PENTAZOCINE VERSUS COMBINED PENTAZOCINE AND DICLOFENAC FOR PAIN RELIEF IN THE FIRST 24 HOURS AFTER CAESAREAN SECTION: A RANDOMIZED CONTROLLED STUDY

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF FELLOWSHIP OF THE NATIONAL POSTGRADUATE MEDICAL COLLEGE OF NIGERIA IN OBSTETRICS AND GYNAECOLOGY

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DECLARATION

I declare that this dissertation titled "**pentazocine versus combined pentazocine and diclofenac for pain relief in the first 24 hours after caesarean section: a randomized controlled study"** is original, the study was done by me and has not been presented to any other college for a fellowship examination or a journal for publication.

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CERTIFICATION

This is to certify that Dr Egede John Okafor, a Senior Resident doctor in the Department of Obstetrics and Gynaecology, Federal Teaching Hospital Abakaliki, Ebonyi State, under our supervision carried out the research on:

Pentazocine versus Combined Pentazocine and Diclofenac for Pain Relief in the First 24 Hours after Caesarean Section: A Randomized Controlled Study

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TABLE OF CONTENT

LIST OF TABLES AND FIGURES

ABSTRACT

BACKGROUND

Pain is one of the important outcomes of caesarean section. Its management still remains a challenge in a low resource setting like ours. The addition of diclofenac to pentazocine provides effective and safe postoperative analgesia.

AIM

To compare the efficacy of intramuscular pentazocine only and combined intramuscular pentazocine with diclofenac as pain relief within 24 hours after caesarean section.

METHODOLOGY

A total 146 parturient women who had uncomplicated caesarean section and live babies at the Federal Teaching Hospital Abakaliki were randomly grouped using computer generated numbers into pentazocine placebo group and pentazocine diclofenac group. The pentazocine placebo group received pentazocine 30mg only analgesic every 4 hours for 24 hours and 3ml of water for injection as placebo 12hrly for 24 hours while the pentazocine diclofenac group women received pentazocine 30mg every 4 hours and diclofenac 75mg every 12 hours all for 24 hours. The level of pain control was assessed using visual analog scale (VAS) at 1, 2, 6, 12, 18, 24 hours. The patient satisfaction and side effects of the drugs were also documented.

DATA ANALYSIS

The information obtained were entered into a predesigned data sheet. The data was analyzed with Statistical package for Social Science (IBM SPSS statistics) version 22.0.

Categorical variables were analyzed using chi square. Means and standard deviation (SD) were calculated for quantitative variables, and the difference between two independent groups was compared using independent sample *t*-test. The level of significance was set at ≤ 0.05.

RESULT

A total of 140 participants completed the study (70 in each group). This gave 95.9% completion rate. The mean pain scores at the 1st, 2nd, 6th, 12th, 18th and 24th hour for the pentazocine only and pentazocine with diclofenac analgesic were 5.01±1.64 and 2.91±1.45, 4.13±1.76 and 2.49±1.34, 3.56±1.86 and 2.07±1.07, 2.83±1.14 and 1.40±0.86, 1.96±0.84 and 1.27±1.09, and 1.50±0.79 and 1.06±0.83 respectively. These were statistically significant ($p<0.005$). Those who received pentazocine and diclofenac started ambulation and oral intake earlier compared to those who received pentazocine only ($p<0.005$). There was no difference in the duration of hospitalization and level of satisfaction in both groups ($p>0.005$). No side effect was noted on the babies in both groups. However, the maternal side effects noted were drowsiness and nausea which occurred more in the pentazocine only group compared to the pentazocine diclofenac group.

Conclusion

Pentazocine and diclofenac combination is an effective and safe post caesarean section analgesic.

Key words: caesarean section, pentazocine, diclofenac, post-operative pain

CHAPTER 1

INTRODUCTION

Caesarean section represents the most significant operative intervention in obstetrics and has saved lives of countless mothers and infants[1]. The rate has been on the increase as a result of better surgical technique, improvement in the intra-operative anaesthesia, availability of blood for transfusion and antibiotics and other social reasons including maternal request for non-medical reasons[2]. The rate varies from country to country and within the same country. It also varies between institutions. Globally, the rate varies between 10% and 35% in most developed countries[2,3]. In Nigeria, the rates between 10.3% and 27.6% have been reported from different institutions[4,5]. The rate of 10.5% was reported at Mile 4 hospital Abakaliki[6]. Our populace has an aversion for surgeries, with morbid fear for death and pain during and after surgeries[6]. Studies in which parturient women were questioned about their fears and expectations, pain during and after cesarean section was the greatest concern in about 20% of the respondent [7,8]. Therefore, post-operative pain management is as important as the pre- and intra- operative care and may influence future health seeking behaviour of the patients.

Postoperative pain is one of the main postoperative adverse outcomes causing distress to patients[9]. It leads to patient discomfort and suffering, decreased level of satisfaction, prolonged recovery and hospital stay, and higher health care costs and risk of developing chronic persistent pain[10,11]. This is even more in obstetrics where post caesarean section pain may interfere with ambulation, breastfeeding, and early maternal bonding with the infant. This might lead to thrombo-embolic events, uterine sub-involution and post-partum haemorrhage as well as stress

on the health care system[10,12,13]. It could also lead to psychological and emotional distress. Thus, it seems that postoperative pain management of patients within the immediate puerperium is more challenging than other surgical patients[13-15].

Adequate pain relief is essential after caesarean section to promote early recovery, early maternal care for the newborn, and reduction of hospital cost and less stress on the health care system[16]. Effective pain management is therefore a priority of care and a patient's right[17]. Although, there is no 'gold standard' for post-caesarean pain management, an ideal post-caesarean analgesic regimen must be cost-effective, simple to implement and with minimal impact on staff workload. Drug transfer into breast milk must also be minimal, with no adverse effects on the newborn. Several other factors, including patient and physician preferences, maternal medical situations such as pre-eclampsia or bleeding disorders, staff education and drug availability can influence the choice of the analgesic regimen[15]. In the West African sub region drug availability and cost remain important consideration in the choice of post-operative analgesia. Therefore, despite the fact that the current armamentarium of analgesic drugs and techniques are impressive, effective management of post caesarean section pain especially in the West African sub region still poses some unique challenges.

Post-operative analgesia has traditionally been provided by opioid analgesics[14,18]. However, opioid analgesia can be associated with increased incidence of post-operative complications, such as ventilatory depression, sedation, post-operative nausea and vomiting, pruritus, difficulty voiding and ileus, which in turn contribute to delayed discharge from hospital and increased health care cost[18-20]. Some of these adverse

effects can occur even with small doses[19]. Non-steroidal anti-inflammatory drugs when used must be done with caution, because of the potential problems with bleeding, platelet dysfunction and renal insufficiency. A systematic review of 36 studies on 3362 patients comparing efficacy of adding acetaminophen (paracetamol) or its precursor, NSAIDS or their combinations to post-operative opioid management suggests acetaminophen is a useful alternative with mostly low incidence of adverse effects and with most similar or less efficacy compared to NSAIDS. Multimodal analgesia is currently recommended for effective post-operative pain control[9]. Multimodal analgesia is achieved by combining different analgesics that act by different mechanisms (e.g., opioids, NSAIDs, and local anesthetics); resulting in additive or synergistic analgesia, lower total doses of analgesics, and fewer side effects[9,10].

