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Mussel RL, De Sa Silva E, Costa AM, Mandarim-De-Lacerda CA (2003). Mast cells in tissue response to dentistry materials: an adhesive resin, a calcium hydroxide and a glass ionomer cement. *J. Cell. Mol. Med.* 7:171-178.

Booth M, Bundy DA, Albonico P, Chwaya M, Alawi K (1998). Associations among multiple geohelminth infections in school children from Pemba Island. *Parasitol.* 116: 85-93.0.

Fransiscus RG, Long JC (1991). Variation in human nasal height and breath, *Am. J. Phys. Anthropol.* 85(4):419-427.

Stanislawski L, Lefeuvre M, Bourd K, Soheili-Majd E, Goldberg M, Perianin A (2003). TEGDMA-induced toxicity in human fibroblasts is associated with early and drastic glutathione depletion with subsequent production of oxygen reactive species. *J. Biomed. Res.* 66:476-82.

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*Full Length Research Paper*

## Reasons for admission and mortalities following admissions in the intensive care unit of a specialized hospital, in Ethiopia

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Many studies have been conducted in the intensive care unit (ICU). But little is known about the outcomes of ICU admissions. This is particularly the case in the ICU of developing countries. Thus, the aim of this study was to assess reasons and outcomes of admissions in the ICU of Jimma University Specialized Hospital (JUSH). A longitudinal study was conducted in the ICU of JUSH from February 7 to April 15, 2011. All patients admitted to the ICU during the study period were followed till discharge or death. Data was coded and entered into the Statistical Package for Social Sciences (SPSS) windows version 16.0 to generate descriptive statistics. Sixty nine patients admitted to the ICU during the study period were followed prospectively till discharge or death. Diseases of cardiovascular origin (30.4%) followed by surgical interventions (18.8%) were the major reasons of ICU admission. There were 26 (37.7%) deaths during the study period in the ICU. Mortality rate in the ICU was found to be significantly high. Diseases of cardiovascular origin were the major reasons for ICU admission. Hence, responsible bodies need to seek for possible ways of reducing this unacceptably high mortality in the ICU by devising quality control mechanisms.

**Key words:** Reasons of admission, outcome of admission, intensive care unit.

### INTRODUCTION

Hospitalization should occur or should be considered depending on each patient's presenting symptoms and physical examination. The decision to admit patients to the medical wards was determined by age, co-existing

illness, physical and laboratory findings, the ability of the patient to comply reliably with an oral medication, and the resources available to the patient outside the hospital (Dipiro et al., 2008; Mandell and Wunderink, 2008). The

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death rate in the medical wards of Jimma University Specialized Hospital (JUSH) was reported to be 12.6%, communicable diseases being the most common reasons for admission (Ali and Woldie, 2010).

Most patients do not require admission to the intensive care unit (ICU) and are admitted to a monitored unit or general medical floor. ICU is a consolidated area of a hospital where patients with acutely life threatening illnesses or injuries receive around the clock specialized medical and nursing care, such as mechanical ventilation and intensive cardiac monitoring (Kohn et al., 2000; Leapfrog Group, 2014). Admission to an ICU may be required if the patient experiences hemodynamic instability requiring frequent monitoring of vital signs, invasive hemodynamic monitoring, or rapid titration of intravenous medications with concurrent monitoring to assure safe and effective outcomes (Dipiro et al., 2008; Mandell and Wunderink, 2008). Apart from causing death, the type and severity of illnesses can directly affect the length of stay in the ICU. Although ICU admission for asthma is relatively uncommon, it remains to be associated with appreciable in-hospital mortality (Lange et al., 2009; Mayr et al., 2006; Gruenberg et al., 2006; Roch et al., 2011; Gupta et al., 2010).

Planned surgery (43%), infection (12.1%), sepsis (10.1%) and cardiac arrest (8.0%) were the most common reasons for ICU admission among which 10.9% of the patients died while they are in the ICU. Similar mortality rate was reported from another ICU, 9.5% (Lange et al., 2009; Mayr et al., 2006). On the other hand, mortality rate as high as 26% has also been reported by one study (Enget al., 1992).

The estimated mean in France, in a multi-center study, is about 15% for ICU mortality and 6 to 25% for hospital mortality after ICU discharge, yielding a hospital mortality rate of 20 to 30%, with substantial variations across studies (Azoulay et al., 2003). A recent systematic review revealed that patients admitted to an ICU over the weekend appear to be at an increased risk of death, while nighttime admissions were not associated with an increased mortality (Cavallazzi et al., 2010). On the other hand, a study reported from Canada concluded that time of admission does not have significant effect on outcome of patients admitted to the ICU (Ala et al., 2011). A study on acute myeloid leukemia showed that survival was inferior in those patients admitted to the ICU compared to those who were not admitted. However, no difference between intensive care and non-intensive care patients was found concerning continuous complete remission at 6 years or survival at 6 years (Schellongowski et al., 2011).

However, much cannot be said about ICUs in Ethiopia since there are no studies so far. Therefore, this study is reporting the findings of the analysis done from the data collected primarily to pick medication errors at the ICU of JUSH (Agalu et al., 2011). This analysis aimed to identify reasons for admission and outcomes of admissions to the

ICU in JUSH.

## METHODOLOGY

### Study area and design

The longitudinal study was conducted as part of broader cross-sectional study on medication errors (Agalu et al., 2011, 2012) from February 7 to April 15, 2011 in the ICU of Jimma University Specialized Hospital (JUSH), a teaching hospital located in Jimma town, Southwestern Ethiopia, 350 km from Addis Ababa. JUSH is the only referral hospital in Southwest Ethiopia with 450 beds and 558 health professionals where a multidisciplinary team of diverse professionals provide a range of health care services for approximately 9000 inpatients and 80,000 outpatients each year. The ICU has 6 beds serving patients from the different departments of the hospital (Jimma University Specialized Hospital, 2014).

### Participants

All critically ill patients who were admitted to the ICU of JUSH during the study period were included in the study. All patients admitted to the ICU during the study period were followed till discharge or death. Patient cards and medication documentation charts were also reviewed.

### Data collection and management

Data was collected using a pre-tested structured data collection format by one trained clinical pharmacy post-graduate student together with principal investigator. Since this paper is the product of the broader study on, accessory data was compiled from that study. The content of the format included demographic variables, diagnoses and co-morbidities, dates and time of prescription, name of the medication, dosage forms, doses, frequency, and duration of medications prescribed. Demographic information about patients was obtained from patient card and medication charts. Diagnosis made by physicians was taken from patient cards. Finally, the data was edited, coded, entered into SPSS windows version 16.0 and finally cleared. Descriptive statistics were generated to meet the objective.

### Ethical considerations

Prior to the study, ethical approval was obtained from the Ethical Review Board of Jimma University. The management of the hospital was requested for cooperation with formal letter. Written consent was obtained from the nurses, physicians and patients included in the study and names of patients and the health professionals were replaced with their initials. All data obtained in the course of the study were kept confidentially and used solely for the purpose of the study.

