control
 Outcome: 10 Duration of labour



Ingested remedies did not decrease the length of labour. The duration of labour in the control group is significantly shorter.

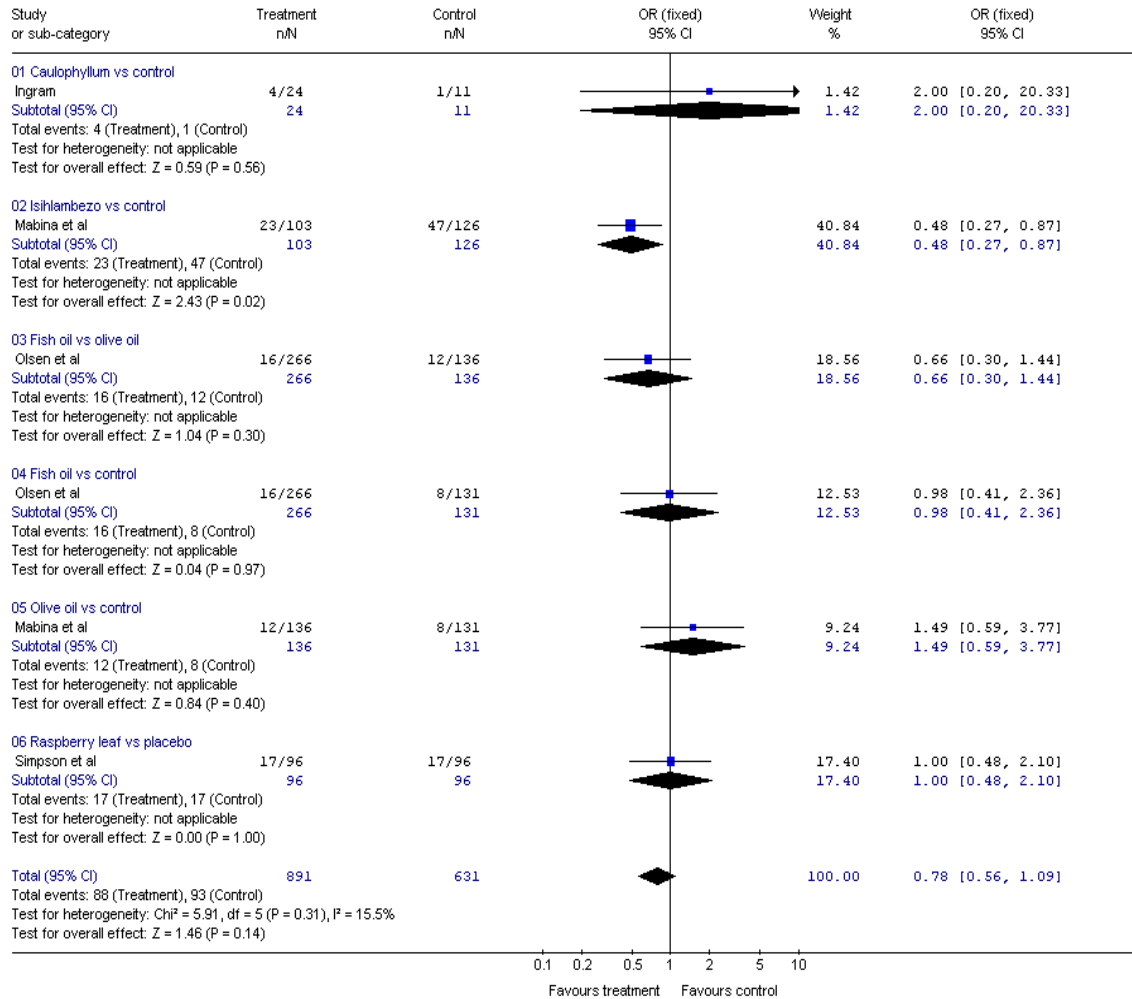
4.10.5 Vaginal delivery not achieved within 24 hours



Fewer women in the treatment group (ingested herbal remedy) did not achieve vaginal delivery within 24 hours. Ingestion of raspberry leaf, fish oil, *isihlambezo* and olive oil do not assist in achieving delivery within 24 hours. Slightly more women deliver before 24 hours in the control group.