In most other centres in Nigeria, including the study centre, pentazocine and tramadol are the main stay of post-operative caesarean section pain management[9]. No study has been done in our centre to compare the efficacy of opioid verses combination of opioid and diclofenac for pain control after caesarean section. Thus, this study will compare these two groups of agents and suggest a better modality of pain management in post-caesarean section patients.

CHAPTER 2

AIM AND OBJECTIVES

2.1 AIM

To compare the efficacy of pentazocine only and combined pentazocine with diclofenac as pain relief within 24 hours after caesarean section.

2.2 SPECIFIC OBJECTIVES

1. To determine the efficacy of intra muscular pentazocine as the only pain relief in the first 24 hours after caesarean section.
2. To determine the efficacy of intramuscular pentazocine-diclofenac combination as analgesia in the first 24 hours after caesarean section.

2.2 NULL HYPOTHESIS

There is no difference between analgesia produced by intramuscular pentazocine alone and intra muscular combined pentazocine and diclofenac after caesarean section.

2.3 ALTERNATIVE HYPOTHESIS

Analgesia produced by combined pentazocine and diclofenac is more efficacious than pentazocine only analgesic after caesarean section.

2.4 RESEARCH QUESTION

Is the efficacy of pentazocine only analgesic comparable to its combinations with diclofenac in the first 24 hours after caesarean section? Pain management after caesarean section is very important in view of the consequences of the unrelieved pain after surgery and the peculiar nature of caesarean delivery. The choice of analgesic is also very important as the use of only potent opioids may result to opioid dependence and other opioid side effects. Therefore, combination of opioid with diclofenac or

paracetamol may reduce these side effects and at the same time provide adequate analgesia. Thus, this research aims to establish the analgesic or their combinations that will produce the more satisfactory analgesia within the first 24 hours after caesarean delivery.

CHAPTER 3

LITERATURE REVIEW

3.1 PATHOPHYSIOLOGY OF PAIN IN CAESAREAN SECTION

Caesarean section (CS) was introduced in clinical practice as a life-saving procedure both for the mother and baby. Postoperative pain is a common complaint after caesarean deliveries[21,22] and it is often moderate to severe for 48 hours after the procedure[23]. The pain thereafter becomes variable in terms of duration and intensity[24]. A study done by Kolawole et al[25] at Ilorin showed that 95% of the patient who had caesarean section had some degree of pain in the immediate postoperative period and that the first 24 hours was found to be particularly painful. He also found that 79.6% and 54.5% of the patients reported moderate to severe pain in the recovery room and on the day one respectively. Pain has been described as unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage[9,22,26]. Post-cesarean pain consists of a somatic and visceral components[16,27]. Visceral pain originates from uterine incision and contractions (increased by breastfeeding), peritoneal irritation and gastro-intestinal transit. The somatic component arises from nociceptors within the surgical wound. Nerves supplying the anterior abdominal wall are derived from T6 to L1 and pass through the plane between the layers of the transversus abdominis and internal oblique muscles[16,27].

The nociceptive axon carries this impulse from the peripheral via the A delta- and C-fibres into the dorsal horn of the spinal cord and through mainly the spinothalamic and the spinoreticular tracts to the supraspinal control areas, including the reticular formation, mid brain, thalamus, hypothalamus, the limbic system of the amygdale and the cingulate cortex, basal ganglia, and celebral cortex. Neurons originating from these areas synapse with the neuronal cells of the descending spinal pathway which terminate in the dorsal

horn of the spinal cord[28-31]. The visceral impulse is also transmitted through the unmyelinated fibre to the dorsal horn[32]. Besides, disruption of the endometrium during surgery leads to increased local production of eicosanoids (PGE2, PGF2, TXA2, LT) by the endometrium. These sensitize uterine afferent nociceptive fibres, sensitize the uterus to enhance uterine contractility through the action of agents like oxytocin, vasopressin and histamine. These will cause spasm of the uterine arteries leading to muscle hypoxia with the release of k^+, H^+ ions that will cause visceral hyperalgesia. At the same time, circulating prostaglandins directly sensitize central nervous system[33,34].

Tissue damage from the surgery produces disruption of cells, degranulation of mast cells, secretion by inflammatory cells and and induction of enzymes such as cyclo-oxygenase-2 (COX-2). The chemical mediators produced act as endogenous modulators of nociception and include proteinases, pro-inflammatory cytokines (eg TNFα, IL-1β, IL-6), anti-inflammatory cytokines (eg IL-10) and chemokines (eg CCL3, CCL2, CX3CL1) and they can also act as signalling molecules in pain pathways[35-39]. Non-steroidal anti-inflammatory drugs (NSAIDs) modulate peripheral pain by reducing prostaglandin E2 (PGE2) synthesis by locally induced COX-2. Inflammatory process also induces changes in protein synthesis in the cell body in the dorsal root ganglion and alters the expression and transport of ion channels and receptors including opioid receptors[38]. This underlies the peripheral action of opioid agonists in inflamed tissues[40]. Opioids also act by binding to the opioid receptors centrally or at the dorsal horn. The effect produced depends on the opioid receptor (mu1 and 2, delta, kappa or peripheral opioid receptor) that is bound[41]. These receptors also bind to the endogenous endorphins and enkephalins which the opioids mimic.

There is inter- individual variability in the severity of post-operative pain. This is influenced by multiple factors such as individual sensitivity to pain, psychological factors (eg state of anxiety and somatization), age, and genetic factors. Also, co-morbidities, preoperative cognitive function, general health and perioperative drug therapy also influence pain perception in the post-operative period[42-44]. It may also be genetically determined[24]. Therefore, post operating pain is individual and contextualized. Thus the intensity of post-caesarean pain should ideally be predicted so as to customize analgesia. The design of multifactorial predictive models for post-operative pain and analgesia requirement is still in its infancy; recent research has evidenced some important predictors including maternal expectations, anxiety, and thermal and electrical pain threshold on the lower back near the dermatomes of the surgical wound[42,43,45].

3.2 IMPORTANCE OF POST CAESAREAN SECTION PAIN RELIEF

Prompt and adequate postoperative pain relief is an important component of caesarean delivery that can make the period immediately after the operation less uncomfortable and more emotionally gratifying. Postoperative pain produces adverse physiologic effects as unrelieved pain activates the pituitary-adrenal axis, which can suppress the immune system and result in postsurgical infection and poor wound healing. Sympathetic activation can have negative effects on the cardiovascular, gastrointestinal, and renal systems, predisposing patients to adverse events such as cardiac ischemia and ileus. This manifests on multiple organ systems such as hypoventilation, atelectasis, pneumonia, stress induced hypercoagulable state and increased incidence of deep venous thrombosis[26,46]. Proper management of postoperative pain can improve patient

comfort, decreased perioperative morbidity, and decreased cost by shortening the time spent in the hospitals[16].