## RESULTS

About 69 patients were admitted to the ICU during the data collection period (9 weeks period). Majority of these patients were females 38 (55.1%) and in the age group of 18 to 50 years, 44 (63.8%) (Mean age of  $32.87 \pm 17.03$  years). About 54 (78.3%) of them were admitted to other

**Table 1.** Characteristics of patients admitted to the ICU of JUSH, April 2011 (n=69).

Characteristic		Frequency (%)
Age (years)	<18	12 (17.4)
	18-50 years	44 (63.8)
	>50 years	13 (18.8)
Sex	Male	31 (44.9)
	Female	38 (55.1)
Level of consciousness	Conscious	37 (53.6)
	Unconscious	32 (46.4)
Regimens taken	Complex	49 (71.0)
	Not complex	20 (29.0)
State of admission	From emergency department	15 (21.7)
	From other wards	54 (78.3)
Length of ICU stay	<4 days	28 (40.6)
	>=4 days	41 (59.4)

wards before they come to the ICU, about 32 (46.4%) were unconscious and 49 (71.00%) received complex regimen (average of  $5 \pm 2$  drugs). Patients stayed  $5.654 \pm 5.22$  days in the ICU till death/transfer to other wards. Average number of co-morbid conditions per patient was  $3 \pm 2$ . (Table 1).

Twenty six (37.7%) patients died during the 9 weeks period. Eighteen (69.2%) patients who died in the ICU were in the age group of 18-50 years while 14 (53.8%) of the patients who died in the ICU were males. Nineteen (73.1%) of the patients who died in the ICU were admitted in other wards prior to ICU admission while 7 (26.9%) of the deaths were among patients directly admitted to the ICU from the emergency department (Table 2).

Common diagnoses that lead to ICU admission were diseases of cardiovascular origin 21 (30.4%), followed by surgical interventions for various reasons 13 (18.8%) and respiratory tract infections 8 (11.6%) (Table 3). Infectious diseases were the commonest (51.7%) co-morbid conditions in patients admitted to the ICU followed by cardiovascular disorders (21.7%) (Table 4). On the other hand, cardiogenic shock (18.8%), surgical interventions (8.7%), traumatic brain injury (7.2%) and severe community acquired pneumonia (7.2%) were common specific diseases that led to ICU admission (Table 5).

## DISCUSSION

According to this study, the commonest diagnoses that lead to ICU admission were diseases of the cardiovascular system (30.4%) followed by surgical interventions of

various reasons (18.8%) and respiratory tract infections (11.6%). Similar finding was reported from Austria (Lange et al., 2009) but it was different from what was found in the medical wards of JUSH (Ali and Woldie, 2010), where infectious diseases were the commonest causes of admission.

In this study, infectious diseases were the commonest (51.7%) co-morbid conditions followed by cardiovascular disorders (21.7%). This is similar with the finding in the medical wards of JUSH. This might be explained by the fact that majority of the ICU admissions in the JUSH come from the medical wards where patients with chronic diseases often have co-morbid infectious (Ali and Woldie, 2010). Unlike the previous study where severe community acquired pneumonia, pyogenic and chronic meningitis, and malaria were common (Ali and Woldie, 2010), the present study showed that cardiogenic shock, surgical interventions and traumatic brain injury were the major reasons that lead to ICU admission. This difference might be due to the difference in the ward where ICU only serves severe cases as compared to the general medical wards.

The death rate in the ICU was 26 (37.7%) which was higher than findings reported in earlier works from France (multi-center study), ICU of Asthma in London and JUSH (Ali and Woldie, 2010; Gupta et al., 2004; Azoulay et al., 2003). On the other hand, it is lower than the finding of a study from Australia (Lange et al., 2009). The differences observed in this regard might be related to the difference in patient profile and the ICU setting in which the patients were managed.

Being the part of broader study in medication errors and based on accessory data, this study did not assess

**Table 2.** Distribution of mortalities in the ICU of JUSH, April 2011 (n=69).

Patient characteristic	Outcome of ICU admission		Total	
	Discharged from ICU	Died		
Sex of patient	Male	17	14	31
	Female	26	12	38
	Total	43	26	69
Age of patient (years)	<18	10	2	12
	18-50	26	18	44
	>50	7	6	13
	Total	43	26	69
Length of hospitalization (days)	<4	11	17	28
	>=4	32	9	41
	Total	43	26	69
State of the patient	Conscious	31	6	37
	Unconscious	12	20	32
	Total	43	26	69
Presence of co-morbidities	Yes	36	24	60
	No	7	2	9
	Total	43	26	69
Reasons for ICU admission	Cardiovascular disorders	10	13	23
	Infection	10	5	15
	Respiratory disorders	2	0	2
	Surgical interventions	9	4	10
	Trauma	4	3	7
	Urinary tract disorders	2	0	2
	Others*	4	1	5
	Total	43	26	69

Others\*: CNS disorders, GI disorders, burn, Guillain Barre syndrome (GBS), endocrine disorders, autoimmune disorders

**Table 3.** Reasons for ICU admission in the ICU of JUSH, April 2011.

Disease category	Frequency (%)
Cardiovascular disorders	21 (30.4)
Surgical interventions	13 (18.8)
Respiratory tract infections	8 (11.6)
Trauma	7 (10.1)
Infections	6 (8.7)
Hemodynamic disorders	2 (2.9)
Endocrine disorders	2 (2.9)
Urinary tract disorders	2 (2.9)
Respiratory tract disorders	2 (2.9)
Others*	4 (5.8)
Total	69 (100)

Others\*: CNS disorders, Burn, Guillain Barre syndrome (GBS), gastrointestinal (GI) disorders.

the severity of disease conditions during admission.

Similarly, it did not calculate prognostic score, standard mortality ratio, comorbidity index and did not use Glasgow Coma Scale to determine the level of consciousness. It has to be noted that this study did not consider death of patients after discharge from the ICU. Moreover, it did not determine all the possible causes for death including medication errors. Since patient cards and medication charts were reviewed prospectively, all the diseases and co-morbidities patients had not been identified during data collection.

All these might affect the quality of data, thus should be used as the possible insights for the future studies in the ICU.

In conclusion, diseases of cardiovascular origin were the major reasons for ICU admission and there were significant deaths among admissions in the ICU. Hence, responsible physicians and others concerned need to seek for possible ways of reducing this unacceptably high mortality in the ICU by determining the causes for it. Supporting such efforts with further studies to identify

**Table 4.** Major co-morbidities in the ICU patients of JUSH, April 2011.

Specific disease	Frequency (%)
Infections	31 (51.7)
Cardiovascular disorders	13 (21.7)
Uterine rapture	2 (3.3)
Endocrine disorders	2 (3.3)
Neurologic disorders	2 (3.3)
Trauma	2 (3.3)
Others*	11 (18.3)
Total	60 (100)

Others\*: Coagulation related disorders, cerebro-vascular disorders, gastrointestinal (GI) disorders.

**Table 5.** Specific disease that lead to ICU admission in JUSH, April 2011.

Specific disease	Frequency (%)
Cardiogenic shock	13 (18.8)
Surgery for acute abdomen	6 (8.7)
traumatic brain injury	5 (7.2)
Sever community acquired pneumonia	5 (7.2)
Congestive heart failure	4 (5.8)
Tetanus	3 (4.4)
Eclampsia	3 (4.4)
Diabetic keto-acidosis	2 (2.9)
Surgery for peritonitis	2 (2.9)
Uterine rapture	2 (2.9)
Sepsis	2 (2.9)
Hospital acquired pneumonia	2 (2.9)
Guillain Barre syndrome	2 (2.9)
Others*	18 (26.1)
Total	69 (100)

Others\*: Acute coronary syndrome, soft tissue laceration, asthma, septic shock, hypertension.

predictors of mortality in the ICU is warranted.