4.10.6 Caesarean section

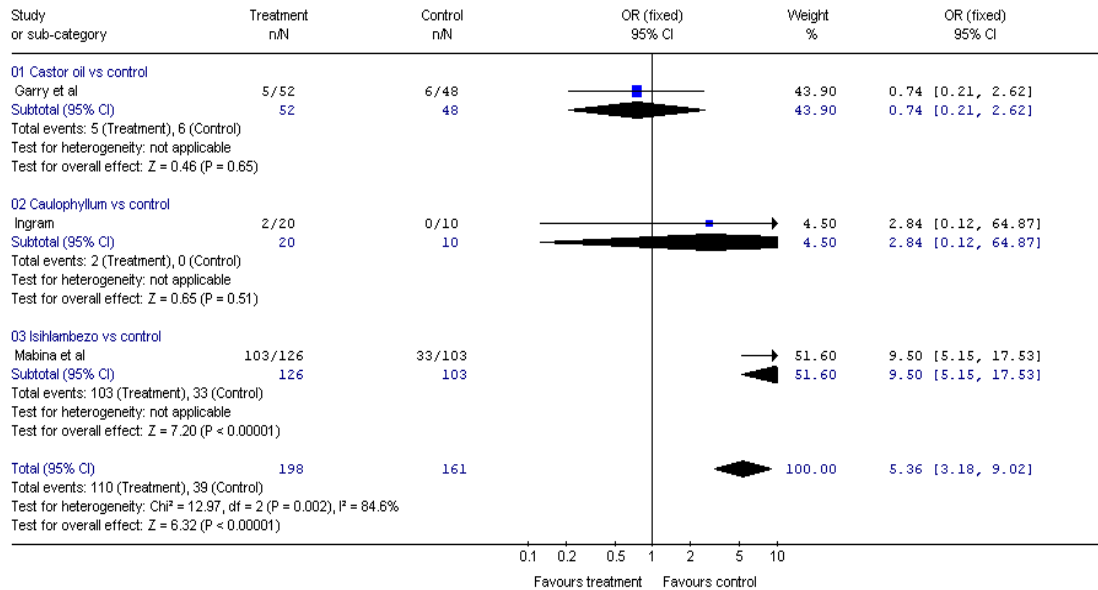
Review: A systematic review on the effects of ingested natural (herbal / homeopathic) remedies for use during the perinatal period
 Comparison: 01 Natural remedy versus placebo or control
 Outcome: 12 Caesarean section



Fewer women who ingest *isihlambezo*, fish oil, caulophyllum and olive oil receive caesarean sections.

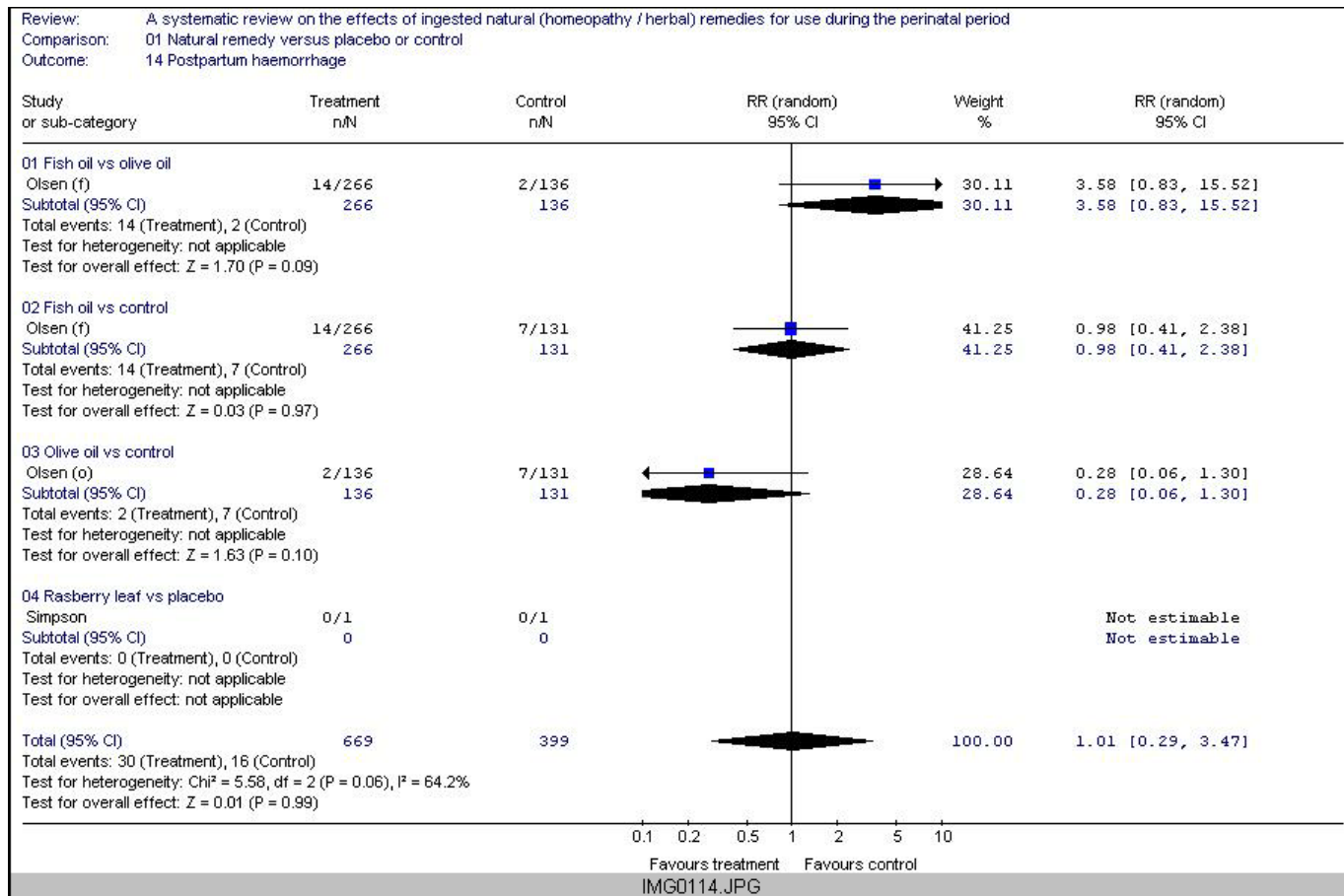
4.10.7 Meconium stained liquor

Review: A systematic review on the effects of ingested natural (herbal / homeopathic) remedies for use during the perinatal period
 Comparison: 01 Natural remedy versus placebo or control
 Outcome: 08 Meconium stained liquor



There is a significant increase of meconium stained liquor in mothers who have ingested castor oil, caulophyllum and *isihlambezo*. Nearly two thirds of the women in the treatment group experience meconium stained liquor.

