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ORIGINAL ARTICLE

Management of complex ankle fracture: A Ghanaian experience

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Ankle fractures are among the most common conditions for surgical emergencies in most developing countries including Ghana. Despite the fact that many ankle fractures are uncomplicated, a high proportion may require surgical intervention. Decision-making depends on recognition of the fracture pattern, availability of surgical implants and anaesthetic materials. In resource-limited settings where patients are unable to afford the cost of surgical implants and anaesthetic materials associated with ankle fractures, suggested modification of the open reduction and internal fixation (ORIF) technique have proven to yield satisfactory results. This study retrospectively assessed the effectiveness of the modified ORIF method among Ghanaians living within the Tamale metropolis, a resource-limited setting located in the Northern Region of Ghana. The study reviewed 70 cases of bimalleolus fractures which were either treated using the ORIF based on the Association for the Study of Internal Fixation (ASIF) protocol or a modified version of the ORIF which involves internal fixation of the malleolus without screws. The findings indicate that the modified method is as good as ORIF (based on ASIF protocol) with added benefits such as shorter operation time, reduced risk of anaesthetic complications and cost of operation (anaesthetic agents and orthopaedic implant cost) as well as reduced number of foreign bodies (implants) leading to a lower risk of wound infections. The use of this method however demands that foot and ankle joint must be handled with extreme care so as not to dislocate the tibia malleolus post-operatively.
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Keywords*:* Bimalleolus, surgical, open reduction, internal fixation, bone fracture, Ghana

INTRODUCTION

As a weight-bearing joint, the ankle can absorb great amount of shock and pressure up to about 6 times the individual's body weight (Carr *et al.*, 2003). Excessive amount of energy across the ankle joint can lead to fracture. Ankle fractures are considered the most common of all fractures treated in hospitals (Yang *et al.*, 2011). In the United States of America (USA), the incidence per year of ankle, tibia and fibula fractures is about 492,000. (Praemer *et al.*, 1992; Weening and Bhandari, 2005) and in the United Kingdom (UK), documented incidence rate of fractures is 14.8% per 10,000 persons per year (Van Staa *et al.*, 2001). In Africa however, the incidence is expected to be higher due to additional high incidence of road traffic accidents (Twagirayezu *et al.*, 2008). Road traffic accidents are said to account for about 46.3% of ankle fractures in Nigeria (Ifesanya and Alonge, (2012) and about 71.5% of lower limb fractures in Rwanda (Twagirayezu *et al.*, 2008)

The management of ankle fracture in the general populace has been documented to range from non-operative restriction to open reduction and internal fixation (ORIF). Irrespective of management method, anatomic alignment of the ankle joint and complete healing are major factors which can ensure long-term treatment success (Dahners, 1990; Egol *et al.*, 2000) and to prevent arthritis due to abnormal pressure distribution because of malunion of the ankle fracture (Ramsey and Hamilton, 1976). The quality of bone and related cartilage injury, age and alignment of the joint surface (Walheim and Akerman, 1936; Klossner, 1962) as

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well as the type of fracture (Lindsjo, 1985) are other factors to consider during management. However, ORIF is said to offer a potential for more rapid recovery than non-operative treatment (Lindsjo, 1985; Porter *et al.*, 2008). Congruent joint, fracture union, functional motion, normal strength and optimal recovery time are the main objectives of any management method of ankle fracture (Jelinek and Porter., 2009). In a resource-limited setting where availability and accessibility to surgical implants and anaesthetic materials is a major problem coupled with the fact that the community dwellers may not be able to afford the cost of surgical implants and anaesthetic materials, a modification of the method may be necessary. This study retrospectively assessed the effectiveness of the modified ORIF method among Ghanaians living within the Tamale metropolis and its surrounding environs, a resource-limited setting located in the Northern Region of Ghana.

PATIENTS AND METHODS

Study site and participants

A total of 70 patients who received complex ankle fracture or bimalleolus fracture management at the Tania Specialist Hospital between September 2005 and September 2010 were included in this retrospective study. Patient characteristics (age and gender), fracture type, mechanism of injury and treatment type were retrospectively reviewed. After review of patient data, the subjects were grouped into two based on method of treatment. Group one (n = 35) was treated with open reduction and internal fixation (ORIF) using principles of the Arbeitsgemeinschaft Osteosynthesefragen (AO/ASIF) group. The second group (n = 35) was treated with modified ORIF without syndesmosis and medial malleolus lag screws. All surgical cases were performed by a consultant orthopaedic surgeon and were usually done after initial physical and photographic assessment of the patient to confirm the position and 'personality' of the fracture. Radiographs taken at 2 and 6 weeks of treatment in both methods were also reviewed.

Treatment Procedure

All patients treated by ORIF with AO/ASIF principles followed the under listed protocol;

a. Open reduction of laterally dislocated tibia malleolus and stabilization with lag screw(s)
b. Open reduction of fibular fracture with unstable syndesmosis
c. Reduction of lateral dislocated Talus
d. Fixation of syndesmosis with screw(s)
e. Application of below knee splint for 7-10 days
f. Application of knee circular POP after 7-10 for six weeks
g. Removal of POP and start of physiotherapy and partial body weight bearing (15 kg) for start increasing over six more weeks

The major outcome is the anatomic fixation of the ankle joint which allows for early return to functional range of motion.

The rest of the patients who were treated with modified ORIF without bimalleolus lag screws followed the under listed procedure;

a. Open reduction of laterally dislocated tibial malleolus and stabilization with Vincryl-2 suture (first as pair-string and fortified with Z-shape suture) over deltoid ligament without lag screws.
b. Reduction of laterally dislocated Talus
c. Fixation of syndesmosis with screw(s)
d. Application of below knee splint with extreme care for 10 days
e. Application of knee circular POP for six weeks
f. Removal of POP and start of physiotherapy and partial weight bearing of 15 kg body weight for the start, increasing over six more weeks.

Statistical Analysis

All categorical variables were expressed as proportions and were compared using Fisher's exact test. In all statistical tests, a value of $P<0.05$ was considered significant. All analysis was performed using GraphPad Prism 5.10 for windows (Graphpad software, San Diago, CA. USA).