**Competing interests**

The authors declare that they have no competing interests.

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*Full Length Research Paper*

## Whole-body vibration and benefits for people with osteoarthritis: A systematic review

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Whole body vibration (WBV) can be an important tool to treat patients with osteoarthritis (OA). The purpose of this study was to systematically review published research concerning the use of WBV in people with OA. In PubMed and Scopus, the number of publications (NP) is respectively to the keywords arthrosis, 289,586 and 10,569, osteoarthrosis, 299,158 and 3,952, arthritis, 251,453 and 236,849 and osteoarthritis, 56,323 and 80,008. Putting together the information found in the analyzed 4 papers, the numbers of subjects were ranging from 15 to 52 and frequencies ranging from 24 to 40 Hz. Self-report of the status of disease (WOMAC) was used in 2 papers, while the pain levels were evaluated by the visual analog scale (VAS) in 2 papers. Different tests were used in these studies, as (i) TUG, (ii) step test, (iii) 20-meter walk test, (iv) timed get up and go test (TGUG), (v) chair stand test (CST), (vi) 6-minute walk test (6MWT), (vii) knee muscle strength (extension/flexion) and (viii) proprioception (threshold for detection of passive movement (TDPM) to evaluate the effects promoted by the exercises due to the WBV. In conclusion, these studies indicate that the WBV could bring some benefits to patients with OA.

**Key words:** Osteoarthrosis, arthrosis, arthritis, PubMed, Scopus, whole body vibration, oscillating/vibratory platform.

### INTRODUCTION

Joints are functional units of the body that aid in the transmission of mechanical loads between contacting the

bones during normal daily activities or in special situations related with sports and work. All the components

of the joint, including the articular cartilages (AC), bone, muscles, ligaments/tendons, nerves and synovial fluid participate in load transmission (Arokoski et al., 2000; van den Berg, 2010).

AC are found on the epiphyses of long bones and function to cushion, to act as load-bearing structures and, in consequence, to reduce the friction in the articular surfaces. AC composed of a smooth, lubricated, reversibly compressible tissue that protects the underlying bones from biomechanical damage during joint loading. Failure in one or more of the components of the joint can cause joint malfunction, which, in turn, may lead to the accumulation of damage in other joint components and impairment of the entire body (Eyre et al., 2006; Wu et al., 2011).

### Articular cartilages and osteoarthritis

AC have received much of the attention in osteoarthritis (OA) studies, because gross AC damage is the most obvious pathologic feature leading to joint dysfunction. Miehle (1987) has reported that in contrast to German-speaking regions, where the expression "arthrosis" is used, English-speaking countries prefer the term "osteoarthritis" to express disorders of the articular cartilage. Arthritis, arthrosis, osteoarthritis and osteoarthrosis are other terms used in the investigations of the clinical disorders associated with the AC (Lieveense et al., 2002).

Patients diagnosed with AC defects are at increased risk for the early development of OA (Gilligly et al., 1998; Charlton et al., 2008). OA is the most common form of arthritis in the USA (Lawrence et al., 2008; Loeser, 2006; National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), 2013), and the most prevalent and degenerative joint disorder worldwide (Reginster, 2002; Stein et al., 2010). In addition to being the most prevalent form of arthritis, knee pain associated with OA is the leading cause of disability in older adults (Peat et al., 2001). The central feature of OA is the destruction and loss of the AC of the articulating bones, which can lead to the dysfunction of the joint (Loeser, 2006; NIAMS, 2013). Moreover, AC degenerates with the development of fibrillation and fissures, and full thickness loss of the joint surface (French et al., 2013). In contrast to other forms of arthritis, such as rheumatoid arthritis, a systemic disorder of the immune system that can affect the skin, lungs, eyes, and blood vessels, OA affects only the function of the affected joint (NIAMS, 2013).

Mechanical forces have strong influence on the

synthesis and rate of turnover of AC molecules, such as proteoglycans (PG). Moreover, regular cyclic loading of the joint, (i) enhances the synthesis of PG, increasing the rigidity of the cartilage and (ii) appears to have fewer effects on the AC collagen fibril network. Continuous compression of the AC diminishes PG synthesis and can cause injuries of the tissue due to possible necrosis. Moreover, it is suggested that OA starts from the cartilage surface due to the PG depletion and fibrillation of the superficial collagen. Several investigations have been published about alterations of structures neighboring the joint and related to abnormalities in the gross appearance, material properties, cellular morphologies, biochemical composition, and gene expression in AC in human beings and in animals with AO (Loeser, 2006; Goldring and Goldring, 2007; Meulenbelt et al., 2007; Bijlsma et al., 2010; van den Berg, 2010; Schroepel et al., 2011; Wang et al., 2011). Characteristics of OA include (i) phenotypic changes in the cells of the superficial layer of the AC, (ii) chondrocyte hypertrophy and apoptosis, (iii) progressive fibrillation and fissures of the AC, (iv) subchondral bone sclerosis, (v) bony outgrowths (osteophyte) formation, and (vi) increased remodeling of the periarticular bone (French et al., 2013; Bijlsma et al., 2010; van den Berg, 2010).

### Osteoarthritis and treatments

AC have received much of the attention in OA studies because gross AC damage is the most evident pathologic characteristics leading to joint dysfunction. There are no proven treatments capable of markedly altering the progression of the OA (The American College of Rheumatology (ACR), 2013; Osteoarthritis Research Society International (OARSI), 2013). Zhang et al. (2008) have reported evidence-based guidelines for the medical management of knee OA based upon systematic reviews of previously published guidelines, meta-analyses, reviews, and studies. Moreover, the ACR and OARSI state the goals of treatment of knee OA as (a) reducing joint pain and stiffness, (b) improving joint function and reducing disability, (c) improving health-related quality of life, (d) limiting the progression of joint damage and (e) avoiding any toxic effects of therapy, if possible.

ACR (2013) and ORSI (2013) agree that the preferred treatment of knee OA would involve a combination of pharmacologic and nonpharmacologic therapies, with pharmacologic therapies added to the nonpharmacologic modalities as indicated by individual circumstances.

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### Nonpharmacologic modalities of treatment

Exercise appears to be the most recommended nonpharmacologic treatment for knee OA. ACR and OARSI suggest aerobic exercise and resistance training (to strengthen periarticular muscles such as the quadriceps) as treatments that have been shown to modestly, yet significantly, improve the range of motion (ROM) of the knee, reduce pain, improve function and reduce disability.

Additional benefits of exercise programs mentioned in the ACR guidelines include less analgesic consumption, fewer visits to a physician, improved knee joint position sense, and improved performance of activities of daily living lasting up to six months.

Additional nonpharmacologic treatments recommended by the ACR and OARSI include walking aids such as walkers, canes, or crutches used in the contralateral hand. These aids can reduce loading in the affected knee leading to reduced pain and improved physical functioning. Further recommendations include wedged insoles, medial patella taping, and knee braces to correct abnormal biomechanics contributing to OA symptoms. These modalities have been shown to reduce pain, instability, and risk of falling. Heat therapy and cryotherapy, acupuncture, and transcutaneous electrical nerve stimulation are additional therapies recommended, to a lesser degree, by the OARSI for the management of knee OA symptoms.