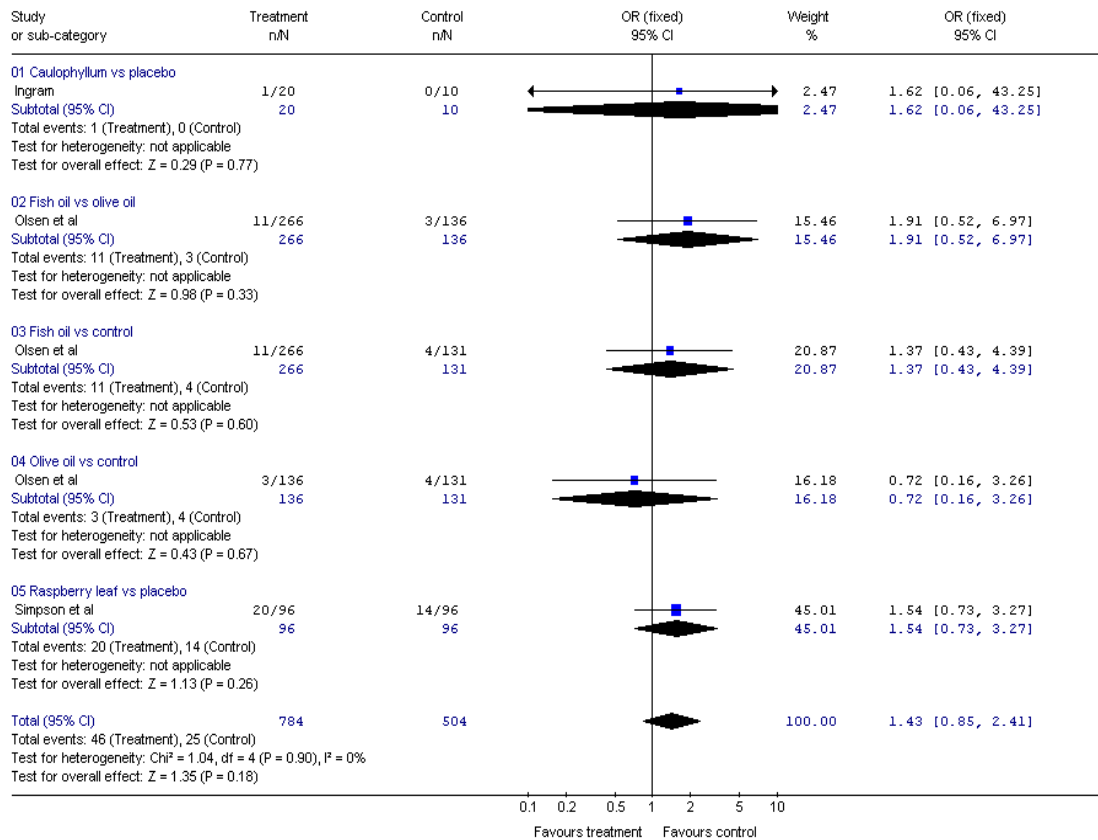
4.10.8 Postpartum haemorrhage



Ingestion of fish oil, raspberry leaf and olive oil has no effect on the incidence of post partum haemorrhage.

