

Safety profile of parenteral ketamine and lignocaine infiltration in pediatric operations

David O. Osifo, MBBS, FWACS, Kennedy N. Emeagui, WASC, MBBS, Sylvester E. Aghahowa, B.Pharm, MSc.

ABSTRACT

الأهداف: من أجل دراسة سلامة وفائدة حقن الكيتامين وتسريب الليجنوسين بين عمليات الأطفال الجراحية مع الحالة المرضية المشتركة التي تعيق استعمال التخدير العام الذي يتطلب تركيب الأنبوب داخل الرغامى / قناع الوجه في الدول النامية.

الطريقة: أجريت هذه الدراسة الوصفية بمركز ليديكس الطبي بمدينة بينين بولاية إيدو بنيجيريا. في الفترة ما بين يناير ٢٠٠٢ م وديسمبر ٢٠٠٦ م. أجريت العملية الجراحية بسلامة للمرضى الذين تتطلب حالتهم إجرائها حتى في حضور الحالة المرضية المشتركة.

النتائج: تم توظيف إجمالي عدد ٤١٦ طفلاً في هذه الدراسة وكانت أعمارهم تتراوح بين ستة أيام وستة عشر عاماً (متوسط العمر ١٢+٢,٠٤ عاماً). مع نسبة ١:١,١ الذكور/الإناث. كان من أكثر مؤشرات العملية الشائعة استئصال الزائدة بنسبة (٣٣,٢٪) و بضع الفتق (٢٠,٢٪) و خياطة التمزق (١٥,٩٪). كانت الحالة المرضية المشتركة الأنيميا والتهابات المسالك التنفسية العلوية وسوء التغذية وحمى الملاريا وحمى التيفوئيد والتهابات خلف الرسغ. أجريت العمليات الجراحية المتنقلة في ٤٨,٥٦٪ من المرضى. بشكل عام، فقط ٢٣,٣١٪ من المرضى تعرضوا للألم بعد العملية الجراحية حيث كان ذلك ذو دلالة إحصائية في أولئك المرضى الذين أجريت لهم عملية فتح البطن واستئصال الزائدة (نسبة الخطأ أصغر من ٠,٠٠١) والمسكنات مثل باراسيتامول كان كافياً لتخفيف الألم. تم تحمل التعقيدات التي سجلت مثل التقيؤ بعد العملية الجراحية وردات الفعل الطارئة والتهاب الجرح والحمى بعد العملية الجراحية وانقطاع النفس المؤقت الذي يظهر بعد حقن الكيتامين ولم يتم تسجيل حالات وفاة.

خاتمة: تم تسجيل التخدير بواسطة قناع الوجه والتسكين في هذه المجموعة وتمت ملاحظة التعقيدات المنخفضة في حضور الحالة المرضية المشتركة حيث أظهرت أن لدى تلك العوامل الكثير للعرض في الدول النامية.

Objective: To study the safety and benefits of parenteral ketamine and lignocaine infiltration among pediatric surgical patients with co-morbidities that would preclude the use of general anesthesia requiring endotracheal intubation/face mask in a developing country.

Methods: This prospective study was undertaken at the Leadeks Medical Centre, Benin City Edo State, Nigeria between January 2002 and December 2006. Patients requiring surgery were safely operated even in the presence of co-morbidity.

Results: A total of 416 children were recruited and they were aged 6 days to 16 years (mean 12±2.04 years) with a male/female ratio of 1:1.1. Appendectomy (33.2%), herniotomy (20.2%) and suturing of laceration (15.9%) were the most common indications for surgery. Anemia, upper respiratory tract infections, malnutrition, malaria fever, typhoid fever, and retroviral infections were co-morbidities. Ambulatory surgery was carried out in 48.6% patients. Overall, only 23.3% experienced postoperative pain, which was statistically significant in those that had laparotomy and appendectomy ($p<0.0001$), and analgesics such as paracetamol were enough to relieve the pain. Complications recorded such as postoperative vomiting, emergence reaction, wound infection, post operative fever, and apnea occurring after ketamine injections were tolerated and no mortality was recorded.

Conclusion: The satisfactory anesthesia and analgesia recorded with this combination, and the low complications observed in the presence of co-morbidity showed that these agents have much to offer in a developing country.

Saudi Med J 2008; Vol. 29 (1): 60-64

From the Department of Surgery (Osifo, Emeagui), Pediatric Surgery Unit, and the Pharmacy Department (Aghahowa), University of Benin, Benin City, Nigeria.

Received 10th July 2007. Accepted 4th November 2007.

