UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

SCHOOL OF MEDICINE AND PHARMACY

DEPARTMENT OF ANESTHESIOLOGY

Impact of Use of Caffeine Supplements to Treat Post Dural Puncture Headache (PDPH) in Kigali city hospitals/Rwanda "descriptive/cross-section study"

A dissertation submitted to College of Medicine and Health Sciences, School of Medicine and Pharmacy in partial fulfillment for the requirements of the award of a Masters' degree in anesthesiology

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DECLARATION

DECLARATION AND AUTHORITY TO SUBMIT THE DISSERTATION

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Title of the project:

Impact of Use of Caffeine Supplements to Treat Post Dural Puncture Headache (PDPH) in Kigali city hospitals/Rwanda "descriptive/cross-section study"

a. *Declaration by the Student*

I do hereby declare that this ***dissertation*** submitted in partial fulfillment of the requirements for the degree of **MASTERS OF SCIENCE** in **Anesthesiology** at the University of Rwanda/College of Medicine and Health Sciences, is my original work and has not previously been submitted elsewhere. Also, I do declare that a complete list of references is provided indicating all the sources of information quoted or cited.

Date and Signature of the Student

Dr SINAMENYE Jean d'amour  **Date:** August 24, 2021

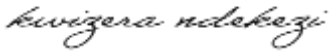
b. *Authority to submit the dissertation*

In my capacity as a Supervisor, I do hereby authorize the student to submit his dissertation.

Prof. Paulin RUHATO BANGUTI

Signature: ...  ... Date: Aug 27, 2021

This dissertation has been submitted for the degree of Master of Medicine in Anaesthesia with my approval as a university supervisor.

Dr Kwizera Ndekezi Jackson  25th August 2021

This dissertation has been submitted for the degree of Master of Medicine in Anaesthesia with my approval as a university supervisor.

Supervisor:	Signature	Date
Dr Alice A. Elder		24th August 2021

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LIST OF ABBREVIATIONS

PDPH **:** Post-dural puncture headache

ERP **:** Epidural blood patch

C/section **:** Caesarean section

CSF **:** Cerebral spinal fluid

ICP **:** Intracranial pressure

HIS **:** International headache society

DH **:** District hospital

CMHS **:** College of Medicine and Health Sciences

UR **:** University of Rwanda

DEDICATION

To my daughter INEZA TONA Kelsy and My son IGANZE Ray Tony

To my wife; BATAMULIZA Alice

To my mother; MUKABURAMBA Xaverine

To my friend doctors and non-physician anesthetists

I dedicate this work

ACKNOWLEDGEMENT

This work would not have been successful without joint efforts from different persons, including patients, nurses, doctors and laboratory technicians whom I express my gratitude.

I would like to thank the university of Rwanda, Kigali university teaching hospital (KUTH), District hospital (Muhima and Kibagabaga), and particularly the department of anesthesia and critical care and department gynecology and obstetrics in each hospital respectively, for supervision and assistance in different ways to make this research possible.

I would like to express my gratitude to Dr KWIZERA NDEKEZI Jackson and Prof. Alice A. Elder who supervised and corrected this work.

I would like also to thank patients who accepted to participate in this research by signing consent providing needed information and giving the samples voluntarily.

Finally, my thanks are presented to all my colleagues, friends and relatives for their endurance and charity throughout my training.

Dr SINAMENYE Jean d'amour

ABSTRACT

Background: The post-dural puncture headache (PDPH) is a severe complication that occurs after spinal or epidural anesthesia. It is a clinical diagnosis and presents with severe frontal headache and posterior headache involving the neck and shoulder. The PDPH may increase the severity, duration of postoperative pain, increase hospital stay, and increase hospital costs. The gold standard of management of PDPH is epidural blood patch (EBP), but when it is not available and contraindicated, other measures are taken. Those measures include no pharmacological and pharmacological, and among pharmacological include caffeine**.** The study aimed to reveal impact of caffeine supplementation on PDPH in postpartum women who underwent c/sections.

Method: This study was a descriptive/cross-section study among women, post spinal anesthesia after C-sections and present with signs of PDPH. Statistical significance was measured with a p-value of 0.05.

Study population and period: The study population included 67 women who had C-sections under spinal anesthesia and presented with signs of PDPH, and those who accepted to consent for participation in the study and fulfill the inclusion criteria. The study was conducted from November 2020 to March 2021.

Results: The study finally recruited sixty-seven women with PDPH. Before caffeine supplements being taken, 21 patients representing 31.3% had mild headache, 32 patients representing 47.8% had moderate headache while 14 patients representing 20.9% had severe headache However, 24 hours after taking caffeine supplements, 51 patients representing 76.1% had no pain, 13 patients representing 19.4% had mild pain, and 3 patients representing 4.5% had moderate pain, while no patient reported severe headache.

Conclusion: The management of PDPH with caffeine supplements in this study showed great improvement on headache intensity with no previous studies in Rwanda.