Uncontrollable pain can impair functions such as ambulation, dietary intake, breast feeding and early maternal bonding with the infant and can impair the mother's ability to optimally care for her infant in the immediate postpartum period[26,47-50]. High quality pain relief is important after delivery to promote early recovery and optimize the mother's ability to care for her new born[51]. Inadequate pain control can also negatively affect the normal development of infants by affecting nursing activities such as breast-feeding[26,49]. Continuous, unrelieved pain also affects the psychological state of the patient and family members. Common psychological responses to pain include anxiety and depression. The inability to escape from pain may create a sense of helplessness and hopelessness, and these may predispose the patient to puerperal blues, postpartum depression, post-traumatic stress disorder and chronic pain[21]. Patients who have experienced inadequate pain management may be reluctant to seek medical care for other health problems and affect subsequent obstetric care. This may be worst in our environment where there is aversion for caesarean section.

3.3 POST OPERATIVE PAIN ASSESSMENT

Pain is a highly personal experience that is communicated outwardly to healthcare providers, family members, and friends by verbal signals, as well as through body and facial expressions. Patients and their caregiver must understand how to properly assess the character and intensity of surgery-related pain and the response to the analgesic therapies. Pain has been accepted as the 'fifth vital sign', and therefore the development of standards for pain evaluation and its clinical management is very important[52].

Assessment of pain is a critical step to providing good pain management in the post-operative period. In a sample of physicians and nurses, Anderson and colleagues found lack of pain assessment was one of the most problematic barriers to achieving good pain control[53]. There are many recommendations and guidelines for what constitutes an adequate pain assessment but the most critical aspect of pain assessment is that done on a regular basis[53]. The assessment procedure and the time frame for reassessment should be directed by hospital or unit policies and procedures[54]. During the postsurgical period, pain assessment must be brief and simple to complete. Numerous pain intensity measures have been developed and validated. Several tools provide a numeric rating of pain intensity (like - visual analogue scale, numeric rating scale (NRS). Simpler tools such as the verbal rating scale, which classifies pain as mild, moderate or severe, also are commonly used. Selecting the pain assessment tool should be a collaborative decision between patient and health care provider. When this is done during the preoperative period, it ensures the patient is familiar with the scale and will be able respond appropriately in the post-operative period[54,55].

3.3.1 VISUAL ANALOGUE SCALE

A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured. For example, the amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain. From the patient's perspective this spectrum appears continuous and their pain does not take discrete jumps, as a categorization of none, mild, moderate and severe would suggest. It was to capture this idea of an underlying continuum that the VAS was devised. Thus Visual

Analogue Scales are more sensitive to small changes than are simple descriptive ordinal scales[56,57].

The simplest form of VAS is usually a horizontal line, 10 cm in length, anchored by word descriptors at each end (no pain at one end and worst pain at the other end). The patient marks on the line the point that she feels represents the perception of her current pain state. The marked part is then measured from the left end to determine the actual score. Score of 1-4 are classified as mild pain, greater than 4 to 8 as moderate pain and above 8 as severe pain. This type of VAS has been used in similar studies with reliable results[10,13,58-9].

VAS can also be presented in a number of ways, including the following: scales with a middle point, graduations or numbers (numerical rating scales), meter-shaped scales (curvilinear analogue scales), "box-scales," scales consisting of circles equidistant from each other (one of which the subject has to mark), and scales with descriptive terms at intervals along a line (graphic rating scales or Likert scales). Numerical rating scales or number scales consist of numbers without a line, although the term is also sometimes used to refer to graphic rating scales[57].

3.5 POST CAESAREAN SECTION PAIN MANAGEMENT

Good analgesia is important after caesarean section to provide the mother with opportunities for mother-child bonding, early ambulation and discharge, hence leading to greater overall patient satisfaction[49]. Adequate pain relief following cesarean section in women, using safe and effective analgesic combinations, is a universal concern as pain relief is a fundamental human right[17,60-1]. Many options are available for the treatment of postoperative pain, including systemic analgesics (ie, opioids and non-opioids) and

regional analgesic techniques (ie, neuraxial and peripheral). Several studies have investigated different protocols of postoperative pain management in women undergoing cesarean section, and some new technologies have been reported[59,62]. There is currently no gold standard for post–cesarean section pain management. Many options are available and the choices of the method of pain control are determined by drug availability, institutional protocols, individual preferences, available resources, and financial considerations[22]. Post-operative analgesia has traditionally been provided by opioid analgesics[14,18] with the attendant complications. NSAIDS have also been used as single agents but not without complications. However, multimodal analgesia is achieved by combining different analgesics that act by different mechanisms and at different sites in the pain pathway. This results in additive or synergistic analgesia, with lowered adverse effects and lowered total dose of analgesics and pain scores, when compared with the administration of individual analgesics[9,14,63].

3.6 OPIOID AS POSTOPERATIVE ANALGESICS

Opioids have been used for thousands of years for the treatment of acute and chronic pain. Around 3400 B.C., the opium poppy was cultivated in lower Mesopotamia by Sumerians who referred to it as Hul Gil, the 'joy plant'. Ancient Egyptian papyrus records mention opium as a treatment for pain and in 1170, the first book of western surgery described using sponges soaked in opium held over the patient's nose for surgical procedures[41]. However, its side effects, in particular respiratory depression, were noted approximately 600 years ago[64]. The 17th century English physician Thomas Sydenham wrote: 'Among the remedies which it has pleased Almighty God to give man to relieve his suffering; none is so universal and so efficacious as opium'.

The use of opioids in obstetric patients started in 1907 in Austria with Richard Von Steimbuchel, who described the use of morphine and subcutaneous scopolamine for the analgesic management of women in labor. The technique was also used by Carl Gauss and Bernard Kronig in Germany[64]. Opioid drugs, such as meperidine (pethidine), are used extensively in labour. Post operative analgesia has also traditionally been provided by opioid analgesics and are still the pillar playing a central role in post caesarean pain management[14,18].

The opioids are preparation acting on the body's opioid receptors, which normally respond to endorphins and enkephalins which are mood changers especially during stress. Thus morphine, diamorphine, meperidine, meptazinol, codeine, buprenorphine, tramadol, pentazocine and the morphine antagonists such as naloxone are all opioids. They are used for analgesia, sedation and reduction of anxiety and are able to reduce the hyperventilation induced by pain and maintain carbon dioxide at near normal concentrations. In the absence of evidence favouring any particular opioid, the opioid offered is often based on institutional preference[65]. In Nigeria, like in most developing countries, where there is depressed economy and poor health care financing; potent opioids such as morphine and pethidine which have been found to be useful and effective analgesia after major surgical procedures are often lacking[66]. Thus, pentazocine and tramadol are the most commonly used opioids as single agents[10]. However, limited studies are available in literature comparing these two opioids as unimodal or as components of multimodal analgesia after caesarean section[10].