### Pharmacologic modalities of treatment

Because of its safety and efficacy, the simple analgesic acetaminophen is recommended as the preferred pharmacologic treatment for mild to moderate knee OA pain, especially for long-term use. Evidence presented by the ACR shows some disagreement regarding the efficacy of acetaminophen as compared to nonsteroidal antiinflammatory drugs (NSAIDs). While some studies indicate that acetaminophen is as effective as NSAIDs in relieving mild to moderate joint pain, other studies suggest a greater improvement in pain with NSAIDs. Yet additional studies suggest that they may be equally effective in relieving mild to moderate joint pain, with NSAIDs being more effective in treating severe pain.

In patients not effectively responding to oral analgesics, treatments involving injections directly into the joint such as glucocorticoids and hyaluronic acid (HA) are recommended, to a lesser degree, by both groups. For patients whom have not responded to other pharmacologic treatments or in cases where other treatments are contraindicated, both groups recommend the use of weak opioids (e.g. tramadol, codeine) and narcotic analgesics for the relief of moderate to severe knee OA pain. Stronger opioids (e.g. oxycodone, fentanyl, morphine) should

be reserved for the treatment of severe pain in extreme circumstances. The negative influence of such side effects on fall risk and quality of life in the knee OA patient underscore the limitations of opioids as a treatment (Goodwin et al., 2005; ACR, 2013; OARSI, 2013).

Glucosamine and chondroitin sulphate, two naturally occurring components of cartilage proteoglycans, are often taken as nutritional supplements by individuals with OA. They are recommended, to some degree, by the OARSI for the treatment of knee OA, although mixed evidence exists regarding efficacy in pain reduction and functional improvement. Small amount of evidence is presented by the OARSI suggesting that they may have beneficial structure-modifying effects in the knee joint.

### Surgical interventions

When a combination of nonpharmacologic and pharmacologic treatments fails to provide adequate pain relief and functional improvement in severe knee OA cases, there are a number of surgical procedures recommended by the ACR and OARSI. Total joint arthroplasties are recommended by both groups with evidence indicating reduced pain, improved function, and improved health-related quality of life in many cases. Osteotomy is recommended by both groups as a means of correcting abnormal biomechanics in the knee, and slowing the progression of OA. Finally, arthroscopic debridement to remove debris such as loose cartilage and meniscus fragments is recommended by both groups, but less strongly. In spite of the evidence in favor of their effectiveness in treating severe cases of knee OA, the combination of the financial costs, and the psychological and physical health risks associated with surgery (Lingard and Riddle, 2007; Patella et al., 2008; Webb et al., 2008; Haas et al., 2008), especially in a population characterized by advanced age and frequent comorbidities, make surgical treatment of knee OA undesirable in many cases, and unfeasible in others. An alternative treatment, such as, whole body vibration (WBV) could prove beneficial.

### Whole body vibration and the oscillating/ vibratory platform

Vibration is a mechanical stimulus that is created by an oscillating/vibratory motion that it usually delivered through an oscillating/vibratory platform. Vibration can be characterized by its magnitude and its frequency. The magnitude is determined by the amplitude, or peak to peak displacement of the oscillation. The frequency is measured in oscillations per second. Together, these factors determine the intensity of the vibration (Rittweger, 2010).

Vibration has long been studied for its negative effects

on the body, usually as the result of exposure in the workplace to either high intensity vibration or chronic exposure to large amounts of vibration over many years. These negative effects have been summarized in previous reviews and include damage to nerves, blood vessels, and joints (including the spine), as well as disruption of proprioception, vision, and hearing (Jordan et al., 2005; Lings and Leboeuf-Yde, 2000; Seidel, 1993; Abercromby et al., 2007). In spite of the existing negative reports, much research has been conducted regarding the potential beneficial effects of the WBV on the body.

Cardinale and Wakeling (2005) emphasize that vibration is a natural stimulus that we experience everyday as our bodies are acted upon by external forces, while interacting with our environment. They note that vibrations are commonly experienced in sporting activities and that the transmission of these vibrations throughout the body is dependent upon the properties of numerous different tissues including bone, cartilage, and muscle. Previous reviews provide evidence of the numerous effects including increased muscle strength and power, improved balance, improved blood circulation, improved bone mineral density, improved health-related quality of life, and hormonal fluctuations (e.g. growth hormone, IGF-1, cortisol, and testosterone) resulting from WBV exposure (Gómez-Cabello et al., 2012; Prisby et al., 2008; Bruyere et al., 2005; Jordan et al., 2005; Cardinale and Wakeling, 2005; Cardinale and Bosco, 2003).

Cardinale and Bosco (2003) report that vibration was first utilized as an exercise intervention by Russian scientists in the mid 1980's. More recently, whole body vibration training (WBVT) has been utilized both scientifically and recreationally using commercially available platforms designed to produce sinusoidal vibrations of adjustable frequency and amplitude. While there appears to be mixed evidence regarding the ability of WBVT to stimulate a significant cardiovascular response (Jordan et al., 2005), some have concluded that WBVT can elicit cardiovascular and metabolic responses in some people similar to other forms of mild exercise (Cardinale and Wakeling, 2005). Because of its wide range of potential physiological benefits, and because it can be applied in a relatively low-effort, low-impact manner with no complicated technique to learn, some have suggested that WBVT may be of particular benefit to the elderly and special populations characterized by impaired mobility (e.g. patients with stroke, Parkinson's disease, osteoporosis, or arthritis) (Prisby et al., 2008; Cardinale and Wakeling, 2005; Cardinale and Bosco, 2003; Arias et al., 2009; Pinto et al., 2010).

*In vitro* studies have been conducted that suggest that vibration may have a beneficial effect on cartilage synthesis (Liu et al., 2001; Takeuchi et al., 2006). Mechanical loading, such as vibration, may regulate chondrocyte function through some yet to be determined pathway, and

suggested the possible involvement of chondrocyte cell surface receptors for certain cartilaginous extracellular matrix (ECM) molecules (Liu et al., 2001). Takeuchi et al. (2006) found that, in cultured chondrocytes, vibration significantly increased the synthesis of chondroitin sulfate, an ECM component, and that the effect was even greater in the presence of hyaluronic acid (HA). They also reported increased expression of proteins involved in the intracellular signal transduction system in groups of chondrocytes treated with vibration. An additional proposed benefit from this study is improved nutrient delivery and waste removal among chondrocytes as a result of a more even distribution of HA and movement of the ECM, caused by vibration.

Despite these interesting and promising findings, it must be noted that in terms of frequency, amplitude, and duration, the vibration parameters applied in these settings were quite different than what is typically applied in human populations. Furthermore, no evidence of similar beneficial effects exists *in vivo*, and the long-term effect of WBV on articular cartilage is still unknown (Prisby et al., 2008). Nevertheless, the existence of a safe and efficient stimulus to combat the effects of aging on chondrocytes would be groundbreaking in the treatment of OA.