Key words: *Post dural puncture headache, pain management, quality of pain, caffeine supplementation*

CHAPTER 1. BACKGROUND

1.1 General introduction

The post-dural puncture headache (PDPH) is a complication of neuraxial anesthesia and is estimated to be between 0% and 5% following spinal anesthesia and up to 81% following accidental dural puncture during epidural anesthesia. (1)(2) At Aga Khan University Hospital, Nairobi, more than a quarter of the studied obstetric patients who received spinal anesthesia developed PDPH. (5)

PDPH is a clinical diagnosis characterized by severe frontal occipital headaches which radiate to the neck and shoulder. (2) This headache may be increased by any head movement in upright position and decreased by lying down. (3)

PDPH can increase the pain after surgery and length of hospital stay, and increased hospital costs. (4) Angel et al, found that 40% of women with severe and moderate PDPH were found to return for treatment, despite treatment with or without epidural blood patch (EBP), even if discharged from the hospital. (4)

The most effective management of PDPH includes epidural blood patch (EBP), but other alternative treatments are available when EBP is not successful or contraindicated. (1) Caffeine was used since 1949 as central nervous system stimulant, reducing PDPH by stimulating cerebral vasoconstriction. (1) The dosage of 75 to 500 mg caffeine can be administered orally, intramuscularly, and intravenously. (2)(6) The pure caffeine or combination tablet other drugs can be found as example of paracetamol 500mg with 30 to 50mg of caffeine tablet form. (7) The half-life of caffeine is 20 min and onset is 42min, but for the capsule is 67min, its peak effect is up to 5hours, and its duration is 8hours. (8)(9) (10).

The Rwanda's annual health report of 2014 and annual statistics 2016 showed that many patients undergo Caesarean sections under spinal anesthesia. (11) (12). There are no data on PDPH incidence, risk factors and management. There was no protocol of PDPH management as there was no data on caffeine use. This study aimed at detecting the impact of caffeine supplements on women with PDPH.

1.2 LITERATURE REVIEW

2.1 Definitions of concepts

2.1.1 Spinal Dura Mater

The connective tissue layer made the dura mater exiting the foramen magnum and extends to the second segment of the sacrum. (6) It is made of collagen fibers and few cells inside the dural mater surface, while the outside dura mater is covered by cells. (13) The dural mater surrounds the brain and spinal cord and play role of attaching it in the denticulate ligaments that are situated between nerve roots. (14) It is connected to the vertebrae and disk annulus with big part to the cervical and dorsal regions than lumbar region. (15)

2.1.2 Spinal anesthesia

The spinal anesthesia in neuraxial technique of anesthesia that consists of introducing the local anesthetics drug into intrathecal space containing the CSF that surrounds spinal cord. (16) The spinal anesthesia is most often done in the lumbar part, in middle to lower lumbar levels to prevent spinal cord damage and accidental intrathecal injected drugs into the upper thoracic and cervical regions that can lead to complications. (16)

Spinal anesthesia is commonly used in surgical operations done below umbilicus, involving the pelvis, and lower limbs. (16) There are absolute contraindications to the neuraxial blockade like elevated intracranial pressure (ICP), infection of injection site. (16) The relative contraindication includes pre-existing neurological disease, emergency procedures, bleeding disorders, valvular heart disease, and hypertrophic obstructive cardiomyopathy. (16)(23)

The most spinal anesthesia complication include high spinal, spinal hematoma but backache, PDPH, nausea, vomiting, and hypotension, are relatively common. (16)

2.2 Post dural puncture headache

2.2.1 Pathophysiology of postdural puncture headache

The pathophysiology of PDPH is unclear, but the continuous loss of cerebral spinal fluid was suggested as trigger after spinal anesthesia. (17) (18) The CSF leakage lead to intracranial pressure change and induce pulling tension to subdural vessels and nerves. (18) The signs and symptoms was associated with the traction that shifts the brain caudally which increase pressure and apply the pressure on pain sensitivity to the sinuses, cranial nerves and meninges and the pressure on pain-sensitive structures such as sinuses, cranial nerves, and meninges. (24) The CSF loss was compensated by vasodilation, which cause sensation of pressure in PDPH patients. (18)(24) This explains the cause of increase of headache by upright position which increase venous dilation and release of headache by laying down with possible decrease in venous distention. (18)

2.2.2 Risk factor of postdural puncture headache

The different PDPH risk factors include age, female sex, pregnancy, history of headache, needle size, needles type, and some inexperienced health providers can be one trigger cause even if statistically is not approved. (19)(25) The obstetrical patients have greater risk to develop PDPH due to dehydration, and increased estrogen that influence the tonicity of cerebral vessels. (3) The large needles has been associated with greater risk of PDPH and using smaller needles, the risk of developing PDPH has decreased from 66% in 1998 with 17 and 18G needles, to 33-36% with 22G Quincke needles and 0.4 to 20% using smaller quincke needles of 24 to 32 G. (7) The different quinckle, cutting needle size produce PDPH differently post spinal anesthesia with incidence of 36% with 22G needle, 25% with 25G needle, 2% to 12% with 26G needle and less than 2% for smaller than 26G. (26)

2.2.3 Clinical presentation of postdural puncture headache

The PDPH begins within 24 to 48h hours after the dural puncture and decrease commonly in 7 to 10 days. (20) The standing and sitting position exacerbate headache than lying down which improves headache. Other clinical findings include neck stiffness, hearing loss, vision, and pain sensitivity to light. (20)(27)