4.10.9 Serious neonatal morbidity (Apgar 1<7, fetal distress, birth asphyxia, NICU, congenital abnormalities)

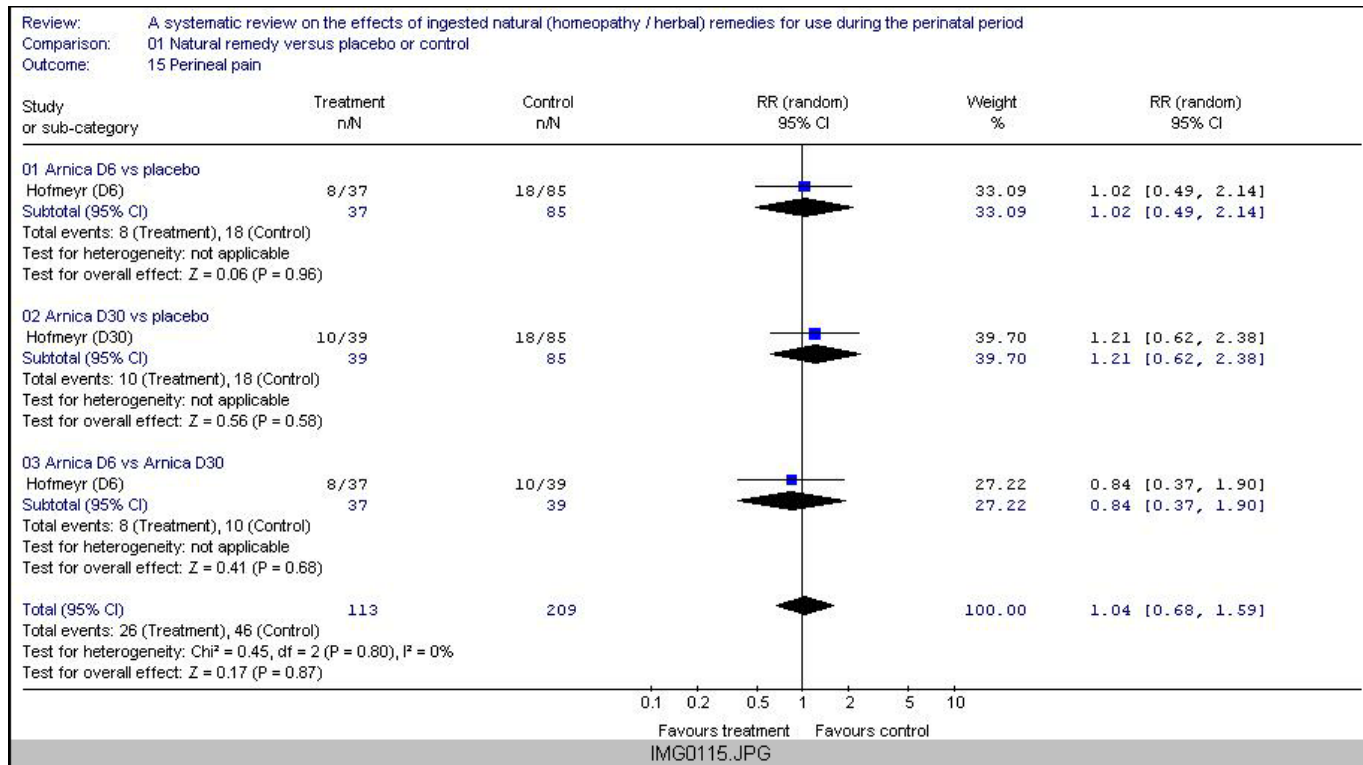
Review: A systematic review on the effects of ingested natural (herbal / homeopathic) remedies for use during the perinatal period
 Comparison: 01 Natural remedy versus placebo or control
 Outcome: 19 Serious neonatal morbidity (Apgar 1<7, fetal distress, birth asphyxia, NICU, congenital abnormalities)



There is a tendency that caulophyllum, fish oil, olive oil, and raspberry leaf have a negative effect in the neonate as fewer infants in the control group experience neonatal morbidity.

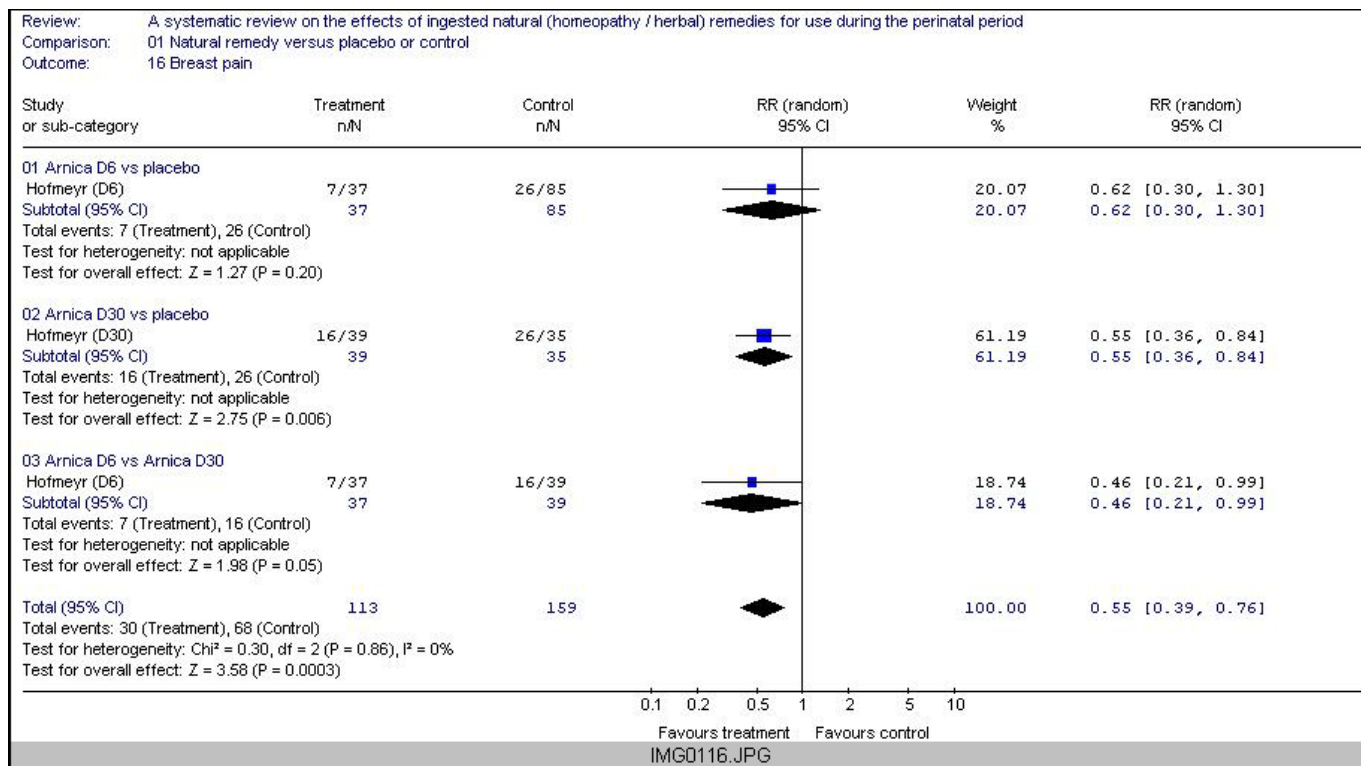
4.11 Effects of treatment for perineal pain, post delivery

4.11.1 Perineal pain



This small study showed that ingested arnica does not relieve perineal pain.