RESULTS

From this study, plate 1A shows a radiograph of pre-operative fracture (*in the direction of the black arrow*). Plate 1B shows a radiograph of the ankle joint after stabilization using the modified ORIF method (*in the direction of the white arrow*) compared to Plate 1C which is a radiograph of the fracture after heal-

ing following the ORIF (AO/ASIF) (*indicated with a white arrow*).

From the retrospective review of available data, the general cause of injury was road traffic accident which accounts for 88.6% (62/70) of all recorded ankle fracture cases followed by direct blow (10.0%) and falls from heights (1.4%) as shown in Table 1.

Table 1: Aetiology of fractures

Aetiology	No. (%)
Road traffic accident	62 (88.6)
Direct blow	7 (10.0)
Fall from a height	1 (1.4)
Total	70 (100)

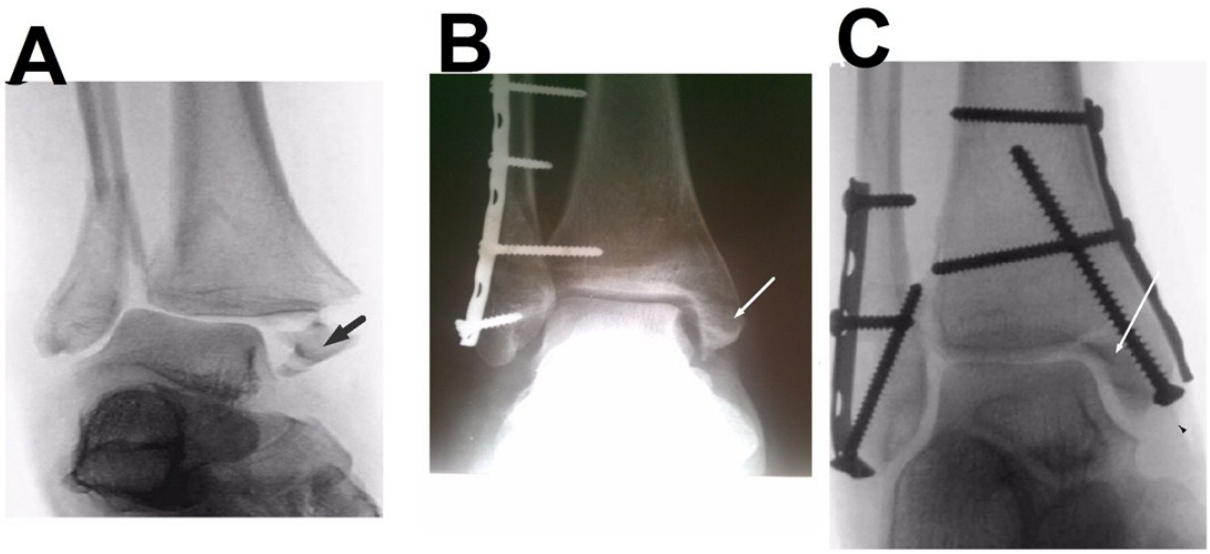

Plate 1: Radiographs of **A)** pre-operative fractures with an arrow (black) showing the medial malleolus; **B)** post-operative treatment without medial malleolus screw(s) indicated by the arrow (white); **C)** post-operative treatment with medial malleolus screw(s) indicated by arrow (white).

In this study, 85.7% (60/70) of the patients were males with only 14.3% (10/70) being females. The mean age of the patients was 36 ± 9 years with a range of 11-65 years. Majority of the patients (62.9%) were within the 31-50 year age bracket as shown in Table 2. The recovery period for the patients ranged from within 3 months to 6 months with about 67.4% (47/70) gaining full recovery within 3 months and the remaining 32.9% (23/70) recovering within 3-6 months post-operation. When the rate of recovery between the subjects treated with the AO/ASIF was compared to those treated without the malleolus lag screws, there was no significant difference (P = 0.8075). There was no significant difference in the recovery period between men and women as shown in Table 2. Although younger subjects tendered to heal early there was no statistical significant difference in healing among the subjects with respect to patient age. After one year of follow up there were no post-operative complications such as deep wound infections and reflex sympathetic dystrophy in both groups.

DISCUSSION

This study reports ankle fracture incidence of 88.6% resulting from vehicular road traffic accident (RTA). This high figure could be attributed to the high number of motor cycles in the three Northern regions. According to the Regional motor traffic unit majority of users of these motor cycles are without driving licence leading to careless and reckless driving culminating in the high incidence of

Table 1: Relationship between fracture healing time and patient age, method of fixation and gender

Variable	Healing time		Total	P value
Age (Yrs)	Within 3 months	3-6 months		
10-20	2(100.0%)	0(0.0%)	2	
21-31	9(52.9%)	8(47.1%)	17	
31-40	12(57.1%)	9(42.9%)	21	
41-50	13(56.5%)	10(43.5%)	23	
51-60	3(60.0%)	2(40.0%)	5	
61-70	0(0.0%)	2(100%)	2	
Method of stabilization				
ORIF(AO/ASIF)	22(62.9%)	13(37.1%)	35	P = 0.8075
ORIF (without screws)	20(57.1%)	15(42.9%)	35	
Gender				
MALE	35(58.3%)	25(41.7%)	60	P = 1.000
FEMALE	6(60.0%)	4(40.0%)	10	

road traffic accidents (*personal communication*). The high vehicular related ankle injury reported in the present study is in conformity with results of similar studies in other parts of Africa which indicated that road traffic accidents are the leading cause of ankle fractures in Africa (Twagirayezu *et al.*, 2008).