2.2.4 Diagnosis of postdural puncture headache

According to diagnostic criteria of the international headache society (IHS), the onset of headache can appear up to the fifth day and decrease within a week or up to 48 hours after an epidural blood patch (EBP). This complication goes with neck stiffness, tinnitus, hypoacusia, photophobia, and nausea. The IHS criteria are as follows (21): 1. Position headache that aggravated within 15 minutes after upright position and improves within 15minutes after lying down, with at least one of the following and fulfilling criteria 3 and 4 associated with neck stiffness; tinnitus; hypoacusia; photophobia and nausea. 2. The occurrence of dural puncture, 3. Headache occurring within 5days post dural puncture, 4. Spontaneously recovering headache within 1 week or 48 hours after effective treatment of the spinal fluid leak by an epidural blood patch. (21)

2.2.5 Differential diagnoses of postdural puncture headache

Brain tumors, migraine, hematoma, pituitary apoplexy, cerebral venous thrombosis, chemical or infective meningitis, and nonspecific headache are pathologies that have in common same clinical presentation as the PDPH. (6) (22)

2.2.6 Management of postdural puncture headache

The management of PDPH consist of restoring amount of CSF lost, heal the puncture site and control the cerebral venous impairment. (6) It includes bed rest in a flat position, plenty of oral fluids intake, simple analgesics and anti-emetics. (6)(7) If conservative management fails, specific treatments may be initiated. (22) The EBP decreased the incidences of PDPH. (6) It consists of introducing the blood into the epidural space and once the later makes a clot, it seals the puncture site and inhibits further CSF loss. (18) Its success rates are about 70-98% and it is indicated once medical management fails to resolve the headaches. (6) The epidural saline, epidural sumatriptan and epidural dextran 40 were introduced in the same context with EBP and showed promissing results on headaches management. (18)

The fibrinous glue has been used as alternative agents to blood patch to seal the dural puncture site. But, its association with high risk of aseptic meningitis was reported. (6) Some studies reported that the uses of DAVP (desmopressin acetate), Adrenocorticotrophic hormone, and surgical closure of dural gap did not show improved headaches. (6) (18)

Caffeine

Caffeine is a central nervous system stimulant which lead to cerebral vasoconstriction. (1) The oral caffeine absorption peaks its serum level in 30min to get to the brain and it has a long half-life of 3-7.5h. (6) Caffeine acts by inhibiting the adenosine receptors, which results in increased cerebral tone and decrease in cerebral blood flow and it was associated with increased CSF production via Na-K+ pumps activation. (18) The evidence showed that caffeine sodium benzoate dosed at 500mg in 1000ml of normal saline administrated during and after spinal anesthesia was decreasing PDPH. (18) The assessment of pain scale after 300mg of oral caffeine in patients with PDPH, four hours and twenty four hours after caffeine administration showed an improved headache. (6) (18) The combination of caffeine with non-opioid analgesic drug were prescribed to treat PDPH. (18)

3. Study Justification

The number of C-sections is increasing in Rwanda. (11) A high percentage of C-sections are performed under spinal anesthesia. (11) (12) The risk of developing PDPH is probably higher due to lack of efficient training, lack of effective equipment and techniques of spinal anesthesia.

Caffeine is among the pharmaceutical management options of PDPH, which reportedly showed improved headaches, easy to administer, and it can be given in combinations. (18) There is no available data on PDPH management in Rwanda, and especially no previous studies on impact of caffeine supplementation on PDPH management.

4. Research question and Hypothesis:

Question: Can the caffeine supplementation significantly improve PDPH management among postoperative women with PDPH who underwent c/sections in Kigali city hospitals?

Hypothesis: The caffeine supplementation significantly improves PDPH management among postoperative women with PDPH who underwent c/sections in Kigali city hospitals.

5. Aim and objectives

5. 1. Aim:

This study aimed to assess the impact of caffeine supplements on post-dural puncture headache in patients undergoing cesarean section under spinal anesthesia.

5. 2. Specific Objectives:

- To assess the risk factors of PDPH in patients who have undergone C-sections with spinal anesthesia in district hospitals in Kigali and KUTH.
- To assess the impact of caffeine supplements in the treatment of PDPH in post-operative obstetrical patients.

CHAPTER 2. METHODS

2.1 Study design

Descriptive/cross-section study

2.2 Study settings

General settings:

This study was conducted in KUTH, one of the largest referral hospitals, located in Nyarugenge district, Rwanda. Two district hospitals were involved, Kibagabaga located in Gasabo district, and Muhima DH located in Nyarugenge district where cesarean sections rate by district, is around 35% of cesarean are in Gasabo district, 34% in Nyarugenge. (12)

Specific settings:

This study was conducted in the Department of Gynecology and Obstetrics of KUTH and two district hospitals in Kigali.

2. 3 Study population

The participants included women who underwent C-sections under spinal anesthesia and present with signs of PDPH.

Inclusion criteria

The patients who had undergone C-section with spinal anesthesia, presenting signs and symptoms of post-dural headache who accepted the consent for the study.

Exclusion criteria:

- Patients with allergies to caffeine and comorbidities including preeclampsia, eclampsia, arthritis, caffeine intolerance, or history of consumed caffeinated beverages within the previous 4hours, intracranial infections, and tumors.
- Patients with signs and symptoms of PDPH who refused consent

2.4 Sample size

We used a convenience sample of all consented participants between November 2020 and March 2021.