4.11.2 Breast pain



Although the original intention to treat was ingested arnica to relieve perineal pain, it appears to have a significant benefit in that it significantly reduces breast pain.

4.12 Summary results

Only studies that used an experimental or control group were included in this review. Sample sizes for the studies in this review were small, and only nine studies were used. All trials did not use the same method of randomisation, and looked at different outcomes. From this review a clear conclusion regarding the efficacy or side effect of ingested herbal remedies cannot be formulated. We can conclude that ginger is efficacious in the treatment of nausea and vomiting during pregnancy, castor oil has a significant effect in initiating labour within 24 hours of

ingestion, and that arnica has significantly relieves breast pain post delivery. Caution should still be exercised before these remedies are used, due to the small studies reviewed.



Chapter Five: Discussion

5.1. Introduction

Increasingly, systematic reviews of research are being viewed as providing the most reliable conclusions about treatment effects. Meta-analysis displays either a beneficial effect, no effect or a harmful side effect of a particular treatment. Most meta-analyses display no effect of a particular treatment. This leaves the implication that further research would need to be done in order to provide the evidence required. Systematic reviews set the results of individual studies in the context of similar, but separate research papers, in a manner that reduces bias and the play of chance. Differences in outcome of a treatment comparison may simply be due to the play of chance, especially if the numbers of patients involved in the study are small and the treatment outcomes of interest are rare. The collation of studies using meta-analysis, can reduce the play of chance, and lead to more optimal clinical decision-making (The James Lind Library, 2004).



Starting with new tests of medical treatments without first consulting the material that has been systematically reviewed, which, apart from being unethical, could have dangerous consequences for the patient. For example, between the 1960's and early 1980's, more than 50 drug trials were run on drugs that reduced heart rhythm abnormalities in patients experiencing myocardial infarction (heart attacks). It was only realized later that these drugs were actually fatal. If the evidence regarding the effects of these drugs had to meta-analysed, many deaths could have been avoided (The James Lind Library, 2004).

A systematic review sets out to find the effect of an intervention. This systematic review evaluates the effect of ingested herbal remedies during the perinatal period. The review focused specifically on maternal and neonatal outcomes of ingested herbal remedies only. Remedies that are applied to the skin, or utilized in other ways were excluded in order to narrow the research.

This chapter includes a discussion of the findings, the reviewer's conclusion and some suggestions for the implications for research.

5.2 Discussion

The findings of this systematic review were compared to the findings of other research articles and scientific publications. The results of the current systematic review showed that most herbal remedies had a non-significant effect. Some remedies were however shown to be efficacious.

For the treatment of nausea of vomiting in pregnancy, the literature suggests that all forms of ginger can be efficacious. In a retrospective comparative study by Portnoi, Chng, Karimi Tabesh, Koren, Tan & Einarson (2003:1374,1376), participants ingested all forms of ginger, including ginger tea, capsules, fresh ginger, ginger cookies, crystals and sugared ginger and inhaled powdered ginger. The results of the study show that ginger was more effective for the treatment of nausea during pregnancy than other anti emetic preparations (exact nature of preparations are not known). Reported adverse events between the ginger and control group were not statistically significant. The study concluded that ginger has a mild effect for the treatment of nausea and vomiting in pregnancy (Portnoi et al, 2003: 1374).

This corresponds with another article, a randomized controlled study on the treatment of hyperemesis gravidarum with ingested ginger (Fischer-Rasmussen, Kjaer, Dahl & Asping, 1991:163). No adverse events were observed. The study concluded that ginger was better than a placebo for the treatment of hyperemesis gravidarum. (Fischer- Rasmussen, Kjaer, Dahl & Asping, 1991:163). In a randomized comparison of ginger and vitamin B6, there was no difference between ginger and Vitamin B6 for the treatment of nausea and vomiting of pregnancy, but both were shown to be efficacious treatments with mild, but not statistically significant side effects (Sripramote & Lekhayananda, 2003: 846).

The dosage of ginger differs between studies. The manner in which the ginger is prepared for ingestion and the harvesting of the ginger rhizome contribute to the efficacy of ginger as an intervention (Vutyavanich et al, 2001:581). Methods of preparation for ingestion include tea, capsules, powdered, sugared crystals, inhaled, cookies and fresh ginger (Portnoi et al, 2003: 1376). The three articles referred to before confirm the findings of the review. Ginger is efficacious for the treatment of nausea and vomiting of pregnancy, with no significant maternal or neonatal adverse events reported. Relief of nausea symptoms and decrease in vomiting episodes have been attributed to the ingestion of ginger in the review.

Castor oil, caulophyllum, fish oil, olive oil, evening primrose oil, *isihlambezo* and raspberry leaf were all evaluated in this review, in relation to different outcomes, as treatments for duration of gestation, induction or length of labour. Castor oil was reported to be an effective induction agent by Garry (2000:78), but was shown to have no statistically significant effect on duration of gestation in the meta-analyses done in the current review. Olive oil, castor oil, evening primrose oil, fish oil and raspberry leaf were shown to have no effect on duration of gestation in this review. In relation to length of labour, ingestion of evening primrose oil, fish oil, olive oil, raspberry leaf and caulophyllum, did not decrease length of labour in this review. As an induction agent, the review displayed that castor oil did indeed have a significant effect. The Cochrane Review on castor oil concluded that more research would need to be done in order to prove the efficacy of castor oil as induction agent. Data on maternal and neonatal mortality was not presented (Kelly, Kavanagh and Thomas, 2004). The results of the meta-analyses of the current review, supports the Cochrane review by Kelly et al (2004).