In a study done in Ilorin by Kolawole et al[25], pentazocine was prescribed to 86.4% and tramadol to 13.4% of the patients in their series. Although, 85.2% expressed satisfaction with the level of pain relief, 79.6% and 54.6% felt pain in the recovery room and on the

first post operative day. They concluded that multimodal (balanced analgesia) should be encouraged to ensure effective postoperative control. Adeniji et al[10] compared the efficacy of intramuscular tramadol and Pentazocine as single agents with the addition of piroxicam as multimodal agents in the immediate post caesarean section period. They found that though tramadol had faster onset of action, Pentazocine had better pain control in the first 6 hours post caesarean section and also has longer duration of action. In their study, patient satisfaction was highest with the Pentazocine-piroxicam group[10].

Jabalameli et al[67], compared intraincisional injection of tramadol, pethidine and bupivacaine on postcesarean section pain relief under spinal anesthesia and concluded that the administration of subcutaneous pethidine or tramadol after cesarean section improves analgesia and has a significant morphine-sparing effect compared with bupivacaine and control groups. Fernandes also compared the effectiveness, safety, and tolerability of intravenous tramadol and paracetamol with epidural morphine and paracetamol and found that both protocols are satisfactory in the first 48 hours post caesarean section[68].

Opioids can be administered by various routes using different modes of delivery. In our environment the intermittent intramuscular opioids is commonest route of administration[26]. This is because of convenience, familiarity, relative safety and low cost. Though, this has been found to lead to variable levels of pain relief[25]. Thus, there are serious limitations to their use including

1. This mode of administration often requires repeated injections, and this may be uncomfortable for the patient.

2. Intramuscular or subcutaneous administration provokes peaks and valleys of the opioid blood concentration. Valleys can affect pain relief, while peaks increase the incidence of adverse effects. Obtained blood levels are also likely to vary considerably between individuals.
3. In addition, after the injection, pain relief is not immediate. The time interval needed for the resorption of the drug from the site of injection, and for the drug to reach opioid receptors is variable[16].

3.7 NONSTEROIDAL ANTI-INLAMMATORY DRUGS (NSAIDS)

NSAIDS are important component of post caesarean section multimodal analgesia and with additional anti-inflammatory and antipyretic actions. NSAIDs achieve their hyperalgesia suppressing effect by reducing the concentration of prostaglandins peripherally and centrally, and through several other peripheral and central mechanisms[69]. Cyclic prostaglandins are produced by the cyclooxygenase-catalyzed oxidation of arachidonic acid. NSAIDs inhibit cyclooxygenases, a group that comprises two enzymes: COX-1 and COX-2. Both COX enzymes are very similar in structure, but they have a crucial difference in amino acid sequence at their active site[70,71]. Most COX-1 is constitutively expressed and involved in homeostasis, whereas COX-2 is inducible and involved in pathways of pain and inflammation[72]. Prostaglandins produced through metabolism of arachidonic acid by COX-1 are essential for maintaining the integrity of the gastric mucosa, and allowing normal platelet aggregation, and kidney function[71]. Inhibition of COX-1 by NSAIDs results in the reduction of mucosal prostaglandin cytoprotective functions, in some cases leading to gastric erosions and ulcers. In contrast,

inhibition of COX-2 produces analgesia with fewer adverse effects, particularly gastric erosions, ulcerations, and bleeding (lack of effect on platelet aggregation times)[73,74]. However, some studies have shown that COX-2 inhibition may delay gastric ulcer healing[75]. Most of the available NSAIDS in our centre are non-selective for COX-1 and -2.

A survey found that 54.5% of units use NSAIDs postoperatively in the maternity ward, and in another survey 81%[21]. The use of NSAIDs has been found to be extremely effective in preventing postoperative caesarean section pain thus; National Institute of Clinical Excellence in Britain stated that NSAIDs should be offered after caesarean section[76]. NSAIDs are very effective for relieving pain related to menstrual cramping and this has made interest to grow in the use of NSAIDs to treat the visceral component of post-cesarean section pain. Several different NSAIDs and administration routes have been investigated, including intramuscular[77] and rectal diclofenac[78], intramuscular piroxicam[10], oral naproxen and ibuprofen[80,81] and others. In all these the NSAIDS are used in combination with another form of analgesia. In general, the addition of NSAIDs to a post-cesarean section analgesic regimen has been very successful, both at improving the quality of analgesia resulting from neuraxial or systemic opioids, and at reducing opioid-related side effects[77,81]. Despite these well-documented opioid-sparing effects and the compatibility with breastfeeding[82], NSAIDs must be used with caution. They carry the risk of bleeding, platelet dysfunction and renal insufficiency. Concern has also been raised with regard to uterine atony during the postpartum period. Cases of severe uterine atony associated with a ketorolac or diclofenac administration have been reported[81].

Consequently, the use of NSAIDs in women at risk of postpartum hemorrhage, or suffering from a preeclampsia-induced renal impairment deserves caution.

3.8 MULTIMODAL PAIN MANAGEMENT

Multimodal analgesia is achieved by combining different analgesics that act by different mechanisms (such as opioids, NSAIDs, and local anesthetics). It is an evolving effective postoperative pain control as it results in additive or synergistic analgesia, lower total doses of analgesics, and fewer side effects, decreases pain scores and/or the requirement for postoperative analgesics[9,14]. This is irrespective of whether the agent is given systemically or neuraxially.

Combined use of systemic opioids and NSAIDs relieved postoperative pain more effectively than single-drug regimens. Mitra et al[60] compared the analgesic efficacy of diclofenac-tramadol with diclofenac-acetaminophen and found that both combinations achieved satisfactory post caesarean analgesia with diclofenac-tramadol been more efficacious but associated with more side effects. Another study that compared the efficacy of diclofenac-paracetamol combination verses meperidine only drug showed that diclofenac-paracetamol combination was superior to meperidine as post caesarean analgesia[84]. Different other studies have been compared different analgesics as multimodal combination for post caesarean analgesia[9]. The combination of opioid and NSAIDs may be a very important alternative especially in Nigeria where some of the potent opioids are not readily available and where they do are usually very costly. Besides, potent opioids are associated with side effects such as respiratory depression, drowsiness and dependence. Some of the side effects are unwanted especially in post

caesarean section patient as early breast feeding and maternal-infant bonding may be affected.

CHAPTER 4

METHODOLOGY

4.1 STUDY CENTRE

The Federal Teaching Hospital is a conglomerate of Ebonyi State University Teaching Hospital Abakaliki and Federal Medical Centre Abakaliki formed in 2012. Abakaliki is the state capital of Ebonyi state and the state is one of the five south eastern states of Nigeria. It was created in 1996. Ebonyi state is mainly inhabited by the Igbo speaking community and has the population of about 3 million.