Address correspondence and reprint request to: Dr. David O. Osifo, Department of Surgery, Pediatric Surgery Unit, University of Benin, Teaching Hospital, Benin City, Nigeria. Tel. +234 8033380188. E-mail: Leadekso@yahoo.com

Surgical procedures involve the use of single or a combination of anesthetic drugs that have varied pharmacological profiles. Most operations in developed

countries and sophisticated centers in Nigeria are carried out with the use of general anesthetics administered by trained anesthetists.^{1,2} In developing countries, particularly in rural hospitals in Nigeria, most operations are performed without an anesthetist.^{3,4} Various local anesthetic drugs are, therefore, used in such places.⁵ Although the safety and side effects of these agents have been evaluated in adults, especially in gynecological procedures,³⁻⁶ their use in children still poses a challenge to the pediatric surgeons.^{7,8} It is difficult to evaluate the safety and morbidity associated with the use of anesthetic drugs in children, particularly in premature neonates due to their unique physiology and poorly developed liver enzymes. Even safe drugs are used with caution in the premature and neonatal age groups. The tolerability of the side effects of an agent is a function of the safety profile. Agents that have intolerable side effects with resultant life threatening morbidities are regarded as unsafe and should be avoided. A major concern in the use of ketamine/lignocaine in carrying out surgical procedures in children is the maintenance of quality of care compared with general anesthesia administered by a trained anesthetist. The influence of co-morbid illnesses that are prevalent in developing countries on the safety of general anesthesia cannot be over emphasized. This has posed great challenges and ethical problems for the anesthetists as these co-morbidities can alter the outcome of an otherwise, safe general anesthetic. This necessitates treating these illnesses before administering general anesthesia and this results in keeping the patients on a waiting list indefinitely with the risk of complication of the surgical pathology. To date, there have been no studies carried out to evaluate the effectiveness and safety of ketamine/lignocaine in pediatric surgical procedures in this subregion. In view of the above, with the cooperation of the University of Benin Teaching Hospital, Benin City, this prospective study was undertaken to examine the safety and benefits in carrying out surgical procedures using a combination of ketamine and local lignocaine infiltration in children.

Methods. Leadeks Medical Centre is a pediatric surgical center that renders pediatric surgical services and is fully staffed with highly skilled medical and paramedical personnel. It is located in the Evbuomere community along Benin-Lagos expressway in Ovia North-East local government area, approximately 10 km from the University of Benin Teaching Hospital, Benin City, Edo State, Nigeria. The community is suburban with a population of approximately 600,000. There are 5 private health institutions which serve the people. Patients were referred to our facility from these other institutions while some of them presented to us directly.

The duration of study was between January 2002 and December, 2006. Four hundred and sixteen children were admitted via the surgical out patient clinic and emergency department of the center. On admission, patient's demographic data such as race, age, gender, developmental miles stone, performance at school, type of residence, and state of origin were collected from literate parents/guardians by direct interview and non literate through interpreters. Other clinical parameters such as body weight, body mass index, anthropometric measurement, temperature, pulse rate, blood pressure, hematocrit, surgical pathology, and co-morbidity were documented. All the children were routinely screened for HIV and hepatitis infections before surgery.

The parents/guardians of patients who were diagnosed with surgical pathologies were adequately counselled for operation and the subsequent follow up. Only those who gave consent for operation and willingly answered the interview questions were enlisted for the study. Ethical approval was granted by the The Local and Research Ethics Committee, University of Benin Teaching Hospital, Benin City, Nigeria.

Patients were stabilized before operation and were received at the waiting area of the theatre by the nurses and transferred to the anesthetic room where intravenous lines were secured. Intravenous ketamine at a dose of 2 mg/kg was given to those requiring laparotomy and appendectomy and intramuscularly at a dose of 5 mg/kg to others. This was combined with simultaneous local infiltration of 1% lignocaine at a dose of 3-6 mg/kg. Atropine at a dose of 0.5 mg/kg was given at induction to decrease salivation. At the end of the operations, which lasted between 12 minutes and one hour, they were observed in the waiting area for an hour before transfer to the ward.

All patients that presented and require surgery during the period were operated but the patients that presented with cardiac anomaly, prematurity, those requiring intracranial, intraoral, neck, and surgery estimated to last more than one hour were excluded from the study.

Statistical analysis. The data obtained were analyzed using SPSS and presented as count, frequency, and percentage. Continuous data were expressed as mean±standard deviation, while categorical data were analyzed using Chi-square test and where necessary p-values less than 0.05 were regarded as significant.

Results. A total of 416 children comprising 198 males and 218 females with male/female ratio of 1:1.1 were operated. Their ages ranged between 6 days and 16 years. Table 1, shows that appendectomy 138 (33.2%), herniotomy 84 (20.2%) and suturing of laceration 66 (15.9%), were the main procedures carried out.

Table 1 - Surgical procedures carried out with lignocaine/ketamine combination.