The ingestion of castor oil has been associated with various maternal and neonatal side effects, and have been recorded in case reports. Amniotic fluid embolism was on significant condition reported in a woman that had ingested castor oil during pregnancy, but a direct cause-effect relationship between the embolism and ingestion of castor oil was not established (Steingrub, Lopez, Teres, Steingart, 1988:642). Conversely, in a prospective evaluation study by

Garry (2000:78) no such adverse events are reported. In this review, maternal nausea was found as a significant side effect when olive oil, fish oil and raspberry leaf were ingested. The meta-analyses revealed that significantly fewer mothers in the control group experienced nausea as a side effect.

El Mauhoub, Khalifa, Jaswal & Garrah (1983:57) reported neonatal adverse events such as moderate growth impairment, convulsions, cranio-facial dysmorphism, limb reductions, and vertebral defects associated with the ingestion of castor oil during pregnancy. In a prospective evaluation study by Garry (2000:78) no such adverse events are reported. The findings of the review do not find any statistically significant neonatal adverse events.

Other significant maternal side effects associated with the ingestion of castor oil, caulophyllum, evening primrose oil, fish oil, olive oil, raspberry leaf and *isihlambezo*, evaluated in this review are vaginal delivery not achieved within 24 hours, the rate of caesarean section, meconium stained liquor, and the rate of post partum haemorrhage. For vaginal delivery not achieved within 24 hours, rate of caesarean section and the rate of post partum haemorrhage, the remedies had no significant effect. Ingestion of *isihlambezo* has been reported to be associated with an increased rate of passage of meconium stained liquor and caesarean section (Mabina, Pitsoe and Moodley, 1997:1008). This is confirmed by the results of the meta-analysis. The results showed that ingestion of castor oil, caulophyllum, and *isihlambezo* are associated with a statistically significant increase in meconium stained liquor. Evening primrose oil has been associated with vacuum extraction, arrest of descent, and prolonged rupture of membranes (Dove and Johnson, 1999:320).

5.3 Implications for practice

In most of the studies used for this review, individual sample sizes were small. Strict selection criteria and rigour in including the studies lend support to the findings in the review. Health professionals have a responsibility toward their gravid clients, in advocating best clinical practices with regard to the latest

evidence as well as protecting them and their fetus from potentially harmful treatments. As the use of herbal medications is on the rise, this review indicates that substantial evidence to advocate or contra-indicate the use of herbal or homeopathic substances is not yet available.

The implication for practice is that the health professional should assume the responsibility of contacting a qualified naturopath or homeopath, registered with an allied health professions council, and discuss possible adverse and beneficial events, before treating the client. In the South African setting, this could mean setting up professional dialogue for specific management with registered traditional healers or other practitioners. When health professionals consult with their clients at antenatal visits, enquiries should be made into the use of herbal products to open discussions about safety and efficacy. Gravid clients with complications like epilepsy and cardiac conditions should be warned about possible drug interactions with any herbal medication.



In South Africa the use of *isihlambezo* is widespread, and the composition of the concoction varies from area to area (Mabina et al, 1997:1009). It may be useful to health practitioners to open dialogue with clients in a non-threatening and culturally sensitive manner in order to pinpoint specific safety issues. This will help to ensure that the client has an idea of the reported adverse events with regard to *isihlambezo*. It is also recommended that the health practitioners and registered traditional healers form a professional relationship and do not practice in isolation from each other.

5.4 Implications for research

The primary aim of the review was to establish whether there are serious maternal and / or neonatal adverse effects associated with ingestion of herbal / homeopathic remedies, and also to explore efficacy issues. Sample sizes were small, and most of the literature available were did not include a control group, but were case reports, letters or anecdotal articles on the usages of different remedies. The controlled trials, as stated before, had relatively small

sample sizes and even with meta – analysis could not provide substantial evidence on most outcomes.

It is clear from the review that larger randomised controlled trials need to be conducted, especially in areas where use of a specific herbal or homeopathic remedy is entrenched in culture or tradition. Even in developed societies where tradition does not play a strong role, the return to alternative therapies, especially during pregnancy lends support to the motivation for larger trials on specific substances.

5.5 Conclusion

It is evident from the review that ingestion of some herbal / homeopathic substances are efficacious. Health professionals should take cognisance of the prevalence of herbal and homeopathic use amongst their clients, and provide clients with enough information to make a balanced decision on whether to use these substances or not. Clinicians and researchers should be encouraged to pursue further trials in this field, in order that substantial evidence can be built up regarding the safety and efficacy of herbal / homeopathic remedies during pregnancy.