Federal Teaching hospital is a tertiary institution in Ebonyi state. It receives a referral from all parts of the state and neighbouring states of Abia, Benue, Cross-River, and Enugu. The hospital runs a busy obstetric unit. The antenatal clinic holds daily Monday through Friday with about 5000 antenatal registrations per year. The antenatal clinics are conducted by the consultants and the residents in the department. There are about 3500 deliveries per annum with an average caesarean section rate of 20% (obtained from the birth records).

4.2 STUDY POPULATION

The study involved low risk parturients who had elective or emergency caesarean section, under spinal anaesthesia in the Federal Teaching Hospital Abakaliki and who willingly accepted to be part of the study. The details of the study were explained to the patients before the surgery and informed consent obtained.

4.3 SAMPLE SIZE

Sample size (N) will be calculated using the following formula[85].

$N= (U+V)^2 [P_1 (1-P_1) +P_2 (1-P_2)]/ (P_1-P_2)^2$

U= Power of 90% = 1.28

V= Confidence interval of 95%= 1.96

P_1= Expected patient satisfaction using combined pentazocine and diclofenac analgesics is 90%

P_2= Expected patient satisfaction using pentazocine only analgesic is 70%

N= 61, therefore minimum of 73 parturients (N+20%) will be allocated to each group. Studies have shown approximately 90% patient's satisfaction using opioid and NSAID combination and approximately 70% satisfaction with opioid analgesics[10].

4.4 STUDY DESIGN

This was a double blind randomized control study in which a computer generated random numbers sealed in an envelope with the drugs. Each number was coded with a particular drug: either placebo or diclofenac and each participant chose a number that corresponded with the one in the envelope. All the participants received pentazocine 30 mg 4 hourly for 24 hours. In addition each participant received 3 ml of water for injection 12 hourly for 24 hours or diclofenac 75 mg 12 hourly for 24 hours. All the drugs were administered by intramuscular route and each patient was treated along the line of packed analgesic as stated. All the drugs administered were made by the same pharmaceutical company.

4.4.1 INCLUSION CRITERIA

1. Uncomplicated caesarean section under spinal anaesthesia
2. Live baby
3. Fully conscious patient.

4.4.2 EXCLUSION CRITERIA

1. Caesarean section under general anaesthesia
2. Stillbirth
3. History of allergy to pentazocine or diclofenac.
4. Severe obstetric haemorrhage
5. Delirium
6. History of preexisting opioid dependency
7. Sickle cell haemoglobinopathy
8. Peptic ulcer disease patients
9. Those that declined consent
10. Inability to rate pain due to psychiatric illness or illiteracy.

The study compared the effectiveness on intramuscular 30mg pentazocine given 4 hourly as the only post caesarean section analgesic with combined intramuscular 30mg pentazocine 4 hourly and diclofenac 75mg 12hourly. All drugs were administered in the first 24 hours. The intention was to treat and there was no crossover of analgesics. Additional dose of pentazocine was used as break through analgesic at patients request or VAS $\geq$ 6. All the patients received spinal anaesthesia at surgery. The spinal anaesthesia performed at L2-L3 or L3-L4 or L4-L5 interspace with the patient in the sitting

position using a 25-gauge whitacre spinal needle. Then, 2ml of 0.5% hyperbaric (heavy) bupivacaine which is equivalent to intrathecal 20mg bupivacaine hydrochloride was administered. After injection the patient was placed in supine position and the operating table slightly tilted to the left. The patients did not receive any other analgesic at the end of the surgery. However, the agent(s) for the study were administered within one hour after the surgery, according to the number chosen. The injections were administered by trained research assistants who were not involved in the data collection or analysis. The investigator and the participants were blinded to which treatment each subject received until the end of the study when the envelope number code was revealed.

The primary outcome measure was postoperative pain control, while the secondary outcome measures included patient satisfaction and maternal and neonatal adverse outcomes. Pain control was assessed using a visual analog scale (VAS). Each participant was taught on the VAS at the enrolment (before the surgery).The VAS shown below is a 10 cm-long scale marked from 0-10, where 0 represents ‘no pain’ and 10 represents ‘worst possible pain’. Score of 1-4 are classified as mild pain, greater than 4 to 8 as moderate pain and above 8 as severe pain. Each participants was told to make a mark on the horizontal line between 0 and 10 to indicate how much pain she felt. This then was measured from 0 to where the participant marked the line to determine her pain score. Trained research assistants, who were also blinded to the agents of the study, undertook the assessment at 1, 2, 6, 12, 18, 24 hours after the surgery. The side effects of the drugs were also noted.

How severe is your pain now? Place a vertical mark on the line below to indicate how bad you feel your pain now

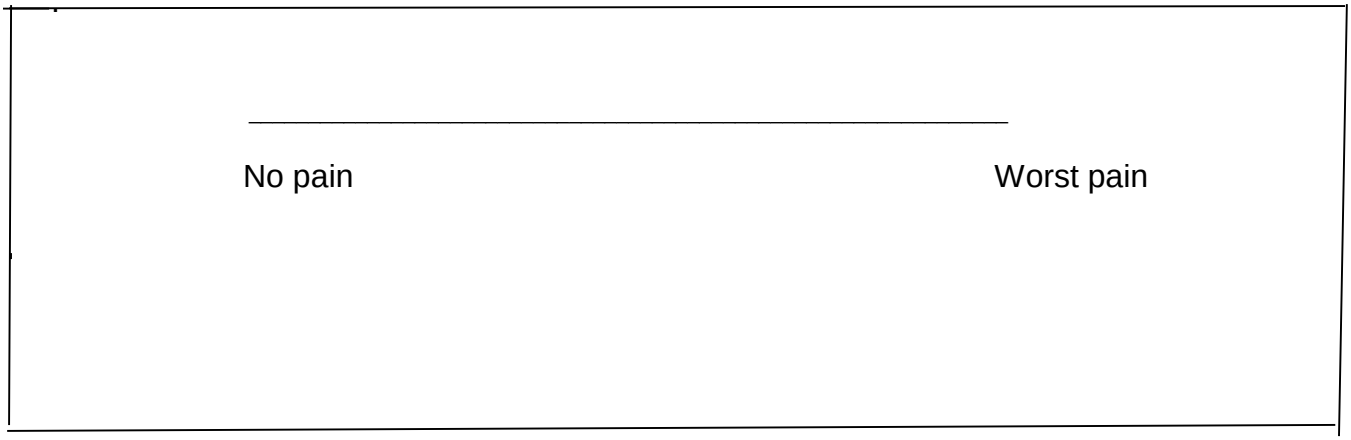

Figure 1: VISUAL ANALOGUE SCALE

4.5 DATA ANALYSIS

The information obtained were entered into a predesigned data sheet. The data was analyzed with Statistical package for Social Science (IBM SPSS statistics) version 22.0. Categorical variables were analyzed using chi square. Means and standard deviation (SD) were calculated for quantitative variables, and the difference between two independent groups was compared using independent sample *t*-test. The level of significance was set at ≤ 0.05.