## AIM OF THE STUDY

In this study, the terms arthritis, arthrosis, osteoarthritis and osteoarthritis will be used to characterize disorders associated with the AC. As no previous systematic reviews of the effects of WBV exercise on people with OA have been published, the purpose of this study was to review published research concerning the use of WBV in people with OA using PubMed and Scopus databases.

## METHODOLOGY

### Databases used in this study

PubMed and SciVerse Scopus online databases were searched on the 13th of June 2014. PubMed comprises more than 23 million citations for biomedical literature from MEDLINE, life science journals, and online books (<http://www.ncbi.nlm.nih.gov/pubmed>).

SciVerse Scopus is the world's largest abstract and citation database of peer-reviewed literature and quality web sources. It contains 53 million records, 70% with abstracts, nearly 21,915 titles from 5,000 publishers worldwide (<http://www.info.sciverse.com/scopus/about>).

### Search strategy used to find the publications involving WBV and clinical articular diseases

Searches were performed using the keywords: (i) arthrosis, (ii) arthrosis and "whole body vibration", (iii) osteoarthritis, (iv) osteoarthritis and "whole body vibration", (v) arthritis, (vi) arthritis and "whole body vibration", (v) osteoarthritis, (vi) osteoarthritis and "whole body vibration", (vii) arthrosis and "vibratory platform", (viii)

**Table 1.** Publications involving arthrosis/arthrititis/osteoarthrosis and vibration.

<b>Keywords searched</b>	<b>NP (PubMed)</b>	<b>NP (Scopus)</b>
Arthrosis	289,586	10,569
Arthrosis and "whole body vibration"	20	0
Osteoarthrosis	299,158	3,952
Osteoarthrosis and "whole body vibration"	27	1
Arthritis	251,453	236,849
Arthritis and "whole body vibration"	14	6
Osteoarthritis	56,323	80,008
Osteoarthritis and "whole body vibration"	15	22
Arthrosis and "vibratory platform"	1	0
Arthritis and "vibratory platform"	1	0
Osteoarthrosis and "vibratory platform"	1	0
Osteoarthritis and "vibratory platform"	1	2
Arthrosis and "oscillating platform"	1	0
Arthritis and "oscillating platform"	0	0
Osteoarthrosis and "oscillating platform"	1	0
Osteoarthritis and "oscillating platform"	0	0

NP: Number of publications.

arthrosis and "vibratory platform", (ix) osteoarthrosis and "vibratory platform", (x) osteoarthritis and "vibratory platform", and (xi) arthrosis and "oscillating platform", (xii) arthritis and "oscillating platform", (xiii) osteoarthrosis and "oscillating platform", (xiv) osteoarthritis and "oscillating platform".

#### **Inclusion and exclusion criteria to select the publications**

Papers were included for review if they met the search criteria and described a study using whole body vibration generated by an oscillating platform used to treat people with clinical articular diseases and the paper was available only in English. Review articles, case reports and investigations only with healthy subjects were excluded. Papers about the effect of the occupational use of the vibration in workers and involving studies with animals were also deleted. Investigations performed involving whole body vibration and other therapeutic procedures were not considered to be analysed.

Data were independently abstracted by the authors and disagreements were resolved by consensus of, at least, three co-authors.

#### **RESULTS**

Table 1 shows the number the publications (NP) found with the keywords when they were searched in PubMed and Scopus databases. In PubMed, NP using the keywords arthrosis, osteoarthrosis and arthritis was almost the same. Considering the Scopus database, intriguingly, NP was extremely lower to arthrosis and osteoarthrosis; however, NP with the keyword arthritis is closed to PubMed. The search using the keywords involving articular disorders (osteoarthrosis or osteoarthritis or arthrosis or arthritis) and source of vibration ("whole body

vibration", "oscillating platform", "vibratory platform") yielded 82 publications in PubMed and 31 publications in Scopus.

The four selected English language publications found with keywords "whole body vibration" and some terms related to articular disorders that reached all the inclusion criteria were analyzed. Descriptions of the type of platform, the subjects (number, sex and age), the frequency and the amplitude used in the platforms used in these 4 studies are as shown in Table 2.

Putting together the information found in the analyzed four papers, the number of subjects ranged from 15 to 52. Moreover, the frequencies used in the studies ranged from 24 to 40 Hz. The self-report of the status of disease (WOMAC) was used in 2 papers (Trans et al., 2009; Avelar et al., 2011) while pain levels were evaluated by the visual analog scale (VAS) in 2 papers (Cloak et al., 2010; Salmon et al., 2012). Different tests were used in these studies, as (i) TUG, (ii) step test, (iii) 20 m walk test (Salmon et al., 2012), (iv) timed get up and go test (TGUG), (v) chair stand test (CST), (vi) 6-minute walk test (6MWT), (Avelar et al., 2010), (vii) knee muscle strength (extension/flexion) and (viii) proprioception (threshold for detection of passive movement (TDPM) to evaluate the effects promoted by the exercises due to the WBV (Trans et al., 2009).

#### **DISCUSSION**

Osteoarthritis, arthritis, arthrosis and osteoarthrosis are terms that have been used in studies related to the clinical

disorders associated with the articular cartilages (Lievens et al., 2002). However, when these terms are used as keywords in searches in different databases, we found an intriguing result. Using the keyword arthrosis, only 10,569 references were found in the Scopus database, while 289,586 were found in the PubMed. A similar finding was observed when the keyword osteoarthritis was used. When these keywords arthrosis and osteoarthritis were used in the searches, the number of publications in both databases was similar. As Scopus and PubMed are important databases, these findings can be relevant to aid in a discussion about the keywords that must be used to try to find references about arthropathy. Searches using the different words related with arthrosis and WBV revealed a reduced number of publications, although WBV is widely available to exercisers and patients, as well as the fact that it is used to treat various musculoskeletal and neurological disorders (Schuhfried et al., 2005; Wunderer et al., 2010). Rittweger (2010) reported that it appears as if this modality is still unknown to the scientific community and our findings seem to confirm this belief. The number of publications about the effects and applications of the WBV has increased strongly in the last three years, as it is possible to see in the databases used in this study.

Review articles, case reports, investigations only with healthy subjects, papers about the effect of the occupational use of the vibration in workers and involving studies with animals, investigations performed involving whole body vibration and other therapeutic procedure were not considered to be discussed (Osugi et al., 2014; Park et al., 2013; Gómez-Cabello et al., 2012; Melnyk et al., 2009; Melnyk et al., 2008).

Following the exclusion criteria, only four papers could be selected for discussion in the current work (Trans et al., 2009; Avelar et al., 2011; Cloak et al., 2010; Salmon et al., 2012). Concerning to the use of WBV in patients with osteoarthritis, the number of publications found in the databanks varied (17 to 52 subjects). As it would be expected, due to the prevalence of this disease (Lawrence et al., 2008), the number of females in the investigations is greater than the number of males. All the authors have reported positive effects of the WBV (Trans et al., 2009; Avelar et al., 2011; Cloak et al., 2010; Salmon et al., 2012) with improvements of some clinical function in patients with osteoarthritis. An important finding in this revision is that although the number of the studies is small, they may constitute first hints for the efficacy of WBV in the treatment of the osteoarthritis.