Bibliography

- Ayers, J.F. (2000). The use of alternative therapies in support of breastfeeding. *J Hum Lact.* **16** (1): 52-56.
- Bak, N. (2003). *Guide to Academic Writing*. University of the Western Cape.
- Bak, N. (2002). *Research Proposal Guide*. University of the Western Cape.
- Beer, A.M & Heiliger, F. (1999). Randomised, double blind trial of caulophyllum D4 for induction of labour after premature rupture of membranes at term. *Geburtshilfe und Frauenheilkunde.* **59**, 431-5
- Belew, C. (1999). Herbs and the childbearing woman. Guidelines for midwives. *J Nurse Midwifery.* **44** (3): 231-52.
- Boris, J., Jensen, B., Salvig, J.D., Secher, N.J & Olsen, S.F. (2004). A randomised controlled trial of the effect of fish oil supplementation in late pregnancy and early lactation on the n-3 fatty acid content in human breast milk. *Lipids.* **39** (12): 1191-6.
- Campbell, A. [Sa]. The historical background of homeopathy. (Online). Available on: <http://www.kcnet.org/~jvanemon/homeo.htm> Accessed on 2004, October 04.
- Clark, G.E. (1998). Childbirth. The Oxford Companion to Classical Civilization. Ed. Hornblower S and Spawforth A. Oxford University Press, 1998. Oxford Reference Online. Oxford University Press. (Online). Available on:
<http://www.oxfordreference.com/views/ENTRY.html?subview=Main&entry=t133.e139> Accessed on 2004, September 18.
- Cook, D.J., Mulrow, C.D & Haynes, B.R. (1997). Systematic reviews: synthesis of best evidence for clinical decisions. *Academia and Clinic Systematic Review Series.* **126** (5): 376-380.

Deadman, P. [Sa]. Obstetrics and gynaecology in chinese medicine by Giovanni Maciocia. (Online). Available on:
<http://www.jcm.co.uk/BookReviews/bookrevs50.phtml> Accessed on 2004, September 08.

Detsky, A.S., Naylor, C.D., O'Rourke, K., McGeer, A.J & L'Abbe, K.A. (1992). Incorporating variations in the quality of individual randomised trials into meta-analyses. *J Clin Epidemiol.* **45**, 225-265.

Dorfman, P., Lassere, M & Tetau, M. (1987). Homeopathic preparation for labour: two fold experiment comparing a less widely known therapy with a placebo. *Cahiers de Biotherapie.* **94**, 77-81.

Dove, D. & Johnson, P. (1999). Oral evening primrose oil: its effect on pregnancy and selected intrapartum outcomes in low risk nulliparous women. *Journal of Nurse-Midwifery.* **44** (3): 320-324.

Edmunds, J. (2004). Breastfeeding herbs. Midwifery Today E-News 6(14). (Online). Available on:
http://www.midwiferytoday.com/enews/enews0614.asp?q=herb*#main. Accessed on 2004, September 09.

El Mauhoub, M., Khalifa, M.M., Jaswal, O.B & Garrah, M.S. (1983). "Ricin syndrome". A possible new teratogenic syndrome associated with ingestion of castor oil seed in early pregnancy: a case report. *Ann Trop Paediatr.* **3** (2): 57-61.

Ernst, E. (2002). Herbal medicinal products during pregnancy: are they safe?. *BJOG.* **109**, 227-235.

Feinstein, A.R. (1985). *Clinical Epidemiology: The Architecture of Clinical Research*. Published by Saunders. Philadelphia; 39-52.

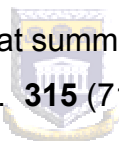
Fischer-Rasmussen, W., Kjaer, S.K., Dahl, C. & Asping, U. (1991). Ginger treatment of hyperemesis gravidarum. *Eur J Obstet Gynecol Reprod Biol.* **38** (1): 19-24.

Gabbay, S. (1999). (Online). Available on: <http://www.holistic-nutrition.com/Castoroil.htm> Accessed 2004, September 09.

Garry, D., Figueroa, R., Cucco, V. & Guillaume. (2000). Use of castor oil in pregnancies at term. *Alternative Therapies in Health and Medicine.* **6** (1): 77-79.

Goldstein, L. (2004). Herbs and natural remedies. Midwifery Today E-News. 6(14). (Online). Available on: http://www.midwiferytoday.com/enews/enews0614.asp?q=herb*#main Accessed 2004, September 08.

Greenhalgh, T. (1997). Papers that summarise other papers (systematic reviews and meta-analyses). *BMJ.* **315** (7109): 672-5.



Higgins, J.P.T & Green, S. (2005). Cochrane handbook for systematic reviews of interventions 4.2.4. In: The Cochrane Library, Issue 2. Chichester, UK: John Wiley & Sons, Ltd. Section 4, 6.

Hofmeyer, J., Piccioni, V. & Blauhof, P. (1990). Postpartum homeopathic arnica Montana: a potency finding pilot study. *BCJP.* **44** (11): 619-621.

Ingram, T. (2003). The effect of caulophyllum on the length of labour. M.Cur thesis. University of Johannesburg (Rand Afrikaans University).

James Lind Library. (2004). Up-to-date, systematic reviews of all reliable evidence. (Online). Available on: http://www.jameslindlibrary.org/essays/systematic_review/up_to_date.html Accessed 2005, January 19.

Kelly, G.A. [Sa]. Meta-Analyses: an introduction. (Online). Available on: <http://www.pitt.edu/~super1/lecture/lec3221/001.htm> Accessed 2004, November 13.

Kelly, A.J., Kavanagh, J & Thomas J (2004). Castor oil, bath and/or enema for cervical priming and induction of labour (Cochrane Review). In: The Cochrane Library, Issue 3. Chichester, UK: John Wiley & Sons, Ltd.