4.6 ETHICAL CONSIDERATION

Ethical approval was obtained from the ethics committee of the Federal Teaching Hospital Abakaliki. Informed written consent was obtained from each participant included in the study. Consented clients were made to sign or thumb print. The research was done at no cost to the participants.

CHAPTER 5

RESULT

This study was done over a 10 months period (March-December 2015) and a total of 146 parturients who had uncomplicated caesarean sections participated. Three of them opted out of the study and three were not given the drugs according to the protocol. These were not included in the analysis. Thus, 140 were analyzed, 70 in each group. All of them were married. One hundred and thirty-five (97.1%) were Igbos and the remainder were from

Ibiobio, Itsakor and Idoma. All were Christians. Majority of the participants 74(52.9%) had secondary education while 61 (43.6%) had tertiary education and only 5(3.6%) had primary education as their highest level of education. Also majority 63(45%) were of social class 3 while 22(15.7%) were social class 1 and 4 (2.9%) were social class 5. One hundred and twenty four 124(86.6%) were booked while 16 (11.4%) were unbooked. These are shown in table 1.

As shown in table 2 below, 26(37.1%) of those who received pentazocine and placebo had emergency caesarean section while 44(62.9%) had elective surgery. Among those who received pentazocine and diclofenac, 24(34.3%) had emergency caesarean section and 46(65.7%) had elective caesarean section. Those who had primary caesarean section included 45(64.3%) in the pentazocine-placebo group and 51(72.9%) of the pentazocine-diclofenac group while 25(35.7%) had repeat caesarean sections in the former group and 19(27.1%) in the latter group. These were not statistically significant (p>0.005). The mean age, parity, gestational age and duration of surgery are comparable in both groups as shown in table 3. These were not statistically significant (P>0.005).

TABLE 1: Social demographic variables of women who had caesarean section at FETHA

LEVEL OF EDUCATION	**PENTAZOCINE (%)**	**PENTAZOCINE DICLOFENAC (%)**	**TOTAL (%)**	X^2	P-value
Primary	2(2.9)	3 (4.3)	5(3.6)	0.270	0.874
Secondary	38(54.3)	36(51.4)	74(52.9)		
Tertiary	30(42.9)	31(44.3)	61(43.6)		
TOTAL (%)	**70 (100)**	**70(100)**	**140(100)**		
TRIBE					
Igbo	67 (95.7)	69(98.6)	136(97.1)		

Others	3 (4.3)	1(1.4)	4(2.8)	7.610	0.179
TOTAL (%)	**70(100)**	**70(100)**	**140(100)**		
RELIGION					
Catholic	50(71.4)	49(70.0)	99(70.7)		
Protestants	9(12.9)	11(15.7)	20(14.3)	0.581	0.901
Pentecostal	11(15.7)	10(14.3)	21(15.0)		
TOTAL	**70(100)**	**70(100)**	**140(100)**		
SOCIAL CLASS					
1	12(17.1)	10(14.3)	22(15.7)		
2	17(24.3)	21(30.3)	38(27.1)	0.008	0.930
3	32(45.7)	31(44.3)	63(45.0)		
4	8(11.4)	5(7.1)	13(9.3%)		
5	1(1.4)	3(4.3)	4(2.9)		
TOTAL	**70(100)**	**70(100)**	**140(100)**		
BOOKING STATUS					
Booked	63(68.6)	61(87.1)	124(88.6)	0.282	0.595
Unbooked	7(10.0)	9(12.9)	16(11.4)		
Total (100)	**70(100)**	**70(100)**	**140(100)**		

Table 2 showing the distribution of the type of surgery among women who had caesarean section at FETHA

Type of surgery	**Pentazocine (%)**	**Pentazocine diclofenac (%)**	**Total**	**X^2**	**P-value**
Elective	44 (62.9)	46 (65.7)	90	0.124	0.724
Emergency	26(37.1)	24 (34.3%)	50		
Total	**70 (100)**	**70 (100)**	**140**		
Primary	45(64.3)	51(72.9)	96	1.193	0.275

Previous	25(35.7)	19(27.1)	44		
Total	**70(100)**	**70(100)**	**140**		

Table 3: Mean parity, age and gestational age of delivery, estimated blood loss and duration of surgery among women who had caesarean section at FETHA.

Variable	**Group(N=70)**	**Mean ±SD**	**t**	**P value**	**95% Confidence interval of the difference**
Age (yrs)	Pentazocine	30.69 ±1.26	0.552	0.582	-0.996 to 1.768
	Pentazocine diclofenac	30.30 ±1.16			
Parity	Pentazocine	2.87 ±1.56	0.582	0.562	-0.377 to 0.691
	Pentazocine diclofenac	2.71 ±1.55			
Gestational age (weeks)	Pentazocine	39.08 ±1.80	-2.006	0.47	-10.213 to -0.72
	Pentazocine diclofenac	40.09 ±2.67			
Duration of surgery(mins)	Pentazocine	63.10 ±12.29	1.058	0.292	-1.925 to 6.354
	Pentazocine diclofenac	60.89 ±12.47			
Estimated blood loss (ml)	Pentazocine	482.86 ±97.76	0.991	0.324	-16.359 to 49.216
	Pentazocine diclofenac	466.43 ±98.44			

As shown in table 4, the mean pain scores using the visual analog scale in the first 24 hours collect at the 1st, 2nd, 6th, 12th, 18th and 24th hour were higher in the pentazocine-placebo group compared to pentazocine diclofenac group (P<0.001). The mean pain scores in both groups continued to improve with time but the pentazocine diclofenac group maintained the comparative advantage of better analgesia. Age, parity or type of caesarean section (primary or repeat) did not significantly influence on the pain scores (p>0.005). Although those who had elective caesarean section had lower mean pain

score than those with emergency caesarean section as well those with primary compared with repeat caesarean section, but these were not statistically significant. Meanwhile, 19(27.1%) of those who received pentazocine only analgesic also received rescue analgesic and non in the pentazocine-diclofenac group received rescue analgesic ($p<0.001$).