Proponents of open reduction and internal fixation suggest that restoration of the normal anatomy will reduce the risk of subsequent osteoarthritis due to incongruence (Weber, 1966). In areas where surgical implants are not readily available or accessible, surgeons find it difficult to manage complex ankle fractures leading to complications such as arthritis and bacterial infections (Ifesanya and Alonge, 2012). According to Steiner and Kotisso (1996), it is not clear whether or not internal fixation should have a place in Africa. It is often argued that there would be too many infections and other complications because in Africa there is neither adequate training in internal fixation nor adequate infrastructure in the operating theatre (Steiner and Kotisso, 1996). This perception is however changing with the establishment of specialist hospitals around Africa. In this study internal fixation of bimalleolus fracture without lag screw has proven successful with added benefits such as a shorter duration of surgical process, reduced risk of anaesthetic complications, reduced cost of operation (anaesthetic agents and orthopaedic implant cost) and reduced number of foreign bodies (implant) leading to a lower risk of wound infections. Clinical studies have consistently failed to show any difference in outcome between fractures treated operatively and those managed conservatively. The findings of the present study is similar to Yde and Kristensen (1980) who compared operations based on ASIF techniques with closed treatment and immobilisation in a plaster cast and found no difference in outcome at a minimum follow-up of three years. The modified ORIF procedure without lag screws also ensures early restoration of anatomical function similar to the ORIF based on ASIF principles. There were no post operative complications such as deep wound infections and reflex sympathetic dystrophy which are usually associated with the ASIF procedure as reported by Paudel (2011) giving this procedure an added advantage.

CONCLUSION

The results of this retrospective study suggest that the modified ORIF treatment protocol for complex ankle injuries is safe, satisfactory and equally effective with good functional outcome similar to the AO/ASIF ORIF treatment protocol which uses screws for internal fixation. The use of the modified ORIF protocol however demands that foot and ankle joint must be handled with extreme care so as not to dislocate the tibia malleolus post-operatively.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

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ORIGINAL ARTICLE

Anti-diarrheal activity of leaf extract of *Juniperus procera* and its effect on intestinal motility in albino mice

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This study was designed to evaluate the anti-diarrheal property of *Juniperus procera* using albino mice. An aqueous extract of *J. procera* leaves was administered to albino mice at 150, 300, and 450 mg kg^{-1} (*p.o*). Wet feces, intestinal accumulation (enteropooling) and intestinal motility were recorded. The aqueous extract of *J. procera* significantly ($p < 0.0001$) decreased the mean number of wet faeces produced by the albino mice in a dose dependent manner as well as decreasing the distance travelled by the charcoal meal ($p < 0.0001$) from 28.5 ± 1.1 cm when treated with 150 mg kg^{-1} to 11.8 ± 0.5 cm when treated with 450 mg kg^{-1} through 20.0 ± 1.0 cm when treated with 300 mg kg^{-1}. Results obtained for the extract especially the 450 mg kg^{-1} dose was almost equivalent to diphenoxylate and atropine sulphate (the reference drugs used). In conclusion, aqueous extract of *J. procera* demonstrated anti-diarrheal activity and could be an inexpensive and readily available anti-diarrheal remedy.

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Keywords*: Juniperus procera*, diarrhea, intestinal motility, castor oil, enteropooling

INTRODUCTION

Diarrhea is a gastrointestinal tract (GIT) dysfunction, which is considered as a common symptom of infection and one of the causes of intestinal motility disorder (Maresca *et al.,* 2003). It causes loss of water and important nutrients from the GIT in addition to increasing intestinal motility (Jimba *et al.,* 2002). The rate of material movement through the intestinal lumen is directly associated with its motility. As diarrhea causes high intestinal motility the increased motility also heightens diarrheal effects through increasing the rate of movement of intestinal content (Qnais *et al.,* 2005; Hejazian *et al.,* 2007).

Diarrhea is the cause of death in about 2.2 million people each year (Guerrant *et al.,* 2001; Meite *et al.,* 2009) despite the availability of synthetic drugs. Medicinal plants have been recommended as good alternatives due to their cost as well as availability. Chebula, swertia, and black pepper are some medicinal plants that are used in India and China to treat diarrheal (Das *et al.,* 2009). Many species of the Genus *Juniperus* belonging to the family *Cuperssaceae* are claimed to cure diarrhea. The anti-diarrheal properties of *J. phoenicia*, *J. communis*, *J. oxycedrus* and *J. thurifera* have been validated (Cosentino *et al.,* 2003; Karaman *et al.,* 2003, Qnais et al., 2005). Also, WHO has encouraged the use of traditional medicinal plants for the treatment and prevention of diarrhea since the 1980s (Syder and Merson, 1982; Park, 2000).

Castor oil is known to induce GIT enteropooling similar to that observed in diarrhea (i.e. accumulation of substances in the gut lumen) (Galvez *et al.,* 1993; Gorard *et al.,* 1994; Akomolafe *et al.,* 2003). Its effect is mediated by ricinolic acid that can induce a hypersecretory response by the gut wall leading to diarrhea (Capasso *et al.,* 1994; Chitme *et al.,* 2000; Das *et al.,* 2009). In this study *J. procera*, an evergreen indigenous gymnosperm in Ethiopia is

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tested as an antidiarrheal plant. This plant has a wide range of traditional uses including charcoal and timber productions, fire wood, fencing etc. Its leaves are smoked to deter insects (personal observation) in rural areas of the country. In the northern parts of the country people are known to use this plant to treat menorrhagia, emmenagogue, constipation, toothache, gum pain, and biliousness (Abebe and Ayehu, 1993).

MATERIALS AND METHODS

Plant Material Collection

Fresh leaves of *J. procera* were collected from the campus of Natural Science College of Addis Ababa University (AAU) at an attitude around 2450 m a.s.l. in June 2010. The collection was made after identification and taxonomic authentication by the help of a botanist and sample specimen is kept in the Herbarium of Faculty of Life Science, AAU under voucher № 006. The collected leaves were allowed to dry under shade for 20 days and the air dried leaves were then ground.

Preparation of the extract

A measured amount of the ground leaves of *J. procera* was dissolved in warm distilled water in 1:10 (w/v) with continuous stirring for 30 min according to the method in Qnais *et al.,* (2005) and Oben *et al.,* (2006). The solution was filtered using cotton and filter paper. The filtrate was completely lyophilized under reduced pressure. The resultant powder was weighed and dissolved in Tyrode, a physiological salt solution. This physiological salt solution was prepared daily with the following compositions (mM): 118 NaCl, 4.7 KCl, 25 $NaHCO_3$, 1 $NaH_2PO_4.H_2O$, 0.5 Na_2HPO_4, 11.1 glucose, 2.5 $MgCl.6H_2O$, and 2.5 $CaCl_2.2H_2O$. The pH used during this preparation was 7.4.