King, H. (1998). Gynaecology. The Oxford Companion to Classical Civilization. Ed. Hornblower S and Spawforth A. Oxford University Press. Oxford Reference Online. Oxford University Press. (Online). Available on: <http://www.oxfordreference.com/views/ENTRY.html?subview=Main&entry=t133.e300> Accessed 2004, September 18.

Klier, C.M., Schafer, M.R., Schmid-Siegel, B., Lenz, G. & Mannel, M. (2002). St. John's wort (*Hypericum perforatum*) – is it safe during breastfeeding? *Pharmacopsychiatry*. **35** (1): 29–30.

Lee, L. (1999). Introducing herbal medicine into conventional health care settings. *Journal of Nurse-Midwifery*. **44** (3): 253-266.

Mabina, M.H., Pitsoe, S.B. & Moodley, J. (1997). The effect of traditional medicines on pregnancy outcome : the King Edward Hospital VIII experience. *S Afr Med J*. **8**, 1008-1010.

Medicine. [Sa]. (Online). Available on: <http://www.webindia123.com/medicine/systems/homeo/origin.htm> Accessed on 2004, September 09.

Menella, J.A. & Beauchamp, G.K. (1991). Maternal diet alters the sensory qualities of human milk and nursing's behaviour. *Paediatrics*. **88** (4): 737-744.

McFarlin BL, Gibson MH, O'Rear J. & Harman P. A national survey of herbal preparation use by nurse-midwives for labour stimulation. Review of the literature and recommendation for practice. *J Nurse Midwifery*. **44** (6): 602-3.

Merriam-Webster's Medical Desk Dictionary. (2002). Merriam Webster's Inc. (Online). Available on: <http://dictionary.reference.com/search?q=gravid> Accessed 2005, August 16.

Nikodem, V.C., Danziger, D., Gebka, N., Gulmezoglu, A.M. & Hofmeyer, G.J. (1993). Do cabbage leaves prevent breast engorgement? A randomised, controlled study. *Birth*. **20** (2): 61-4.

Olson, G. (2001). When pregnant patients use nutritional and herbal supplements. *Contemporary Ob/Gyn*. **10**, 63-81.

Olsen, S.F. & Sorenson, J.D. (1992). Randomised controlled trial on effect of fish oil supplementation on pregnancy duration. *Lancet*. **339**, 1003-07.

Price, M. (2001). History of ancient medicine in Mesopotamia & Iran. (Online). Available on: http://www.iranchamber.com/history/articles/ancient_medicine_mesopotamia_iran.php Accessed 2004, July 14.

Reader's Digest Universal Dictionary. (1988). The Readers Digest Association Limited. Published by William Collins Sons & Co. Glasgow: 16-1216.

Review Manager (RevMan) [Computer Program] (2002). Version 4.2 for Windows. The Cochrane Collaboration. Oxford: England.

Scarborough, J. (1998). Botany. The Oxford Companion to Classical Civilization. Ed. Hornblower S and Spawforth A. Oxford University Press. Oxford Reference Online. Oxford University. (Online). Available on:

<http://www.oxfordreference.com/views/ENTRY.html?subview=Main&entry=t133.e109> Accessed on 2004, September 18.

Shelton, M.G. (1980). Standardised senna in the management of constipation in the puerperium: a clinical trial. *S Afr Med J.* **57** (3): 78-80.

Simpson, M., Parsons, M., Greenwood, J. & Wade, K. (2001). Raspberry leaf in pregnancy: its safety and efficacy in labour. *Journal of Midwifery & Women's Health.* **46** (2): 51-9.

Smith, C.A. (2004). Homoeopathy for induction of labour (Cochrane Review). In: The Cochrane Library, Issue 3. Chichester, UK: John Wiley & Sons, Ltd.

Sripramote, M. & Lekhyananda, N. (2003). A randomised comparison of ginger and vitamin B6 in the treatment of nausea and vomiting of pregnancy. *J Med Assoc Thai.* **86** (9): 846-53.

Steingrub, J.S., Lopez, T., Teres, D. & Steingart, R. (1988). Amniotic fluid embolism associated with castor oil ingestion. *Crit Care Med.* **16** (6): 642-3.

Stapleton, H. (1995). The use of herbal medicine in pregnancy and labour. Part II: events after birth including those affecting the health of babies. *Complement Ther Nurs Midwifery* **1** (6): 165-7

Strandberg, T.E., Jarvenpaa, A.L., Vanhanen, H. & McKeigue, P.M. (2001). Birth outcome in relation to liquorice consumption during pregnancy. *American Journal of Epidemiology.* **153** (11): 1085-88.

Vutyavanich, T., Kraisarin, T. & Ruangsri, R. (2001). Ginger for nausea and vomiting in pregnancy: a randomised, double masked, placebo controlled trial. *Obstetrics & Gynaecology.* **97** (4): 577-582.

Willets, K.E., Ekgangaki, A. & Eden, J.A. (2003). Effect of ginger on pregnancy-induced nausea: a randomised controlled trial. *Aust J Obstet Gynaecol.* **43** (2): 139-44.

Young, G.L. & Jewell, D. (1996). Creams for preventing stretchmarks in pregnancy (Cochrane Review). In: The Cochrane Database of Systematic Reviews. Issue 1. Chichester, UK: John Wiley & Sons, Ltd.