In addition, in general, exercise therapy has been considered to be an important and supportive treatment for people with musculoskeletal disorders (French et al., 2013). WBV exercises are performed in oscillating platforms, and Madou and Croni (2008) have reviewed the effects of WBV on physical and physiological capability in special populations and they concluded that WBV provides

alternative and/or additional therapeutic interventions to improve physical and functional performance. The specific loading parameters and the value of WBV as compared with conventional interventions need to be the source of future research.

OA is associated with multiple impairments of muscle and articular functions, balance and pain that cause a decrease of the quality of life of the subject (van den Berg, 2010; ACR, 2013; ORSI, 2013). In addition, there is no cure to this disease and, concerning to non-pharmacologic and non-invasive therapy, the aim of the treatment is to optimize and to improve the neuromuscular and articular functions, as well as to increase the muscular strength. With these purposes, the vibrations generated in the oscillating/vibratory platforms would be expected that WBV exercises would seem an important alternative to the management of patients with osteoarthritis due to some benefits related to the action in the muscle performance reported in the papers presented as shown in Table 3. Salmon et al. (2012) have reported that the time to complete the step test at 5 min after the WBV improved significantly from the pretest with a moderate correlation with the VAS scores. Avelar et al. (2011) found that the performance of patients in all the functional tests (BBS, TGUT, CST and 6MWT) and in all domains of the WOMAC have improved in the group submitted to the WBV. Cloak et al. (2009) demonstrated that the absolute centre of mass distribution has improved over 6 weeks due to the WBV. Trans et al. (2009) reported that in the patients with osteoarthritis, the muscle strength and knee-extension significantly increased due to the WBV.

The potential mechanisms by which WBV improves neuromuscular performance and pain are not well understood, although a few theories on how WBV can stimulate the neuromuscular system have emerged. It is extensively theorized that the WBV stimulus causes short and rapid changes in muscle fiber length which result in skeletal muscle reflex contractions (Ritzmann et al., 2010). These reflexive contractions result in an increased neuromuscular load placed on the muscle (Roelants et al., 2006). On the other hand, another mechanism could be the proprioceptive feedback potentiation of inhibition of pain by vibration receptors in the skin stimulate inhibitory interneurons in the spinal cord, which in turn act to reduce the amount of pain signal transmitted from A- $\delta$  and C fibers across the midline of the spinal cord and from there to the brain (Melzack and Wall, 1965). This mechanism increases pain threshold (Lunoeberg et al., 1987). This could explain how WBV applied to the lower limbs could improve VAS scores.

In conclusion, the number of publications found in the databases searched involving WBV and osteoarthritis is small, and, in general, the protocols are different. In addition, the number of publications about the effects and applications of the WBV has increased strongly in the last

**Table 2.** Data about the devices of the oscillating platform, the subjects, the frequency and the amplitude used in the oscillating platforms.

Reference	Subjects (sex, age, groups)	Platform manufacturer	Oscillation frequency and amplitude	Inclusion criteria
Salmon et al. (2012)	17 Adults (13 Female and 4 Male aging 66.9 ± 9.39) with symptomatic knee OA.	Power Plate VP (2004 Model Power Plate Personal, USA)	35 Hz and amplitude of 4-6 mm	Knee AO was determined by a questionnaire based upon self-REPORTED Previous diagnosis by a physician and symptoms consistent with ACR Clinical Classification Criteria for OA of the knee.
Avelar et al. (2011)	23 Participants (3 male and 20 female) divided in 2 groups: squat training with WBV (12, age 75 ± 5), and squat training without WBV (11, age 71 ± 4).	Commercial model of VP was used (FitVibe, GymnaUniphy NV, Bilzen, Belgium)	Frequency of 35 -40 Hz, amplitude of 4 mm, and acceleration that ranged from 2.78 to 3.26 g.	Diagnosed with OA in at least one knee in accordance with the clinical and radiographic criteria of the ACR
Cloak et al. (2010)	38 Female dancers (19 years ± 1.1) with self reported unilateral FAI were randomized in 2 groups: WBV and Control.	VP (Bosco, Greece) while bare foot. NEMES (Nemes Bosco-system, Rome, Italy)	Frequency from 30 up to 40 Hz	Self reported unilateral chronic ankle instability. Subjects completed a CAIT questionnaire to determine their inclusion.
Trans et al. (2009)	52 Female patients with knee-OA (age 60.4 years ± 9.6) were randomized in 3 groups: WBV-exercise on a stable platform (VibM; n = 17, age 61.5 ± 9.2, WBV-exercise on a balance board (VibF; n = 18, mean age, 58.7 ± 11.0)), or control group (Con; n = 18, mean age, 61.1 ± 8.5).	Conventional stable WBV platform (VibM, Xendon, Sweden) (VibM) or a balance board with a built-in vibration device (Vibrosfäre, ProMedVi, Sweden) (VibF). Both machines are applying WBV/oscillation muscle stimulation to the lower extremities.	The training Intensity was increased by with the the frequency (24–30 Hz)	The patients were recruited from the outpatient clinic and were all otherwise healthy. 52 patients fulfilled the ACR criteria for knee AO including both clinical and radiographic signs of OA, and all patients' diagnosis of knee OA.

WOMAC: Western Ontario and McMaster Universities Arthritis Index, OMERACT-OARSI: Osteoarthritis Research Society International (OARSI) and the Outcome Measures in Rheumatology Committee criteria, CPG: Conventional physiotherapy, WBV: whole body vibration, FAI: Functional ankle instability, VP: vibration platform, ACR: American College of Rheumatology, CAIT: Cumberland Ankle Instability Tool questionnaire, g: gravity

**Table 3.** Study protocols, measures, results and conclusions from the selected papers.

Reference	Study protocols	Measures	Results	Conclusion
Salmon et al. (2012)	Participants stood on the platform with knees slightly flexed and received tri-planar (mostly vertical), sinusoidal WBV, 10 times (60 s increments with 60 s rest periods) between each about WBV. The total exposure time was 10 min.	Outcome measures included time(s) required to complete the tests: TUG, step test, 12 MWT, as well as knee pain levels as measured using a 10 cm VAS	The time to complete the step test at 5 min after WBV improved significantly from the pre-test with a moderate correlation with the VAS scores. Post-hoc analyses did not indicate improvements from pre-test seen at 5 min after WBVT, and one hour after WBVT. Acute bout of WBVT was effective in improving the ability of individuals with knee OA to perform a step test and 12 MWT.	Our findings suggest that WBVT may be an effective nonpharmacologic modality to treat some knee OA symptoms and improve ADLs.

Table 3. Contd.