Experimental animals

Adult albino mice weighing between 35-45 g were used. All mice were provided with a standard pellet food and water *ad libitum*. The mice were starved for 18 h before the experiment but were provided with water.

Drugs and chemicals

A reference anti-diarrhoeal drug (diphenoxylate), castor oil (laxative agent), atropine sulphate and charcoal meal were used. All the chemicals were of pharmacological grades and obtained from BDH Merck Ltd, UK.

Experimental Procedures

Anti-diarrheal test

Five groups of mice (n=6) were set for the experiment and labeled A-E. Group A serving as a negative control was given 0.2 ml PSS. Groups B, C and D were given the extract at doses of 150, 300 and 450 mg kg^{-1} respectively. Diphenoxylate was given to Group E, the positive control at a dose of 5 mg kg^{-1}. All administrations were by gavage. Castor oil (1 ml) was given orally to all mice an hour before the treatment (described above). Observations were made for 4 hrs and the number of both wet and dry feces was recorded. The experiment was performed in triplicate according to standard procedures. Average number of feces was taken to calculate percentage diarrheal inhibition according to the following formula (Oben *et al.*, 2006).

$$\%\ inhibition = \frac{No.of\ WFC - No.of\ WFT}{No.of\ WFC}\ x\ 100$$

WFC = wet feces in control and WFT = wet feces in test group

Intestinal motility test

Intestinal motility test was done according to the methods of Qnais *et al.,* (2005) and Meite *et al.,* (2009) with slight modifications. Five groups of mice (n=6) were organized and made to fast for 18 hrs. Group A served as a control and received 0.5 ml of PSS. The reference drug, atropine sulphate (5 mg kg^{-1}) was given to group E that had served as a positive control. Groups B, C and D received the extract at a dose of 150, 300 and 450 mg kg^{-1} of body weight respectively. All administrations were made orally by gavage. Mice were given 1 ml of charcoal meal (5 g of activated charcoal suspended in 50 ml PSS) 30 min later through the same route.

After another 30 min all mice were sacrificed and their abdomen was open. The experiment was performed in triplicate according to standard procedures. The distance traveled by the charcoal meal from the pylorus to the caecum was measured and the percentage of inhibition of movement was calculated as follow (Oben *et al.,* 2006):

$$\% \, Inhibition = \frac{MTLI - MDCC}{MTLI} \, x \, 100$$

MTLI = mean total length of the intestine and MDCC = mean distance covered by the charcoal

Anti-enteropooling test

As in test for antidiarrheal and intestinal motility, triplicate experiments were conducted to test the anti -enteropooling property of the plant. Four groups of mice (n=6) were assigned as A, B, C, and D. Group A served as a control receiving PSS (0.5 ml) by oral administration. Group B, C and D respectively received *J. procera* leave extract at a dose of 150, 300 and 450 mg kg^{-1} by the same route. Castor oil (1 ml) was given orally to the mice after an hour. Two hours later all mice were sacrificed to isolate the small intestine. Intestinal contents were collected by mixing the intestine content and the volume was measure using graduated cylinder.

Statistical analysis

Continuous variables were presented as mean ± SEM and categorical variables presented as proportion. To compare differences between groups, *one way Analysis of Variance* (ANOVA) was performed followed by Tukey test as *post hoc*. In all test p value < 0.05 was considered significant.

RESULTS

Anti-diarrheal activity

As shown in figure 1A, the aqueous extract of *J. procera* significantly ($p < 0.0001$) decreased the mean number of wet faeces produced by the albino mice in a dose dependent manner. Even though, the mean reduction in the number of wet faeces produced when the extract was administered at 450 mg kg^{-1} was not as much as that produced when 5 mg kg^{-1} of the standard drug was administered, the difference did not reach significant level ($p = 0.74$). The extract also in a dose dependent manner increased the percentage inhibition of wet faeces production as the treatment dose was increased from 150 through 300 to 450 mg kg^{-1} of *J. procera* ($p < 0.001$) (Figure 1B). The percentage inhibition induced by the 450 mg kg^{-1} of the extract was not significantly different from the inhibition induced by 5 mg kg^{-1} of the standard drug ($p = 0.45$) (Figure 1B).

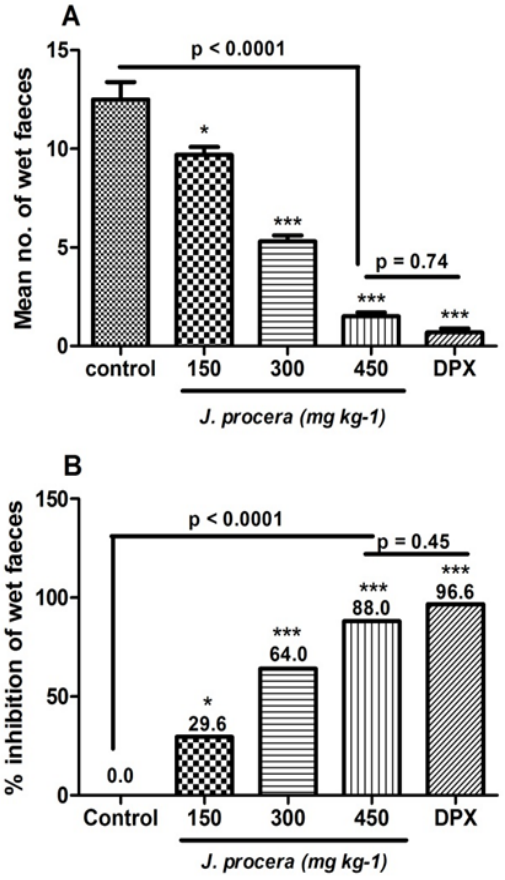

Figure 1: Effects of *J. procera* (150, 300 and 450 mg kg^{-1}) and 5 mg kg^{-1} diphenoxylate (DPX) treatment 1 hr after castor oil (1 ml) induced diarrheal on the number of wet faeces produced (A) and the percentage inhibition of wet faeces (B). Data are presented as mean ± SEM and proportion. Significantly different from control: *p<0.05 and ***p<0.001 by Tukey post hoc test (n = 6).