2.5. Data collection

An assigned and trained research assistant who was trained for 1 week about numerical pain scale use and data collection sheet filling, collected data on the following variables: Age, weight, Height, BMI, Pregnancy, Admission from, time and date of c/section, Spinal needle characteristics, Level of puncture, number of attempts, onset of headache post c/section, aggravating and relieving factors, numerical pain scores, caffeinated beverages, other treatment received, caffeine supplement use.

The research assistant had to collect data regularly in working days of the week during day time. The pain score was immediately recorded before administration and after administration of caffeine (at onset, first half-life, 2 half-life, and at 24hours). The research assistant assessed pain using the numerical pain scale tool that was provided by the primary investigator.Very cheap caffeine-containing oral tablets called betapyn, sekalgic, and action based on adult dose respectively was prescribed to every patient diagnosed with PDPH and assessed their effects on a pain scale. Monitoring was to record pain scores recorded and then record pain scores at 42 minutes, 6 hours, 12 hours, and 24 hours and assessing side effects amenable to treatment. The headache intensity was measured by using a numerical pain scale and classified as mild, moderate, and severe as respectively 1-3 score, 4-6 score, 7-10 score. Caffeine supplements were prescribed by primary doctors to treat headaches upon PDPH diagnosis. Before and after caffeine supplements, the non-pharmacological management modalities were observed.

2. 6. Data entry and Statistical analyses

All data were entered into EPI-info software and exported to SPSS statistics version 22 for analysis. We used descriptive statistics to calculate rates, percentages and the comparisons between pre and post-caffeine exposure pain scores. All comparisons were made by using the chi-square test and a $p<0.05$ was considered as statistically significant.

2. 7. Ethical considerations:

Ethical issues:

The approval was obtained from the Institutional Review Board (IRB) of CMHS UR, and respective ethic committees of every hospital plus signed informed consents from study participants.

Data confidentiality:

The obtained data were stored confidentially in a locked cupboard. Electronic data being password-coded and hard copies were discarded after 5years. Only the researcher collected questionnaires from respondents to ensure the integrity of the given data.

CHAPTER 3: RESULTS

The total number of patients enrolled was 73 participants. During our study period, 6 patients were omitted due to missing data on data collection sheets. The missing data were patient's demographics, and lack of data on puncture level. Figure 1. Shows the enrollment flowchart of participants and the final number of participants we enrolled.

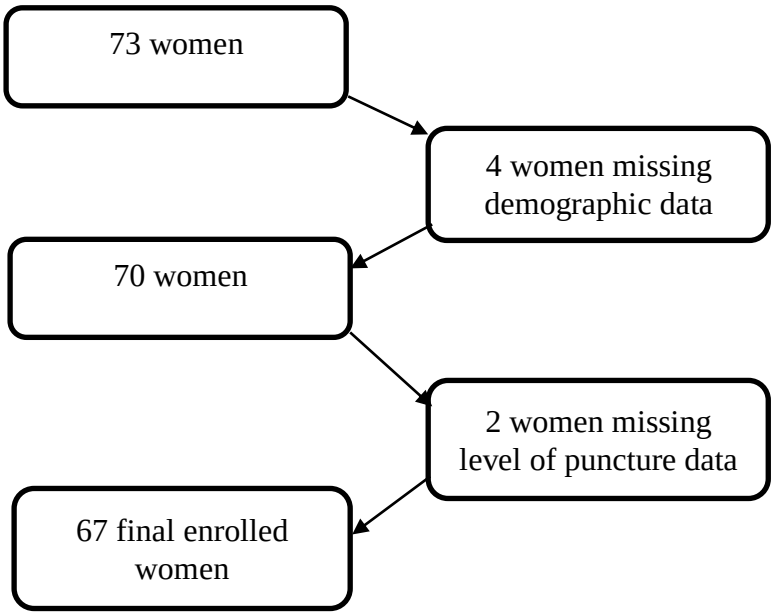

Figure 1. Patients' enrollment flowchart

Among patients who participated in this research, 30 representing 44.8% were from Muhima, 21 representing 31.3% from Kibagabaga, and the rest 16 representing 23.9% were from KUTH. Most of the respondents were aged 20-27 years, representing 47.8% of the total respondents. Most of the patients weighted between 61 and 78 Kg, representing 49.3%; while there was no much difference into their heights. The relationship between height and weight was better reported as BMI which indicated that only 28 respondents were in the range of 18-25kg/m2.

Table 1. Demographic Information

		Count	Percentage %
Hospital name of respondents	Muhima	30	44.8%
	Kibagabaga	21	31.3%
	KUTH	16	23.9%
The age group of respondents	20-27 Years	32	47.8%
	28-36 Years	27	40.3%
	37-44 Years	8	11.9%
	45-52 Years	0	0.0%
Weight range of respondents	42-60 Kg	19	28.4%
	61-78 Kg	33	49.3%
	79-90 Kg	12	17.9%
	90-108 Kg	3	4.5%
Height range of respondents	150-155 Cm	9	13.4%
	156-160 cm	18	26.9%
	161-165 cm	19	28.4%
	166-170 cm	19	28.4%
	171-176 cm	2	3.0%
Pregnancy of respondents	Single	35	52.2%
	Multiple	31	46.3%
BMI of respondents	11.00	1	1.5%
	11-17 kg/m2	3	4.5%
	18-25kg/m2	28	41.8%
	26-32kg/m2	31	46.3%
	33-39kg/m2	5	7.5%