Avelar et al. (2011)	The intervention lasted for 12 weeks, 3 times per week. Participants were randomized in 2 groups. The intensity of squatting exercise training was augmented in the vibration and exercise groups over the 12-week study period by increasing the number of repetitions and reducing the resting time. In the vibration group, acceleration was also increased by varying the vibration frequency (35 – 40 Hz).	Four functional performance tests: BBS, TGUG, CST, and 6- 6MWT, and a self-report of the status of disease (WOMAC)	No statistical difference in functional performance and self-report of disease status between the groups was found, but performance in all the functional tests and in all the domains of WOMAC improved in the vibration group compared to their initial status. In the exercise group, performance improved only two tests (BBS and 6MWT), and there was a reduction in self-reported pain (WOMAC) compared to their initial status.	Although the addition of WBV to squat training failed to result in a significant improvement in functional performance and self-reported status of knee osteoarthritis in the elderly, the intragroup results suggest that WBV may represent a feasible and effective way of improving the functionality and self-perception of disease status in older adults with knee OA.
Cloak e al. (2010)	Participants in the treatment group followed a structured 6 week progressive vibration programme (single leg exercises increasing in duration and vibration frequency as the training progressed). At the beginning of 6 weeks, participants were in 2 groups: WBVG and CG. WBVG did exercises on VP. CG refrained from any ankle specific strength/balance training during the 6-week period and continued their normal training regime.	Absolute centre of mass (COM) distribution during single leg stance, SEBT normalized research distances and peroneus longus mean power frequency (fmed) were measured pré and post 6-week intervention.	Significant improvement in COM distribution over the 6 weeks from $1.05 \pm 0.57$ to $0.33 \pm 0.42$ cm <sup>2</sup> , and 4 of the 8 planes of direction in the SEBT Ant, Antlat, Med and Antmed from $77.5 \pm 7.1$ to $84.1 \pm 5.8\%$ ( $P < 0.05$ ) compared to control groups during the course of the 6 week training intervention. There was no evidence of improvement in peroneus longus (fmed) over time ( $P = 0.915$ ) in either group.	WBVT improved static balance and SEBT scores amongst dancers exhibiting ankle instability but did not affect peroneus longus muscle fatigue.
Trans et al. (2009)	WBVG performed unloaded static WBV exercise. WBVG trained twice a week for 8 weeks, with progressive increase of the intensity. The WBVG performed unloaded static WBV exercise. The two intervention programs consisted of 16 training sessions within an 8-weeks. Training was twice a week with at least 2 days of rest between two sessions. CG did not do any training.	Knee muscle strength (extension/flexion) and proprioception (TDPM) was measured. Self-reported disease status was measured using WOMAC.	Muscle strength increased significantly in VibM compared to Con. Isometric knee-extension significantly increased in VibM compared to Con. TDPM was significantly improved in VibF compared to Con, while there was a tendency for VibM to perform better compared to Con. No effects in the self-reported disease status measures.	This study showed that the WBV-exercise regime on a stable platform (VibM) yielded increased muscle strength, while the WBV-exercise on a balance board (VibF) showed improved TDPM. The WBV-exercise is a time-saving and safe method for rehabilitation of women with knee-OA.

SEBT: Star Excursion Balance Test; WOMAC: Western Ontario and McMaster Universities Arthritis Index; ADLs: activities of daily living; VAS: Visual Analog Scale; BBS: Berg Balance Scale; TGUG: Timed Get Up and Go Test; CS: Chair Stand Test; 6MWT: 6-Minute Walk Test; 12MWT- 12-Minute Walk Test; TDPM: threshold for detection of passive movement; VP: vibration platform; WBVG: WBV group; CG: control group.

the last three years. The analysis of the findings of these studies indicates that the WBV could bring some benefits to patients with OA. In addition, we suggest further larger scale investigations with controlled parameters and well designed protocols into the effects of WBV exercises in people with osteoarthritis. This would be highly desired to improve the quality of life of the patients with this

disease, decreasing pain and the medications, as well as to avoid surgery.

#### ABBREVIATIONS

**OA**, Osteoarthritis; **ECM**, cartilaginous extracellular matrix; **NP**, number of publications; **NSAIDs**, nonsteroidal antiinflammatory drugs; **ROM**, range of

motion; **WBV**, whole body vibration; **WBVT**, whole body vibration training.

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*Full Length Research Paper*

## Medical treatment of the complication of first trimester pregnancy loss with misoprostol

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The objective of the study was to evaluate the efficacy of misoprostol in patients with complication of first trimester pregnancy loss. After the departmental approval, a total of 102 women with first trimester pregnancy failure were recruited for treatment with misoprostol. The inclusion criteria were gestational age of less than 12 weeks and hemodynamically stable. The exclusion criteria were patients with history of hypersensitivity to prostaglandin, bronchial asthma and hemoglobin less than 9 g. Main outcome measures were the successful resolution of miscarriages without surgical intervention; secondary outcomes were incidence of pain, vaginal bleeding, infection, pyrexia and gastrointestinal side effects. A total of 102 women were included in the study. Age ranged from 16 to 40 years and parity ranged from 0 to grand multipara. Women were not selected according to parity but parity was a random occurrence. No relationship was found between parity and response to treatment with misoprostol. Incomplete abortion was found in 82 (80.39%), an embryonic pregnancy in 7 (6.86%) and early fetal demise in 13 (12.74%). 62.74% women completely expelled the conceptual products on treatment with misoprostol alone, while 38 (37.25%) patients required surgical evacuation due to incomplete expulsion of conceptual products. Mean induction to expulsion interval was 15.66 h. Main side effects noted were pain, pyrexia, nausea, vomiting and diarrhea. More than one side effect was noted in 7 (22.54%) patients. Treatment of early pregnancy loss with misoprostol is efficient, acceptable and cost effective for patients with complications of first trimester pregnancy loss.

**Key words:** Misoprostol, medical treatment, miscarriage.

### INTRODUCTION

Post abortion care refers to the services required by women who have problems after pregnancy failure. Treatment is recommended in first trimester pregnancy loss to reduce morbidity like pelvic inflammatory disease

(PID), hemorrhage, blood coagulation defects, and chronic pelvic pain in fertility. Medically, pregnancy loss is usually described as "incomplete" or "missed" abortion. An "incomplete abortion" is usually diagnosed when the

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woman has an open cervix and has passed some, but not all the products of conception. A “missed abortion” is diagnosed when a woman has a closed cervix, a uterus which does not increase in size and a non-viable embryo or fetus (an embryonic pregnancy or an embryonic/fetal demise). Terminology is embryo (0 to 8 weeks) and fetus (9 to 12 weeks).

There are different treatment options available for treatment of early pregnancy loss; the choice lies between expectant, surgical and medical treatment (Khan et al., 2007; Alberman, 1992; Macrow and Elstein, 1993). Expectant management is to wait for spontaneous abortion, but the success rate with the use of this approach for embryonic or fetal death or anembryonic gestation is suboptimal (ranging from 25 to 76%). The interval to spontaneous expulsion is unpredictable, and it may take a month. The uncertainty and anxiety, along with the sadness resulting from pregnancy loss, often make expectant management less appealing to patients (Ballagh et al., 1998; Jurkovic et al., 1998).

Surgical evacuation was the treatment of choice before medical treatment was used, but due to increased morbidity associated with surgical procedure, studies are ongoing to determine the efficacy and safety of medical treatment (Khan et al., 2007). Prostaglandins have emerged as the agents of choice for medical treatment of first trimester pregnancy loss.

Several studies have shown that medical treatment is a safe, effective and acceptable alternative to suction curettage. Misoprostol (15 deoxy-16 hydroxy 16 methyl PGE<sub>1</sub>) is a stable, synthetic form of prostaglandin E<sub>1</sub> analogue. It was originally developed in 1970's for the prevention of non-steroidal anti-inflammatory drugs (NSAID) induced peptic ulcers (Luise et al., 2002; Mazhar et al., 2013; Awan et al., 2008). Several clinical trials have evaluated the use of misoprostol alone for termination of early pregnancy failure (Bogratee et al., 2014; Beucher et al., 2003).