Table 1: Effects of *J. procera* (150, 300 and 450 mg kg^{-1}) and 5 mg kg^{-1} atropine treatment 30 minutes before administration of 1 ml of charcoal meal on the distanced as well as % inhibition of charcoal movement.

Test Group	Total distance of the intestine (cm)	Distance Traveled by charcoal meal (cm)	P value	% Inhibition
Control	69.0 ± 1.0	61.0 ± 1.1		11.6
Extract (150 mg kg^{-1})	68.5 ± 1.0	28.5 ± 1.1	0.00	58.4
Extract (300 mg kg^{-1})	67.5 ± 1.1	20.0 ± 1.0	0.00	70.4
Extract (450 mg kg^{-1})	68.7 ± 1.0	11.8 ± 0.5	0.00	82.8
Atropine (5 mg kg^{-1})	69.0 ± 1.2	9.3 ± 0.5	0.00	86.5

Data are presented as mean ± SEM and proportion. P values are significantly different from control using Tukey post hoc test (n = 6).

Effect of the extract on intestinal motility

As presented in Table 2, the length of the intestine of the albino mice in all the groups was similar. Using one way ANOVA, the aqueous extract of *J. procera* was able to decrease the distance travelled by the charcoal meal in a dose dependent manner ($p < 0.0001$) from 28.5 ± 1.1 cm when treated with 150 mg kg^{-1} to 11.8 ± 0.5 cm when treated with 450 mg kg^{-1} through 20.0 ± 1.0 cm when treated with 300 mg kg^{-1} (Table 1). Inversely, the percentage inhibition of the charcoal meal movement also significantly increased ($p < 0.0001$). There were no significant differences when the highest dose of the extract was compared to the 5 mg kg^{-1} of the standard reference drug (Atropine) in terms of the distance travelled as well as the % inhibition (Table 1).

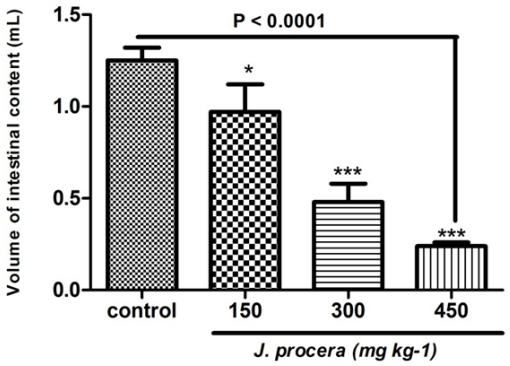

Figure 2: Effects of *J. procera* (150, 300 and 450 mg kg^{-1}) on the volume of intestinal content. Data are presented as mean ± SEM. Significantly different from control: *p<0.05 and ***p<0.001 by Tukey post hoc test (n = 6).

Anti-enteropooling property

From the one way ANOVA using treatment as a factor, the extract significantly reduced ($p < 0.0001$) the content of the animal intestine from 0.97 ± 0.45 mL when treated with 150 mg kg^{-1} through 0.48 ± 0.10 mL when treated with 300 mg kg^{-1} to 0.24 ± 0.02 mL when treated with 450 mg kg^{-1} in a dose dependent manner (Figure 2).

DISCUSSION

The results from this study clearly reveal that the aqueous extract of *J. procera* possesses anti-diarrhoeal property. The aqueous extract of the leaves of this plant may contain different agents that effectively reduced diarrhoea that was induced by a potent diarrhoeal agent, castor oil. Diarrhoea can be characterized by different phenomena including frequent out flow of wet (waterish) faeces, high intestinal motility, high accumulation of important nutrients in the lumen of the intestine, and others (Capasso *et al.,* 1994; Jarbur and Sjovall, 2000). The findings from the present study are in agreement with previous works by Qnais *et al*., (2005). As reported by Venkateran *et al*., (2005), Oben *et al*., (2006) and Das *et al*., (2009) the anti-diarrhoeal properties of plant extracts are expressed by their action of reducing intestinal motility and enhancing intestinal reabsorption, which can be done through inhibition

of prostaglandin release.

A high rate of intestinal absorption might lead to a decrease in intestinal accumulation and together with reduced intestinal motility may result in increased transit time (Jarbur and Sjovall, 2000). This in turn might give chance for further absorption as evidenced by small volume of intestinal contents recorded in this study. Hence, the obtained anti-diarrhoeal activities of *J. procera* in this study might be due to possession of chemicals that facilitate the aforementioned actions. Phytochemical groups like flavonoids, tannins, alkaloids and saponins have been reported to show anti-diarrhoeal activities (Langana *et al.,* 2000; Venkateran *et al.,* 2005; Salgado *et al.,* 2006). Moreover, these substances have also been reported in other *Juniperus spp*. (Qnais *et al.,* 2005). Though further analysis is needed to assert the presence or otherwise of these aforementioned phytochemicals, the positive result of the present study indicates that these secondary metabolites might exist in the leaves of *J. procera*. Reductions in the volume of intestinal contents were also recorded in this study that might be correlated to the ability of the extract to increase intestinal absorption (Oben *et al.,* 2006). In addition to this, the extract might have tannate that can make the intestinal mucosa more resistant and reduce secretion, which is similar with reports made for *J. phoenicia* by Qnais *et al*., (2005).