Table 2. *Risk factor characteristics of enrolled women*

Characteristics		Count	Percentage %
Spinal needle size	18G	0	0.0%
	20G	0	0.0%
	22G	13	19.4%
	24G	0	0.0%
	25G	54	80.6%
	26G	0	0.0%
Spinal needle type	Quinckle	63	94.0%
	Whitacare	0	0.0%
	Sprotte	4	6.0%
Level of puncture	L3-L4	15	22.4%
	L4-L5	52	77.6%
Number of attempts	1.00	24	35.8%
	2.00	34	50.7%
	3.00	8	11.9%
	5.00	1	1.5%
Onset of headache post C/section	2.00	2	3.0%
	3.00	1	1.5%
	4.00	3	4.5%
	5.00	1	1.5%
	6.00	6	9.1%
	8.00	6	9.1%
	10.00	6	9.1%
	12.00	14	21.2%
	13.00	1	1.5%
	14.00	1	1.5%
	15.00	2	3.0%
	16.00	1	1.5%
	24.00	19	28.8%
	48.00	1	1.5%
	68.00	1	1.5%
	136.00	1	1.5%
Aggravating Factors	upright position/ head up	60	89.6%
	Speaking/ movement	3	4.5%
	Sitting	4	6.0%
Numerical pain score	no pain	0	0.0%
	mild pain	21	31.3%
	moderate pain	32	47.8%

	severe pain	14	20.9%
Any other treatment received before caffeine	Yes	24	36.9%
	No	41	63.1%
Any other treatment received after caffeine	Yes	25	37.3%
	No	42	62.7%

The above table depicts all the risk factors that all enrolled participants had. Thirteen patients representing 19.4% had been given spinal anesthesia with a 22G spinal needle size, a 25G spinal needle size was used in 54 patients (80.6%). Out of 67 patients who developed post-Dural Puncture Headache (PDPH), 63 (94%) had spinal anesthesia with Quinckle spinal needle type and 4 (6.0%) with Sprotte needle type. Out of 67 patients who developed PDPH, 15 patients representing 22.4% indicated that the spinal puncture level was L3-L4, while the rest 52 patients representing 77.6%, the spinal puncture level was L4-L5. Twenty-four patients representing 35.8% had only one attempt, 34 patients representing 50.7% had two attempts, 8 patients representing 11.9% had three attempts and 1 respondent had five attempts. Nineteen respondents representing 28.8% reported that the Onset of headache post C/section was after 24 hours, 14 respondents indicated that their headache onset post C/section was after 12 hours.

Sixty respondents representing 89.6% showed that the aggravating factor for headache was upright position/ head up, 3 respondents indicated that the aggravating factor for headache was speaking/ movement while, 4 respondents indicated that the aggravating factor was sitting in the upright position.

Twenty -one patients representing 31.3% had mild pain, 32 patients representing 47.8% had moderate pain, while 14 patients representing 20.9% had severe pain post spinal anesthesia they underwent.

The study revealed that patients who received any other treatment before caffeine supplements were 24 patients representing 36.9%, and forty-one women representing 63.1% did not receive any other medication before caffeine supplements. After caffeine supplements, the need of additional pain medicine was reported in 25 patients representing 37.3% and 42 patients representing 62.7% did not receive any additional pain medicine.

3.1 Pain score after caffeine supplementation

At 0-minute post PDPH diagnosis no patient was found without headache, 21 patients had mild headache, and 32 patients had moderate headache while 14 patients had severe headache. Caffeine supplements showed improved headache after 42 minutes of administration. The rates of severe headache reduced from 20.9% to 4.5% (reduction of 16.4% on severe pain, p-value: 0.028, odds ratio: 1.29 [1.2-2.33]). After 6hours of caffeine supplementation, the rate of moderate headache decreased from 47.8% to 16.4%, corresponding to a reduction of 29.9% (p-value: 0.007, odds ratio: 1.51([0.7-1.9]). The rate of severe headache improved from 20.9% to 4.5%, corresponding to a reduction of 16.4% (p-value: 0.028, odds ratio: 1.29 [1.2-2.33]).

This study showed an improved headache 12 hours post caffeine administration. The percentage of patients who did not have headache increased from 0.0% to 29.9%, corresponding to an increase of 29.9 % (p-value: 0.021, odds ratio: 0.71([0.54-0.86]).

After 24 hours of caffeine supplementation, the percentage of patients who did not have headache increased from 0.0% to 76.1 % (p-value: 0.017, Odds ratio: 0.82 ([0.62-1.3]). The rate of mild headache has decreased from 31.3% to 19.4% corresponding to a reduction of 11.9 %(p-value: 0.043, odds ratio: 3.43([3.3-4.1]). The rate of moderate headache has reduced from 47.8% to 4.5%, corresponding to a reduction of 43.3% (p-value: 0.002, odds ratio: 0.29([0.25-0.3]). The rate of severe headache was reduced from 20.9% to 0.0%, corresponding to reduction of 20.9 %(p-value: 0.001, odds ratio: 0.12([0.1-0.5])

Table 3: *Comparison from time of caffeine supplements administration and pain scores*