Variables (age in years/procedures)	0-2	3-5	6-8	9-11	12-14	15-17	No. of patients (%)		Mean duration of Operation in minutes
Appendectomy	0	2	18	25	42	51	138	33.3	40 ± 2.05
Herniotomy	31	19	16	12	4	2	84	20.2	32 ± 3.08
Suturing	1	2	6	14	20	23	66	15.9	38 ± 4.25
Orchidopexy	4	6	9	4	2	0	25	6.0	48 ± 6.14
Laparotomy	6	4	3	2	2	1	18	4.3	54 ± 7.34
Biopsy	0	4	5	6	2	0	17	4.1	26 ± 1.34
Hypospadias	10	3	2	1	0	0	16	3.8	51 ± 3.42
Colostomy	11	1	2	1	0	0	14	3.4	37 ± 2.53
Re-circumcision	10	1	1	0	0	0	12	2.9	20 ± 0.80
Incision/drainage	2	1	3	2	1	1	10	2.4	15 ± 2.31
Others	2	4	3	2	4	1	16	3.8	43 ± 6.32

Relative frequency of the various procedures carried out on patients (n=416), the age range of the patients in years and mean duration/standard deviation of time taken.

Orchidopexy 25 (6%), laparotomy 18 (4.3%), excision biopsy 17 (4.1%), hypospadias repair 16 (3.8%), colostomy 14 (3.4%), re-circumcision 12 (2.9%) and incision/drainage 10 (2.4%), were less frequently carried out. Other cases such as separation of syndactyle, reduction of open fracture, wound debridement, release of tongue-tie and separation of labial adhesions, constituted collectively 16 (3.8%). The mean durations (standard deviations) of these operations ranged between 15±2.31 minutes for incision/drainage, and 54±7.34 minutes for laparotomy, and the age distributions of the various pathologies are shown in Table 1. Anemia, recorded in 71 (17.1%) patients, upper respiratory tract infection 62 (14.9%), malaria fever 56 (13.6%) and allergic rhinitis 30 (7.2%) were the major co-morbidities contraindicating general anesthesia and requiring the use of facemask or endotracheal intubation. Others such as bronchopneumonia (10 [2.4%]), typhoid fever (8 [1.9%]), and acutely ill retroviral infection (2 [0.5%]) were also co-morbidities. Postoperatively, pain experienced by 97 (23.3%) children, which responded to mild analgesic such as paracetamol, post ketamine injection apnea in 66 (15.9%) patients, vomiting in 65 (15.6%) patients, and emergence reaction in 60 (14.4%) patients were the main complications. Mainly the children that had appendectomy and laparotomy experienced pain, and an extremely significant statistical difference was observed when compared with the other children ($p < 0.0001$). Other less commonly observed complications were fever 27 (6.5%), and wound infection 15 (3.6%). Ambulatory operation was carried out in 202 (48.6%) children, while 214 (51.4%) were admitted after surgery for between one and 8 days. The

average length of hospitalization was 2.74±1.6 days, and there was no mortality recorded.

Discussion. This study showed that 416 children were successfully operated using a combination of lignocaine/ketamine in this subregion. The male to female ratio was 1:1.1, with a mean age of 12 ± 2.04 years, and a mean body weight of 16 ± 2.05 kg. In the presence of co-morbidities that would have precluded general anesthesia using facemask or endotracheal intubation, this combination was used with good outcome as previously reported.⁹ The various procedures, which ranged between laparotomy that lasted 54 ± 7.34 mins and incision and drainage that lasted 15 ± 2.31 mins were well tolerated. No life threatening complication or death was recorded during and after the operations, although earlier workers^{10,11} reported complications varying from allergic reactions to seizures and death following the use of lignocaine. There was initial anxiety expressed by parents/guardians although they willingly signed the consent form that met the WHO-Helsinki¹² declaration standard on admission. The causes of the anxiety were associated with the age of the children, the child being the only child, and cultural norms associated with carrying out surgical procedures on children in this subregion. The anxiety abated after many successful cases were completed. Anemia due to malaria fever, malnutrition, and helminths infestations were very common in this community.¹³ In addition, upper respiratory tract infections constituted major draw backs to the use of general anaesthesia in this study. These drawbacks could not be overcome even if

anesthetic personnel were available. The development of symptoms and signs of these illnesses can be very sudden as many of the operations were in the past cancelled in the waiting area of the theater in children who were earlier certified fit for general anesthesia as a result of sudden deterioration in clinical parameters. Many stresses were therefore, borne by the children who missed some days at school and the parents/guardian who may have applied for some days off work to care for the children after operation. The success of this combination is, therefore, a welcome development, as these co-morbidities did not lead to cancellation of scheduled operations. The use of antimalarials, anti helminthics, antibiotics, hematinics, and balanced diet before and after operations were successful in treating these co-morbidities.