CONCLUSION

The present study clearly shows that like other members of the genus this ever green plant may contains phytochemicals with anti-diarrhoeal properties. Hence, further studies are needed not only to isolate the active principles but also to find such property in parts other than its leaves.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

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ORIGINAL ARTICLE

HIV co-infection and mortality pattern of purulent meningitis: A 5 year retrospective autopsy study at the Korle-Bu Teaching Hospital

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This study utilized retrospective autopsy data to examine the relationship between HIV co-infection and mortality pattern of purulent meningitis. All autopsy log books and available hospital files were reviewed for information on purulent meningitis for which autopsies were performed in 2005 through 2009 at the Pathology Department of the Korle-Bu Teaching Hospital, Accra, Ghana. The mean ± SD of the studied population was 34.6±19.5 years and the prevalence of HIV co-infection among this population was 4.3%. Female participants died at a significantly younger age (31.9±19.7 years; p=0.0103) compared to their male counterparts (36.1±19.2 years). Most of the cases in HIV negative purulent meningitis death had purulent meningitis as the primary cause (i.e. 87.9% *vs* 18.5%) whereas most of the death in HIV co-infection cases had purulent meningitis as the secondary cause of death to other conditions such as CVA, pneumonia, head injury due to road traffic accidents and various malignancies (i.e. 81.5% *vs* 12.1%). Purulent meningitis secondary to other conditions is more likely to be the cause of death in aged subject. The prevalence of purulent meningitis with HIV co infection was low in this study. The mortality pattern is related to the age and gender of the studied population and whether the purulent meningitis is primary or as a co infection with HIV.

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Keywords*:* Autopsy, Purulent meningitis, HIV, Co-infection, opportunistic infections

INTRODUCTION

Purulent meningitis is a life threatening acute bacterial inflammation of the meninges of the brain and spinal cord. It mostly affects children, the aged or the immune-compromised. Ghana lies within the meningitis belt in sub-Saharan Africa and as such outbreaks of bacterial meningitis are not uncommon (Molesworth *et al.*, 2002).

Human immune deficiency virus (HIV) infected patients have a defective immunity and so are susceptible to numerous opportunistic infections caused by both bacteria and fungi including purulent meningitis (Hakim *et al.*, 2000). The association of the meninges has the potential to worsen any opportunistic brain infections. Furthermore, primary infection of HIV is complicated by meningitis thus it is appropriate to expect co-infection of purulent meningitis and HIV especially in places where both conditions are endemic. A number of studies (Silber *et al.*, 1999; Gordon *et al.*, 2000; Hakim *et al.*, 2000) have examined various aspects of the relationship between HIV and purulent meningitis including the mortality pattern looking at the role played by the various opportunistic organisms. However, there is paucity of data on the relationship between these two conditions in Ghana. This study therefore aims to use retrospective autopsy data to examine the relationship between HIV co-infection and the mortality pattern of purulent meningitis.

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MATERIAL AND METHODS

Study Site

All data were gathered from the Department of Pathology, Korle-Bu Teaching Hospital, Accra, Ghana. It is the nation's foremost teaching hospital and has the largest mortuary in the country. This mortuary performs 3,000 to 6,000 autopsies a year. Cases are received primarily from the Accra Metropolis, neighbouring towns and districts, and in some circumstances, from other regions across the country. However, autopsy was not done on all meningitis related deaths within the catchment area. This is because deaths that occurred in the communities and were not reported to the police did not have autopsy done on them.

Data Collection and Analysis

All autopsy log books and available hospital files of subjects who underwent autopsy were reviewed from the period of 2005 through 2009, and all cases of meningitis related deaths were recorded. Data were collected and cross-checked to prevent double entry. For each case of meningitis death, data were collected on age, gender, and category of death by location (Coroner's request or hospital). Coroner's cases are deaths that occurred in the community or within 24-hours of admission to a health facility, where no definitive diagnosis was arrived at before death. Hospital deaths, on the other hand, are deaths that occurred in a health facility while the subject was receiving care for a given diagnosis. The diagnosis of meningitis was based on the ante-mortem clinical and laboratory diagnosis as well as macroscopic autopsy findings. The HIV status was from ante-mortem testing. All cases of tuberculosis (TB) and Cryptococcus meningitis were excluded.

RESULTS

Gender distribution of the studied population

In 2005 through to 2009, a total of 24,787 autopsies were performed. Out of this number, purulent meningitis was recorded as the cause of death in 621 (2.5%) cases. As shown in Table 1, the mean age of the studied population (i.e. the 621 cases with purulent meningitis) was 34.6 ± 19.5 years. Majority of the deaths occurred within the communities with the primary cause of death in recorded. Coroner's cases (85.7%) being purulent meningitis (84.9%) and 95.7% of recorded cases without HIV co-infection. Death within the health facility was found in 14.3% of recorded cases and purulent meningitis was found to be the secondary cause of death to other conditions such as CVA, pneumonia, head injury due to road traffic accidents and various malignancies in about 15% of the studied population. The prevalence of HIV co-infection among this population was found to be 4.3% (Table 1).

When the studied population was classified based on gender, the females died at a significantly ($p = 0.0103$) younger age (31.9 ± 19.7 years) as compared to the male counterpart (36.1 ± 19.2 years). No significant differences were observed in the place of death, type of purulent meningitis as well as HIV co-infection among both sexes (Table 1). As noted in the total population, majority of deaths in both genders are Coroner's cases with purulent meningitis being the primary cause without HIV co -infection (Table 1).

Impact of HIV co-infection on the studied population

From Table 2, HIV related meningitis deaths occurred at a significantly ($p = 0.0432$) older age (41.6 ± 10.1 years) as compared to those without HIV co -infection (34.0 ± 19.3 years) among the total population. Significantly ($p < 0.0001$), HIV negative purulent meningitis death was more associated with Coroner's death (i.e. 87.5% *vs.* 44.4%) whereas HIV related meningitis deaths were more associated with death within the health facilities (i.e. 55.6%*vs.* 12.5%). Majority of the cases that occurred in HIV negative purulent meningitis deaths had purulent meningitis as the primary cause (i.e. 87.9% *vs.* 18.5%) whereas majority of the death that occurred in HIV co-infection cases had purulent meningitis as the secondary cause of death to other conditions such as CVA, pneumonia, head injury due to road traffic accidents and various malignancies (i.e. 81.5% *vs.* 12.1%) (Table 2). These same pattern of results were noted when the studied population

Table 1: General characteristic of the studied population stratified by gender

Variable	Total (n = 621)	Female (n = 220)	Male (n = 401)	P value
Age (yrs)	34.6 ± 19.5	31.9 ± 19.7	36.1 ± 19.2	0.0103
Place of death				
Coroner	532(85.7%)	183(83.2%)	349(87.0%)	0.1905
Permission	89(14.3%)	37(16.8%)	52(13.0%)	0.1905
Type of purulent meningitis				
Primary cause of death	527(84.9%)	187(85.0%)	340(84.8%)	1.0000
Secondary cause of death	94(15.1%)	33(15.0%)	61(15.2%)	1.0000
HIV co-infection				
Yes	27(4.3%)	10(4.5%)	17(4.2%)	0.8398
No	594(95.7%)	210(95.5%)	384(95.8%)	0.8398

Continuous data is presented as mean ± SD and analyzed using unpaired t-test whilst categorical data are presented as proportion and analyzed using Fischer's exact test

were stratified based on HIV co-infection and gender, except for the fact that age was not a significant factor among the male population (Table 2).