Pain score before caffeine				Pain score after caffeine				p-value	OR
Time	Pain	N	%	Time	Pain	N	%		
	No	0	0		No	1	1.5	0.041	2.04 [0.4-2.3]
	Mild	21	31.3		Mild	32	47.8	0.001	1.57 [1.6-2.1]
0min	Moderate	32	47.8	42min	Moderate	31	46.3	0.043	1.33 [1.30-1.99]
	severe	14	20.9		severe	3	4.5	0.018	1.29 [1.2-2.33]
	No	0	0		No	5	7.5	0.031	1.31 [1.29-7.8]
	Mild	21	31.3		Mild	48	71.6	0.006	3.43 [0.2-4.1]
0min	Moderate	32	47.8	6hours	Moderate	11	16.4	0.007	1.51 [0.7-1.9]
	Severe	14	20.9		severe	3	4.5	0.017	4.21 [0.7-5.3]
	No	0	0		No	20	29.9	0.021	0.71 [0.54-.86]
	Mild	21	31.3		Mild	42	62.7	0.031	3.03 [3.01-.4.1]
0min	Moderate	32	47.8	12hours	Moderate	1	1.5	0.003	0.31 [0.3-2.19]
	Severe	14	20.9		Severe	4	6.0	0.021	0.29 [0.25-0.3]
	No	0	0		No	51	76.1	0.017	0.82 [0.62-1.3]
	Mild	21	31.3		Mild	13	19.4	0.043	3.43 [3.3-4.1]
0min	Moderate	32	47.8	24hours	Moderate	3	4.5	0.002	0.29 [0.25-0.3]
	Severe	14	20.9		Severe	0	0	0.001	0.12 [0.1-0.5]

CHAPTER 4: DISCUSSION

PDPH is complication of spinal anesthesia with postural character of the pain, which occurs when a patient is in an upright position (sitting or standing). (21) In 2007, Nafiu et al, in the study done in Korle Bu hospital Accra, showed that 22G cutting needle were associated with PDPH complications. (28) This study showed that 80.6% who developed PDPH received spinal anesthesia with 25G, while it was 19.4% in those spinal needle 22G was used.
J.Salzer et al, showed that 95% of patient who had spinal anesthesia with cutting needle had PDPH.(29) In this study, the little number 13 women (19.4%), and fifty-four women (80.6%) underwent spinal anesthesia with 22G and 25G respectively had PDPH. Among 67 patients who developed post-Dural Puncture Headache (PDPH), 63 (94%) had been administered spinal anesthesia with cutting spinal needle type.

In most of the study, the spinal needle was inserted usually at the lumbar spinal region (L3/4 or L4/5), allowing blockage of structures according to dermatomal parts of the body. (26) During this study, among 67 enrolled women, 22.4% indicated that the level of puncture was L3-L4, while the rest 77.6% of women, level of puncture was L4-L5. Ferede et al, in study done at University of Gonder, showed that patients who had attempt greater than two, had more risk of developing PDPH due to multiple trauma to the dural with experienced anesthesia provider. (30) However, in this index, 50.7% of patients who developed PDPH, had their spinal anesthesia upon two dural puncture attempts, and 11.9% had their spinal anesthesia upon three attempts. This shows that more than 50% of enrolled population had PDPH due to multiple attempts. In US, many studies showed that dural puncture attempts greater than two are associated with PDPH.(28) (30)

Halker RB et al, in the study for caffeine for prevention and treatment for PDPH, showed that PDPH begin within 12 to 24hours post puncture. (33) The results of this index study showed that 19 women representing 28.8%, the Onset of headache was after 24 hours while 14 patients 21.2% had their headache onset 12 hours.

Ljubisavljevic S. in his study about complication of PDPH caused by lumbar puncture, showed that aggravating factors of PDPH, included the upright position and relieving factor include laying supine.(27) In our study, 60 patients representing 89.6% indicated that the aggravating factor for headache was upright position or head up position.
Ferede et al, in their study revealed that 51% of enrolled patients had moderate pain , 17% had severe pain post spinal anesthesia.(30) In this study, 47.8% of enrolled patients had moderate pain while 20.9% had severe pain post spinal anesthesia. Those findings show that a lot of patients who developed PDPH had moderate pain.

In the study done in Medigan Army medical center, Zeger et al. showed that caffeine had overall efficacy rate 80%. (31) In this study, after taking caffeinated supplements, pain scores after 24 hours post PDPH clinical diagnosis, 51 patients representing 76.1% p-value=0.017, odd ratio : 0.82 [0.62-1.3] showed no pain. In comparison to the study done by Ragab A et all, on effectiveness for prevention of PDPH, revealed that, after 24hours post caffeine use, there was a tremendous improvement on headache intensity. (2) This study showed significant improved headache as 76.1% of the patients did not present any headache complaints (p-value=0.017, Odds ratio: 0.82 [0.62-1.3]).

There were limitations in this study. The observation rate of pain evaluation, the numerical pain scale, is not the only reliable pain assessment tool used in postoperative obstetric patients. The data collection was done on day time and we may have missed additional episodes of pain during the night. This study did not address the satisfaction of patients during hospital stay and their pain experience. It is therefore, recommended that further studies to address those issues in Rwanda Health facilities be carried out.

CHAPTER 5: CONCLUSION AND RECOMMENDATION

5.1 Conclusion

The PDPH can have a great impact on patient's overall health and increased morbidity. There multiple risk factors to develop PDPH. The caffeine supplements significantly improved PDPH after 24 hours post administration.