The duration from surgery to ambulation was better in the pentazocine-diclofenac group compared to pentazocine-placebo group 19.97 $\pm$ 2.51 hours versus 18.61 $\pm$ 2.66 hours ($p<0.005$). The duration of surgery to bowel sound present and commencement of oral feeds were 11.60 $\pm$ 2.32 hours versus 9.64 $\pm$1.82 hours ($p<0.001$) and 22.14 $\pm$ 3.07 hours versus 20.37$\pm$2.51 hours ($p<0.005$) respectively in the pentazocine-placebo and pentazocine-diclofenac group. The duration from surgery to passage of flatus was 18.63 $\pm$ 2.14 hours versus 18.56 $\pm$ 2.49 ($p>0.005$) in the pentazocine-placebo group versus pentazocine-diclofenac group respectively. However, the duration of hospitalization in both groups former versus latter is 6.57 $\pm$ 1.25 days versus 6.09 $\pm$ 1.16 days ($p>0.005$). About 54 (77.1%) of those who received pentazocine-placebo were satisfied with the pain relief while 61(87.1%) of those who received pentazocine-diclofenac expressed satisfaction with their pain relief. Meanwhile 38(76.0%) of those who had elective caesarean section and 77(85.6%) of those who had emergency caesarean section were satisfied with the analgesia they had. The side effects reported in both groups were drowsiness and nausea. Although we did not score the degree of drowsiness or sedation, 17(24.3%) of the pentazocine only group reported being drowsy and 6(8.6%) nausea. Among the pentazocine diclofenac group 6(8.6%) reported drowsiness and 2(2.9%) nausea. Two(2.9%) in each group reported that their babies had excessive sleep. There

was no report of undue bleeding, epigastric pain or respiratory depression. Despite these side effects, 66(94.3%) of the pentazocine-placebo group would recommend the treatment to their friends or relatives while 69 (98.5%) of the pentazocine diclofenac group would do the same.

Table 4 showing mean pain scores and duration of activities.

Variable	**Group (N=70)**	**Mean ±SD**	**t**	**P-value**	**95% confidence interval of the difference**
1st Hour VAS	PP	5.01 ±1.64	8.782	0.000	1.782 to 2.818
	PD	2.91 ±1.45			
2nd Hour VAS	PP	4.13 ±1.76	6.217	0.000	1.120 to 2.165

	PD	2.49 ±1.34			
6th Hour VAS	PP	3.56 ±1.86	5.568	0.000	0.958 to 2.013
	PD	2.07 ±1.23			
12th Hour VAS	PP	2.83 ±1.14	8.369	0.000	1.091 to 1.766
	PD	1.40 ±0.86			
18TH VAS	PP	1.96 ±0.84	4.168	0.000	0.360 to 1.011
	PD	1.27 ±1.09			
24TH Hour Vas	PP	1.50 ±0.79	3.222	0.002	0.171 to 0.715
	PD	1.06 ±0.83			
Duration from surgery to ambulation (Hours)	PP	19.97 ±2.51	3.105	0.000	0.69299 to 2.22129
	PD	18.61 ±2.49			
Duration from surgery to flatus passage (Hours)	PP	18.63 ±2.14	0.182	0.856	-0.70546 to 0.84847
	PD	18.56 ±2.49			
Duration from surgery to bowel sound present (Hours)	PP	11.60 ±2.32	5.549	0.000	1.25973 to 2.70855
	PD	9.64 ±1.82			
Duration of surgery to oral feeding(Hours)	PP	22.14 ±3.07	3.738	0.000	0.83430 to 2.70855
	PD	20.37 ±2.50			
Duration of hospitalization (Days)	PP	6.57 ±1.26	2.371	0.19	0.8072 to 0.89071
	PD	6.09 ±1.16			

Note: PP = pentazocine placebo, PD = pentazocine diclofenac, SD = standard deviation

Table 5: comparison of level of satisfaction with the type of surgery and booking status

Variable	**Level of satisfaction**		**Total**	**X^2**	**P-value**
	Unsatisfied	**Satisfied**			
Pentazocine	16(12.9%)	54(77.1%)	70	2.386	0.122
Pentazocine diclofenac	9(12.9%)	61(87.1%)	70		
Total	**25**	**115**	**140**		
Primary CS	16(16.7%)	80(83.3%)	96	0.295	0.587

Repeat CS	9(20.5%)	35(79.5%)	44		
Total	**25**	**115**	**140**		
Emergency	12(24.0%)	38(76.0%)	50	2.001	0.157
Elective	13(14.4%)	77(85.6%)	90		
Total	**25**	**115**	**140**		
Booked	20(16.1%)	104(83.9%)	124	2.209	0.164
Unbooked	5(31.2)	11(68.9%)	16		
Total	**25**	**115**	**140**		

Table 6: Maternal and newborn Side Effects

Side effects	**Pentazocine (%)**	**Pentazocine diclofenac (%)**	**Total**	**X^2**	**P value**
Maternal					
Drowsiness	17(24.3)	6(8.6)	**23**	9.325	0.009
Nausea	6(8.6)	2(2.9)	**8**		
None	47	62	**109**		
Total	**70**	**70**	**140**		
Newborn				0.000	1.000
Excessive sleep	2(2.9)	2(2.9)	**4**		
None	68(97.1)	68(97.1)	**136**		
Total	**70**	**70**	**140**		

CHAPTER 6

DISCUSSION

Pain relief after Caesarean section, despite differences in pain perception, is often restricted to minimum because of the wrong belief that this is the best way to avoid sedation, to maintain the patient as mobile as possible to care for her baby while

preventing thromboembolism and to optimize breast feeding[86]. But, persistent pain will negatively affect mother-child bounding and the success of breast feeding and significantly contribute to the parturient morbidity and cost of care[25,86]. A high quality of analgesia, even if obtained with parenteral morphine, may improve the success of breast feeding and overall quality of care of the patients[10,86]. Unfortunately potent opioids are not readily available in our environment[25]. Thus, we resort to the use of less potent opioids like pentazocine as a major source of post caesarean analgesia. NSAIDs such as diclofenac have been shown to reduce pain caused by uterine cramping and has been found useful for post caesarean pain management[77,81,87].

Limited studies exist in the literature comparing pentazocine with diclofenac through the intramuscular route as post caesarean section analgesics, although these drugs or other related opioids and NSAIDS are often used for the purpose. In this study, the pentazocine and diclofenac were given as fixed interval dosing regimen through the intramuscular route. This is convenient, familiar, relatively safe and of low cost especially in a depressed economy, like ours, with poor health financing[25]. In modern economies, use of potent opioids as patient controlled analgesia (PCA), patient controlled epidural analgesia and continuous epidural infusion are readily available but are costly, requires manpower and costly equipment[86].

The social demographic characteristic of the patients are similar in both groups. Igbo women are known to cope satisfactorily with pain[88] and they constituted about 97% of the parturients who participated in this study. Age, parity and educational status are known to influence pain perception among women in labour[88-9]. The age, parity, education status

and duration of surgery of surgery are similar in both groups and this removes the possible confounding influence of these variables.

The mean pain score over the first 24 hours in the pentazocine- diclofenac group was statistically significant compared to the pentazocine-placebo group. This is consistent with the findings of Wilder-smith et al[90] who studied the effect of intramuscular pentazocine and diclofenac administered simultaneously in women who had elective caesarean section and found a significant post- operative pain control when compared to either drugs alone. Mitra et al[60] compared the analgesic efficacy of diclofenac-tramadol with diclofenac-acetaminophen and found that both combinations achieved satisfactory post caesarean analgesia with diclofenac-tramadol been more efficacious but associated with more side effects. Another study that compared the efficacy of diclofenac-paracetamol combination versus meperidine only drug showed that diclofenac-paracetamol combination was superior to meperidine as post caesarean analgesia[84].This finding is also consistent to the findings of Adeniji and associates[10] in Ilorin who found a lower mean pain score with the combination of pentazocine and piroxicam and tramadol and piroxicam when compared to the use of the either opioids alone. Though, the pain study was for the first 12 hours post operation and they used a higher dose of pentazocine (60mg). A study in Kano with a similar design like this study, though pain study was extended for 48 hours and 50 mg of diclofenac and 60mg of pentazocine administered 12 hourly and 6 hourly respectively, showed statistically significant pain score with combination of intramuscular pentazocine and diclofenac when compared to the use of pentazocine alone[91].