Impact of age on the studied population

When the total studied population was stratified based on age in Table 3, generally, fewer proportion of the female deaths occurred at older ages whereas higher proportion of male deaths occurred as subjects aged as indicated by the Chi-square test for trend. Coroner's death was negatively associated with age as opposed to the positive association between permission death and age (Table 3). Purulent meningitis was less likely to be the primary cause of death as the subjects aged whereas purulent meningitis secondary to other conditions was more likely to be the cause of death as the subjects aged (Table 3).

As the subjects aged, the prevalence of HIV co-infection assumed a "bell-shaped" curve whereas prevalence of HIV negative purulent meningitis assumed a "U-shape" curve. The highest prevalence of HIV co-infection of 8.8% was noted among the 35-44 years group, followed by 8.6% in 25-34 years group, 6.0% in 45-54 years group, 3.9% in 55-64 years group and 2.2% in 65 years and above group. No HIV co-infection was noted up to the age of 24 years (Table 3).

Stratification of the studied population based on age and gender in Table 4 indicated similar patterns of results as in the total population with regards to place of death and type of purulent meningitis. However, the highest prevalence of HIV co-infection of 11.1% was noted among the 55-64 years group followed by 10.0% in 25-34 years group, 8.3% in 35-44 years group, 6.7% in ≥ 65 years group and 3.2% in 45-54 years group among the female. No HIV co-infection was noted among females up to the age of 24 years (Table 4). Among the males, the highest prevalence of HIV co-infection of 9.0% was found among the 35-44 years group, followed by 7.5%, 7.2% and 2.4% among the 25-34 years group, 45-54 years group and 55-64 years group respectively. No male subject up to the age of 24 years and ≥ 65 years had HIV co-infection (Table 4).

DISCUSSION

Opportunistic infections including meningitis are common in HIV infection. This study sought to establish the relationship between HIV co-infection and the mortality pattern of purulent meningitis by examining retrospective autopsy data at the Korle-Bu Teaching Hospital (KBTH). The prevalence of purulent meningitis and HIV co-infection was 4.3% and factors such as age and gender affected the prevalence of purulent meningitis HIV co-infection

Table 2: Distribution of the type of purulent meningitis as well as the place of death of the studied population stratified by HIV co-infection and gender

Variables	HIV positive	HIV negative	P values
Total	***n = 27***	***n = 594***	
Age (yrs)	41.6 ± 10.1	34.0 ± 19.3	0.0432
Gender			
Female	10(37.0%)	210(35.4%)	0.8398
Male	17(63.0%)	384(64.6%)	0.8398
Place of death			
Coroner	12(44.4%)	520(87.5%)	< 0.0001
Permission	15(55.6%)	74(12.5%)	< 0.0001
Type of purulent meningitis			
Primary cause of death	5(18.5%)	522(87.9%)	< 0.0001
Secondary cause of death	22(81.5%)	72(12.1%)	< 0.0001
Female	***n = 10***	***n = 210***	
Age (yrs)	42.7 ± 14.3	30.0 ± 18.0	0.0294
Place of death			
Coroner	3(30.0%)	180(85.7%)	0.0002
Permission	7(70.0%)	30(14.3%)	0.0002
Type of purulent meningitis			
Primary cause of death	1(10.0%)	186(88.6%)	< 0.0001
Secondary cause of death	9(90.0%)	24(11.4%)	< 0.0001
Male	***n = 17***	***n = 384***	
Age (yrs)	40.9 ± 7.0	35.9 ± 19.6	0.2912
Place of death			
Coroner	9(52.9%)	340(88.5%)	0.0005
Permission	8(47.1%)	44(11.5%)	0.0005
Type of purulent meningitis			
Primary cause of death	4(23.5%)	336(87.5%)	< 0.0001
Secondary cause of death	13(76.5%)	48(12.5%)	< 0.0001

Continuous data is presented as mean ± SD and analyzed using unpaired t-test whilst categorical data are presented as proportion and analyzed using Fischer's exact test.

Table 3: The impact of age on purulent meningitis among the total studied population

Variables	≤ 18	19-24	25-34	35-44	45-54	55-64	≥ 65	P value
	n = 149	***n = 69***	***n = 93***	***n = 114***	***n = 100***	***n = 51***	***n = 45***	
Age (yrs)	10.6 ± 6.0	21.6 ± 1.7	30.1 ± 3.0	38.5 ± 2.9	48.9 ± 2.8	58.9 ± 8.1	74.4 ± 2.9	
Gender								
Female	62(41.6%)	27(39.1%)	40(43.0%)	36(31.6%)	31(31.0%)	9(17.6%)	15(33.3%)	0.0039
Male	87(58.4%)	42(60.9%)	53(57.0%)	78(68.4%)	69(69.0%)	42(82.4%)	30(66.7%)	0.0039
Place of death								
Coroner	135(90.6%)	66(95.7%)	84(90.3%)	98(86.0%)	78(78.0%)	40(78.4%)	31(68.9%)	< 0.0001
Permission	14(9.4%)	3(4.3%)	9(9.7%)	16(14.0%)	22(22.0%)	11(21.6%)	14(31.1%)	< 0.0001
Type of purulent meningitis								
Primary cause of death	137(91.9%)	68(98.6%)	83(89.2%)	90(78.9%)	79(79.0%)	40(78.4%)	30(66.7%)	< 0.0001
Secondary cause of death	12(8.1%)	1(1.4%)	10(10.8%)	24(21.1%)	21(21.0%)	11(21.6%)	15(33.3%)	< 0.0001
HIV co-infection								
Yes	0(0.0%)	0(0.0%)	8(8.6%)	10(8.8%)	6(6.0%)	2(3.9%)	1(2.2%)	0.0396
No	149 (100.0%)	69(100.0%)	85(91.4%)	104(91.2%)	94(94.0%)	49(96.1%)	44(97.8%)	0.0396

among the study population.