5.2 Recommendations

1) The patient who underwent C-sections under spinal anesthesia should be followed-up and examined for possible risk factors of PDPH.
2) The hospitals or ministry of health should avail the guideline for the treatment of PDPH
3) The caffeine-containing drug should be available for insurance schemes to be covered by insurance (mutuelle de santé).
4) A multi-centered prospective study for identifications of PDPH risk factors and its management for postoperative women who underwent C/section under spinal anesthesia, have to be conducted. This to avail possibility of prophylactic measures.

6. REFERENCES

1. Kwak K-H. postdural puncture headache. Korean J Anesthesiol. 2017;70(2):136.

2. Ragab A, Facharzt KN. Caffeine, Is it effective for the prevention of postdural puncture headache in young adult patients? Egypt J Anaesth. 2014 Apr;30(2):181–186.

3. Bakshi S, Gehdoo RP. Incidence and management of post-dural puncture headache following spinal anesthesia and accidental dural puncture from a non-obstetric hospital: A retrospective analysis. Indian J Anaesth. 2018;62(11):881-886.

4. Angle P, Thompson D, Szalai JP, Tang SLT. Expectant management of postdural puncture headache increases hospital length of stay and emergency room visits: [Le traitement symptomatique de la céphalée post-ponction durale augmente la durée du séjour hospitalier et les visites à la salle d'urgence]. Can J Anesth 2005 Apr;52(4):397–402.

5. Gisore E, Mung'ayi V, Sharif T. Incidence of post-dural puncture headache following Caesarean section under spinal anesthesia at the Aga Khan University Hospital, Nairobi. East Afr Med J. 2011 Jan 7;87(6):227–230.

6. Turnbull DK, Shepherd DB. Post-dural puncture headache: pathogenesis, prevention, and treatment. Br J Anaesth. 2003 Nov;91(5):718–729.

7. Nath G, Subrahmanyam M. Headache in the parturient: Pathophysiology and management of post-dural puncture headache. J Obstet Anaesth Crit Care. 2011;1(2):57-66.

8. Gonzalez AM, Hoffman JR, Wells AJ, Mangine GT, Townsend JR, Jajtner AR, et al. Pharmacokinetics of caffeine administered in a time-release versus regular tablet form. J Int Soc Sports Nutr. 2014;11(Suppl 1): P23(2014).

9. Institute of Medicine (U.S.), editor. Caffeine for the sustainment of mental task performance: formulations for military operations. Washington, D.C: National Academy Press; 2001. 157 p.

10. Shi J, Benowitz NL, Denaro CP, Sheiner LB. Pharmacokinetic-pharmacodynamic modeling of caffeine: Tolerance to pressor effects. Clin Pharmacol Ther. 1993 Jan;53(1):6–14.

11. 2016_Annual_Statistical_booklets_V9_08_03_2018.pdf.

12. Rwanda_Annual_Health_Statistics_Booklet_2014_.pdf.

13. Yang C, Yang X, Lan X, Zhang H, Wang M, Zhang Y, et al. Structure and mechanical characteristics of spinal dura mater in different segments of sheep's spine. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi Zhongguo Xiufu Chongjian Waike Zazhi Chin J Reparative Reconstr Surg. 2019 Feb 15;33(2):232–238.

14. Nagel SJ, Reddy CG, Frizon LA, Chardon MK, Holland M, Machado AG, et al. Spinal dura mater: biophysical characteristics relevant to medical device development. J Med Eng Technol. 2018 Feb;42(2):128–139.

15. Quiñones D, Viaño J. Abnormalities of the Spinal Dura Mater: Are Multiple Clinical Syndromes with Dural Lesions Associated with Abnormal Connective Tissue? Neuroradiol J. 2011 Aug;24(4):577–587.

16. Olawin AM, M Das J. Spinal Anesthesia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 [accessed 2021 May 29]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK537299/

17. Xavier J, Pinho S, Silva J, Nunes CS, Cabido H, Fortuna R, et al. Postdural puncture headache in the obstetric population : a new approach ? Reg Anesth Pain Med. 2020 May;45(5):373–376.

18. Patel R, Urits I, Orhurhu V, Orhurhu MS, Peck J, Ohuabunwa E, et al. A Comprehensive Update on the Treatment and Management of Postdural Puncture Headache. Curr Pain Headache Rep. 2020 Jun;24(6):24.

19. Makito K, Matsui H, Fushimi K, Yasunaga H. Incidences and risk factors for the post-dural puncture headache after neuraxial anesthesia: A national inpatient database study in Japan. Anaesth Intensive Care. 2020 Sep;48(5):381–388.

20. Calderon R, Copenhaver D. Postdural Puncture Headache. J Pain Palliat Care Pharmacother. 2013 Dec;27(4):406–407.

21. Amorim JA, Gomes de Barros MV, Valença MM. Post-dural (post-lumbar) puncture headache: Risk factors and clinical features. Cephalalgia. 2012 Sep;32(12):916–23.

22. Bleeker CP, Hendriks IM, Booij LHDJ. Postpartum post-dural puncture headache: is your differential diagnosis complete? Br J Anaesth. 2004 Sep;93(3):461–464.

23. Kokki H. Spinal blocks: Spinal blocks. Pediatric Anesthesia. 2012 Jan;22(1):56–64.

24. Candido KD, Stevens RA. Post-dural puncture headache: pathophysiology, prevention and treatment. Best Pract Res Clin Anaesthesiol. 2003 Sep; 17(3):451–469.