In the last two decades, medical termination of pregnancy has become a safe alternative to vacuum aspiration and dilatation and curettage (Blanchard et al., 2005; Borgatta et al., 2004; Creinin and Damry, 1993). The cost savings to the patient and family is extremely important, even if the misoprostol administration did not lead to uterine evacuation. It would soften the cervix and make surgical evacuation an easier procedure.

The objective was to study the efficacy of misoprostol in women with complication of first trimester pregnancy loss as this is cost effective for low resource population. Misoprostol has long been used in our country, but there are few studies regarding its use as abortifacient.

## METHODOLOGY

After the departmental approval, a total of 102 women with first trimester pregnancy failure were recruited for treatment with misoprostol. The women were given detailed information regarding different treatment options available, only women who accepted the

medical treatment with misoprostol were selected. The inclusion criteria were gestational age of less than 12 weeks and hemodynamically stable. The exclusion criteria were patients with history of hypersensitivity to prostaglandin, bronchial asthma and hemoglobin less than 9 g. Gestational age was determined by clinical examination and ultrasound.

All women were given detailed information about the protocol of medical termination of pregnancy and were then admitted. Routine physical examination and investigations were carried out. Investigations included full blood count, urine routine examination, random blood sugar, blood group and rhesus factor, hepatitis screening, liver function tests, renal function tests and blood coagulation profile, quantitative HCG serum testing and STD were also performed.

Main outcome measures were the successful resolution of miscarriages without surgical intervention; secondary outcomes were the incidence of pain, vaginal bleeding, infection, pyrexia and gastrointestinal side effects.

After taking informed consent, misoprostol was inserted intravaginally in posterior fornix by a resident doctor in a dose of 800 mcg (4x200 mcg) with repeat dose every 3 to 4 h for total of 3 doses. Women who resided within Hyderabad city were allowed to go home with advice for follow up visit on third day, while others from rural areas were admitted. Women who did not completely expelled the products of conception on third day were administered a second dose of 800 mcg with advice for follow up on seventh day if the products of conception were still not completely expelled. The medical treatment was considered unsuccessful and a surgical evacuation was performed. Vital signs of vaginal bleeding and abdominal pain were assessed and adverse effects were recorded. Induction to expulsion interval was defined as the time in hours from initiation of therapy until the expulsion of products of conception. All data were collected in a predesigned proforma and were analyzed on SPSS version 16.0

## RESULTS

A total of 102 women were included in the study. Age range from 16 to 40 years and parity ranged from 0 to grand multipara (Table 1). Women were not selected according to parity but parity was a random occurrence. No relationship was found between parity and response to treatment with misoprostol (Table 2).

Incomplete abortion was found in 82 (80.39%), an embryonic pregnancy in 7 (6.86%) and early fetal demise in 13 (12.74%). Sixty four (62.74%) patients completely expelled the conceptual products on treatment with misoprostol alone, while 88 patients (37.25%) required surgical evacuation due to incomplete expulsion of conceptual products.

Mean induction to expulsion interval was 15.66 h. Main side effects noted were pain, pyrexia, nausea, vomiting and diarrhea. More than one side effect was noted in 7 (22.54%) patients (Table 3).

## DISCUSSION

Termination of pregnancy for various reasons is a common obstetrical problem. Induction of abortion needs meticulous and effective care. The rate of maternal mortality and morbidity increases significantly by surgical

**Table 1.** Distribution according to age.

Age (years)	No. of patients	Percentage
16-20	24	23.52
21-30	52	50.98
31-40	18	17.64
>40	8	7.84

**Table 2.** Distribution according to parity.

Parity	No. of patients	Percentage
PG	67	65.68
1-4	17	16.66
>4	18	17.64

**Table 3.** Side effects with misoprostol.

Side effect	No. of Patients	Percentage
Pain	47	46.07
Pyrexia	6	5.88
Nausea	14	13.72
Vomiting	6	5.88
Diarrhea	1	0.98
Heavy vaginal bleeding	7	22.54

methods for termination of pregnancy as compared to medical methods. Medical method has become a safe alternative to vacuum aspiration and dilatation and curettage (Blanchard et al., 2005; Borgatta et al., 2004; Creinin and Damry, 1993).

Misoprostol is the prostaglandin of choice as it is cheap and stable at room temperature. Different doses of oral or vaginal misoprostol have been used; however, the ideal dose and route is yet to be established (Khan et al., 2007). The regimen using repeated doses of misoprostol alone that can be finished within one day have the advantage of requiring less hospital visits and ultrasound examinations.

This study treatment with misoprostol resulted in complete expulsion of products of conception in 62.74% of the cases. In our study, successful abortion were found in 62.74% of the cases which is in accordance with other studies[14-17]. While a higher success rate of 80.4 and 90% was found in studies conducted by Borgatta et al. (2004), Jain et al. (2002, 2001).

Traditional methods of surgical evacuation of uterus are associated with major morbidity in up to 1% women and minor morbidity in 10%. Recently, misoprostol regimen has become more widely available and is now considered to be the gold standard for early pregnancy termination (Demetroulis et al., 2001; Faundes et al., 2007; Gemzell et al., 2007; Graziosi et al., 2004).

It was found that treatment with low dose regimens, that is, dose of 200 to 400 µg every 4 to 6 h were associated with less successful outcome as compared to our regimens of 800 mcg misoprostol. Szymarska et al. (2003) reported 30.0% success rate with the use of 400 µg of vaginal misoprostol and this success variation may be due to this reason. Differences in initial dosage, time interval during administrations, method and routes of drug administration, population and criteria for diagnosis of incomplete abortion were suggested to be relevant in explaining differences in outcome (Graziosi et al., 2004; Jain et al., 2002, 2001).

In our study, vaginal route was used for administration of misoprostol. Vaginal route appears to be the most effective, followed by sublingual with oral being the least effective. Sublingual misoprostol needs a more frequent administration, that is, every 3 h to achieve a similar effectiveness to the vaginal route (Koooper and Mishell, 1996; Kovavisarach and Jamnansiri, 2005; Mailre et al., 2000; Behrashi and Mahdian, 2009).

Incidence of pyrexia (5.88%), nausea (13.72%), vomiting (5.88%), diarrhea (0.98%), and heavy vaginal bleeding (22.54%), respectively. This is comparable to the study conducted by Mazhar et al. (2013). Oral and sublingual administration of misoprostol is associated with more gastrointestinal side effects than vaginal route. Abdominal pain was noted in 54.9% of women. It was much high in comparison to other studies (Wood and Brain, 2002; Neilsen et al., 1999). The incidence of heavy vaginal bleeding >500 ml was 22.54%. It was in contrast with the study conducted by Khan F.M when only 6.2% patient had heavy vaginal bleeding. None of the patient had pelvic inflammatory disease.

Age, parity and gestational age did not affect success route of medical abortion using misoprostol. Similar observation was noted in other studies (Neilsen et al., 1999; Zhang et al., 2005).

## Conclusion

Treatment of early pregnancy loss with misoprostol is efficient, acceptable and cost effective for patients with complications of first trimester pregnancy loss.

## Conflict of Interest

None to declare

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