The 4.3% prevalence of purulent meningitis recorded in this study is compares closely to the 5% prevalence reported in the Western world (Currie and Casadevall, 1994) but contrary to the 20-30% reported in other sub-Saharan African countries and in Eastern Asia (Pinner *et al.*, 1995). The low prevalence recorded among this population could be due to the fact that most HIV-infected patients die of other complications hence the low prevalence.

Palleres *et al.,* (1995) reported that there is no difference in relation to mortality rate between patients with only HIV infection and bacteria and HIV co-infection. This assertion however is inconsistent with observations made from this study. The inclusion of both HIV 1 and 2 patients in our study could account for differences in the age of mortality.

Several studies have examined the relationship between gender, prevalence and mortality rate of purulent meningitis. This study established a trend that fewer females died of purulent meningitis at an older age compared to males. This finding is in conformity to the study of Pfister *et al.,* (1993) who found purulent meningitis to be more prevalent in males. The longer life expectancy of females in Ghana could be the reason for the low mortality rate among the female participants.

Recent studies have reported higher mortality rates in meningitis without HIV co-infection compared to purulent meningitis HIV co-infection (Lynch and Kapila, 1996) which confirms the findings of this study. The low mortality rate among subjects with purulent meningitis HIV co-infection could partly be due to the reduced immunologic response that characterizes HIV infection. This phenomenon is known to reduce inflammatory responses produced in the brain in the initial stages of meningitis infection which is known to be linked directly to mortality (Almirante *et al.*, 1998).

Various reports have established purulent meningitis due to various bacteria as the primary cause of

Table 4: Association between increase in age and place of death, type of purulent meningitis as well as HIV co-infection among the studied population stratified by gender

Variables	<19	19-24	25-34	35-44	45-54	55-64	>64	P value
Female	***n = 62***	***n = 27***	***n = 40***	***n = 36***	***n = 31***	***n = 9***	***n = 15***	
Age (yrs)	10.4 ± 5.8	20.8 ± 1.6	29.9 ± 3.0	38.4 ± 2.9	49.3 ± 3.4	60.8 ± 1.8	76.9 ± 8.2	
Place of death								
Coroner	57(91.9%)	26(96.3%)	34(85.0%)	29(80.6%)	23(74.2%)	5(55.6%)	9(60.0%)	< 0.0001
Permission	5(8.1%)	1(3.7%)	6(15.0%)	7(19.4%)	8(25.8%)	4(44.4%)	6(40.0%)	< 0.0001
Type of purulent meningitis								
Primary cause of death	58(93.5%)	27(100.0%)	33(82.5%)	29(80.6%)	24(77.4%)	6(66.7%)	10(66.7%)	0.0002
Secondary cause of death	4(6.5%)	0(0.0%)	7(17.5%)	7(19.4%)	7(22.6%)	3(33.3%)	5(33.3%)	0.0002
HIV co-infection								
Yes	0(0.0%)	0(0.0%)	4(10.0%)	3(8.3%)	1(3.2%)	1(11.1%)	1(6.7%)	0.067
No	62(100.0%)	27(100.0%)	36(90.0%)	33(91.7%)	30(96.8%)	8(88.9%)	14(93.3%)	0.067
Male	***n = 87***	***n = 42***	***n = 53***	***n = 78***	***n = 69***	***n = 42***	***n =30***	
Age (yrs)	10.5 ± 6.1	22.1 ± 1.6	30.3 ± 3.0	38.5 ± 2.9	48.7 ± 2.5	58.5 ± 3.0	73.2 ± 7.9	
Place of death								
Coroner	78(89.7%)	40(95.2%)	50(94.3%)	69(88.4%)	55(79.7%)	35(83.3%)	22(73.3%)	0.0029
Permission	9(10.3%)	2(4.8%)	3(5.7%)	9(11.5%)	14(20.3%)	7(16.7%)	8(26.7%)	0.0029
Type of purulent meningitis								
Primary cause of death	79(90.8%)	41(97.6%)	50(94.3%)	61(78.2%)	55(79.7%)	34(81.0%)	20(66.7%)	< 0.0001
Secondary cause of death	8(9.2%)	1(2.4%)	3(5.7%)	17(21.8%)	14(20.3%)	8(19.0%)	10(33.3%)	< 0.0001
HIV co-infection								
Yes	0(0.0%)	0(0.0%)	4(7.5%)	7(9.0%)	5(7.2%)	1(2.4%)	0(0.0%)	0.2124
No	87(100.0%)	42(100.0%)	49(92.5%)	71(91.0%)	64(92.8%)	41(97.6%)	30(100.0%)	0.2124

Continuous data are presented as mean ± SD and categorical data are presented as proportion. The association between age and other variables was access using Chi and analyzed using Chi-square test for trend.

death in the aged (Bruyn *et al.*, 1989; Durand *et al.*, 1993; McMillan *et al.*, 2001). Findings of from this study, however, contradict these observations as purulent meningitis secondary to other infections was the major cause of mortality amongst the aged subjects in this study.

As the participants advanced in age, the prevalence of HIV co-infection assumed a "bell-shape" with the total prevalence among the various age groups being far less than the 80% prevalence recorded among participants in a study in Malawi (Kelly *et al.*, 2012). The lower prevalence rate of HIV in Ghana coupled with the up scaling and wide provision of antiretroviral therapy (ART) to these patients which boosts their immunity could have accounted for reduced prevalence rate observed in this study.

CONCLUSION

The prevalence of purulent meningitis and HIV co-infection among studied population was 4.3%, with mortality rate being related to whether the purulent meningitis was primary or secondary to HIV infection. Primary infection with purulent meningitis was associated with a high mortality rate.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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