25. Irene Mansutti, Angelica Bello, Anna Maria Calderini, Maya Valentinis. La cefalea post-rachicentesi:
fattori di rischio, variabili correlate ed interventi.
Revisione della letteratura. Assistenza Infermieristica e Ricerca. 2015 Jul 1;(2015Luglio-Settembre).

26. Xu H, Liu Y, Song W, Kan S, Liu F, Zhang D, et al. Comparison of cutting and pencil-point spinal needle in spinal anesthesia regarding postdural puncture headache: A meta-analysis. Medicine. 2017 Apr;96(14):e6527.

27. Ljubisavljevic S. Postdural puncture headache as a complication of lumbar puncture: clinical manifestations, pathophysiology, and treatment. Neurol Sci. 2020 Dec;41(12):3563–3568.

28. Nafiu OO, Salam RA, Elegbe EO. Post dural puncture headache in obstetric patients: experience from a West African teaching hospital. International Journal of Obstetric Anesthesia. 2007 Jan;16(1):4–7.

29. Salzer J, Granåsen G, Sundström P, Vågberg M, Svenningsson A. Prevention of post-dural puncture headache: a randomized controlled trial. Eur J Neurol. 2020 May;27(5):871–877.

30. Ferede YA, Nigatu YA, Agegnehu AF, Mustofa SY. Incidence and associated factors of post dural puncture headache after cesarean section delivery under spinal anesthesia in University of Gondar Comprehensive Specialized Hospital, 2019, cross sectional study. International Journal of Surgery Open. 2021 Jun;33:100348.

31. Zeger W, Younggren B, Smith L. Comparison of cosyntropin versus caffeine for post-dural puncture headaches: A randomized double-blind trial. World J Emerg Med. 2012;3(3):182–185.

32. Buddeberg BS, Bandschapp O, Girard T. Post-dural puncture headache. Minerva Anestesiol. 2019 Apr;85(5). 543-553

33. Halker RB, Demaerschalk BM, Wellik KE, Wingerchuk, Rubin DI, Crum BA, et al. caffeine for the prevention and trearment of postdural puncture headache: Debunking the Myth. The neurologist. 2007 Sep; 13(5):323-327

APPENDIX

Data collection tool :

I am Dr. SINAMENYE Jean d'Amour, an anesthesia resident, year 3. I am doing a study entitled: The use of caffeine supplements to treat post-dural puncture headache among obstetric patients who undergone c/section under spinal anesthesia in Kigali city hospitals/Rwanda. I hold an IRB approval from the University of Rwanda and respective district hospital ethics approval about my research title. It is with this regard that I request to fill in missing information into the below question or respond to questions.

a. Demographics:

1. Hospital name:.....
2. Study ID:...
3. Age: …..
4. Weight …...
5. Height
6. BMI
7. Pregnancy: single……. Multiple……..
8. Patient's phone contact:.....
9. Admission from which health facility:...
10. Address of the patients: .....
11. When did you undergo c/section: .....

b. PDPH assessment before caffeine supplement use:

1. Spinal needle size…….
2. Spinal needle-type…….
3. Level of puncture……
4. The number of attempts…….
5. The onset of headache post c/section…….
6. Aggravating factors ……..
7. Numerical pain score……..
8. Caffeinated beverages are taken……
9. Any other treatment received…….

C. PDPH assessment after caffeine supplement use:

1. Numerical pain score……

   ✓ Pain score at 0min….

   ✓ Pain score after 42 min….

   ✓ Pain score after 6hours…

   ✓ Pain score after 12 hours….

- ✓ Pain score after 24hours…

2. Any other treatment received……...

Approvals

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 18th/February/2020

Dr SINAMENYE Jean d' Amour
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 023/CMHS IRB/2020

Your Project Title ***"Impact of the the Use of Caffeine Supplements to Treat Post Dural Puncture Headache (PDPH) in Kigali City hospitals/Rwanda"*** has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Involved in the decision		
		Yes	No (Reason)	
			Absent	Withdrawn from the proceeding
Prof Kato J. Njunwa	UR-CMHS		X	
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 17th February 2020, **Approval has been granted to your study.**

Email: researchcenter@ur.ac.rw P.O Box 3286 Kigali, Rwanda www.ur.ac.rw

Please note that approval of the protocol and consent form is valid for **12 months**.

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 18th February 2020

Expiration date: The 18th February 2021

Professor GAHUTU Jean Bosco
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

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CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

21st Jul,2020 Ref.:EC/CHUK/057/2020

Review Approval Notice

Dear Jean d'Amour SINAMENYE,

Your research project: ***"Impact of the use caffeine supplement to treat Post Dural Puncture Headache (PDPH) in Kigali City hospitals/Rwanda "***

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 21st Jul,2020 to evaluate your request for ethical approval of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your research project.

You are required to present the results of your study to CHUK Ethics Committee before publication by using this link:www.chuk.rw/research/fullreport/?appid=101&&chuk.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

Dr Emmanuel Rusingiza Kamanzi
The Chairperson, Ethics Committee,
University Teaching Hospital of Kigali

ETHICS COMMITTEE
CHUK

Scan code to verify

" University teaching hospital of Kigali Ethics committee operates according to standard operating procedures (Sops) which are updated on an annual basis and in compliance with GCP and Ethics guidelines and regulations "