The improved analgesia obtained with the combination of the pentazocine and diclofenac could be explained by the effect of combined action of two different analgesics that interrupt pain transmission at different levels resulting in additive or synergistic analgesia. Pentazocine has both agonist and antagonist action at opioid receptors. It is a weak antagonist at μ opioid receptors. Its analgesic action is derived from an agonist action on ƙ receptors, which interrupts pain pathways in the spinal cord. It also has sedative effect which allays post-operative anxiety. It has no anti-inflammatory or antipyretic function. Diclofenac as an NSAID inhibits prostaglandin synthesis from arachidonic acid by inhibiting cyclooxygenase enzyme. It has long half-life with anti-inflammatory, anti-pyretic and analgesic properties[10,91].

There was significant improvement in the mean pain score for both groups over time. However, the pentazocine-diclofenac group maintained the comparative analgesia advantage. This improvement in the mean pain score could be as a result of the cumulative effect of the repeated dosing of the drugs at regular intervals. It also the follows the natural course of acute posto-perative pain. Adeniji, Adamou and Wilder-Smith and their associates also found similar effects of improved pain score over time in their separate studies[10,90-1].

The patients who received pentazocine and diclofenac combination started ambulation earlier 18.61 hours compared to those who received pentazocine only 19.97 hour ($P<0.001$). The former group also had bowel sound present earlier and started oral intake earlier compared to the latter group (9.64 and 20.37 hours compared to 11.60 and 22.14 hours) $P<0.001$. This is comparable to the finding of Adamou et al[91] who also found earlier mobilization and bowel activity in the pentazocine and diclofenac group compared to

pentazocine only group. This is important as early mobilization and initiation of feeding in a post-caesarean patient will improve patient's psychological and emotional well-being and level of satisfaction. It will also encourage breastfeeding, maternal-child bonding and prevent thrombo-embolic events, uterine sub-involution and post-partum haemorrhage.

There was no statistical difference in the duration of hospitalization between the two groups (P>0.005). Adamou also found that there was no difference in the duration of hospitalization between the groups they studied[91]. This is because many other factors other than pain relieve play role in the decision on patients discharge. Such other factors include the surgeons preference, choice and use of antibiotics, degree of wound healing and type of anterior abdominal wall incision (midline versus Pfannenstiel incision) as well as maternal and child clinical conditions.

Patient's satisfaction was high in both groups: 87.1% in pentazocine and diclofenac group 77.1% pentazocine only group, despite the statistical difference in the mean pain score for both groups. This is similar to the findings of Kolawole and Fawole[25] in Ilorin who found 85.2% of their patient expressed satisfaction on the pain relieved they had. It is also consistent with the findings of Adeniji and Atanda[10] in Ogbomosho who documented 68.4% of the patient's satisfaction among the pentazocine only group, 89.2% among the pentazocine piroxicam group and 70.9% satisfaction among the tramadol-piroxicam group. It however, differed with the findings of Adamou et al[91] in Kano who found significant difference in patient's satisfaction between the pentazocine-diclofenac group and pentazocine only group. The type of surgery, elective versus emergency and primary versus repeat, and the booking status had no influence on the patient's satisfaction.

Patient's level of satisfaction has been described as an imprecise measure of assessing the effectiveness of post-operative pain management. This is because patient often have low expectation of pain relief from the outset and this enhances their coping ability. Thus, they feel grateful for any measure taken to alleviate their pain[25].

The side effect profile was similar in both groups. However, there were more cases of drowsiness among the pentazocine only group compared to pentazocine diclofenac group. No side effects was noted by the breastfeeding babies except excessive sleep. This was similar to the findings of Adeniji et al[10]. However, Adamou noted excessive sleep and poor suckling as side effects in the babies, although not statistically significant[91]. The side effect profile especially that of drowsiness more in the pentazocine compared to combination of pentazocine and diclofenac may have occurred by chance since both groups received the same dose of pentazocine. Though the cumulative effects of both drugs may have helped to reduce the side effects.

In conclusion, the addition of diclofenac to pentazocine achieved a good analgesia and patient satisfaction with minimal side effects in the first 24 hours after caesarean section. This is very important especially in a resource-poor country like Nigeria where potent opioids are not readily available and affordable yet there is need to achieve optimum pain control following caesarean section.

RECOMMENDATION

1. Adequate post caesarean pain control is the patient's right and can be achieved through readily available and affordable drugs like pentazocine and diclofenac.
2. The use of pentazocine and diclofenac for immediate post caesarean section pain control should be made the departmental protocol of Obstetrics and Gynaecology, Federal Teaching Abakaliki and other health institutions where potent opioids are not readily available and affordable.

3. Pain assessment should be part of the vital signs charting in all the surgical units. This will help individualized analgesics after surgery.
4. A multi-centered study with the same design and agents of study like this one will be necessary to validate the outcome of this research.
5. A study involving the use of 30mg pentazocine at less frequent intervals, for example 6 hourly, in combination with diclofenac could be done. This will help reduce sedative effect of pentazocine and other side effects.

LIMITATIONS OF THE STUDY

1. All drugs were administered by intramuscular route which may have contributed to the patient's discomfort.
2. Due to financial constraint I was unable contact a pharmaceutical company to produce the diclofenac and water for injection that had similar container and label.
3. Pain is a subjective experience and we may not have been able to measure how much pain each parturient felt.
4. Costs of the drugs were not considered as part of the outcome variable.

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CONFLICT OF INTEREST: None

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DISSERTATION WORK PLAN

No	ACTIVITY	June 2014	July-Oct 2014	Oct 2014	March 2014-Dec 2015	January 2016	January 2016	January 2016	April-May 2016
1	Proposal to Department	X							
2	Ethical clearance		X						
3	Submission of proposal to college			X					
4	Data collection				X				
5	Data analysis					X			
6	Presentation to Dept						X		
7	Submission to college							X	
8	Examination								X

PENTAZOCINE VERSUS COMBINED PENTAZOCINE AND DICLOFENAC FOR PAIN RELIEF IN THE FIRST 24 HOURS AFTER CAESAREAN SECTION: A RANDOMIZED CONTROLLED STUDY

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF FELLOWSHIP OF THE NATIONAL POSTGRADUATE MEDICAL COLLEGE OF NIGERIA IN OBSTETRICS AND GYNAECOLOGY

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