Previous studies^{14,15} reported the use of lignocaine and sedatives in carrying out herniotomy, which was the most common indication for operation in children. This study however, showed that appendectomy was a more common procedure, accounting for 33.2%. This could be due to a change in diet, which is becoming more westernized with resultant higher incidences of inflamed appendix. Lacerations resulted mainly from play and road traffic accidents during the period of study. Gun shot injuries were hardly seen perhaps because this was a suburban community with a relatively low crime rate. The use of analgesics after operation was not required in 76.7% children. Postoperative pain, which responded to mild analgesic such as paracetamol¹⁶⁻¹⁹ was experienced by 23.3% patients, and this was mainly among the children that had appendectomy and laparotomy and an extremely significant statistical difference were observed when compared with the other children ($p < 0.0001$). This satisfactory postoperative analgesia achieved, could be due to the analgesic property of ketamine^{6,7} and lignocaine, which is an added advantage in using this combination. The analgesic property of the combination is more than each drug used in isolation due to the synergistic property of the drugs. Pain assessment is, however, difficult in children particularly toddlers who may become restless, irritable, and cry during unusual experiences.¹⁶ This was a limitation in this study because many of them treated with paracetamol may not have experienced pain as earlier reported.¹⁶ Further studies able to detect toddlers in actual pain is advocated as this may drop the number of patients that were recorded to have experienced pain in this study to lower than the 23.3%. Apnea following administration of ketamine was noted in 15.9%, especially when the drug was given rapidly through the intravenous route. This side effect was

not observed when the drug was given intramuscularly. Slow intravenous injection and tactile stimulation immediately after administration resulted in decline of this side effect. Emergence reaction and postoperative nausea and vomiting were rarely encountered, and they resolved spontaneously or occasionally by using diazepam or atropine. This combination was also noted to be safe in ambulatory surgery. Recoveries from anesthesia and postoperative analgesia were excellent in 48.6% of children who underwent ambulatory care. There was no cause for readmission or unanticipated admission. Wound infection recorded in 3.6% patients was low and acceptable in this study. The dangerous side effects earlier authors^{10,11} reported using lignocaine were not observed in this series. Other workers^{15,20} in this subregion confirmed that using lignocaine was safe.

In conclusion, we prospectively studied 416 children that underwent operations using ketamine/lignocaine combination. The complications recorded were within tolerable limits, despite the presence of co-morbidities such as upper respiratory tract infection, malaria fever, and anemia. The ease of administration, satisfactory anesthesia, and analgesia, the availability, and affordability of these agents, and the absence of mortality during the period of study, showed that these agents have much to offer in remote areas where there are no anesthetists, sophisticated anesthetic facilities, and compressed gases.

References

1. Aisien AO, Olarewaju RS, Ujah IA, Mutahir JT, Sagay AS. Anaesthesia for minilaparotomy female sterilization in Jos University Teaching Hospital, Nigeria: a fourteen-year review. *Afr J Med Sci* 2001; 30: 119-121.
2. Faponle AF, Sowande OA, Adejuyingbe O. Anaesthesia for neonatal surgical emergencies in a semi-urban hospital in Nigeria. *East Afr Med J* 2004; 81: 568-573.
3. Olasinde AA, Oluwadiya KS. Anaesthesia Practice In A Hospital Developing Countries: An 18months Experience. Available from URL: <http://www.ispub.com/ostia/index.php?xmlFilePath=journals/ijtwm/vol3n1/anaesthesia.xml>
4. Adesunkanmi MR. Where there is no Anaesthetists. A study of 282 consecutive patients using intravenous, spinal and local infiltration anaesthetic techniques. *Trop Doct* 1997; 27: 79-82.
5. Otoide VO, Omuemu C, Ojobo S. Elevated serum glucose levels following ketamine intravenous anaesthesia: a report of two cases. *Int J Obstet Anaesth* 2001; 10: 206-208.
6. Pun MS, Thakur J, Poudyal G, Gurung R, Rana S, Tabin G et al. Ketamine anaesthesia for paediatric ophthalmology surgery. *Br J Ophthalmol* 2003; 87: 535-537.
7. Slonim AD, Ognibene FP. Sedation for pediatric procedures using ketamine and midazolam in a primarily adult care unit: a retrospective evaluation. *Crit Care Med* 1998; 26: 1900-1904.
8. Amitari Y. Death following accidental lignocaine overdose in a child. *N Eng J Med* 1986; 314: 182-183.

9. Kaye AD, Kucera I, Sabar R. Perioperative anesthesia clinical considerations of alternative medicines. *Anesthesiol Clin North Am* 2004; 22: 125-139.
10. Mofenson HC. Lignocaine toxicity from topical mucosal application. *Clin Pediatr* 1983; 22: 190-192.
11. Curley RK. An unusual cutaneous reaction in lignocaine. *Br Dent J* 1984; 113-114.
12. Juliana E, Idanpaan-Heikkila. Ethical principles for the guidance of physicians in medical research-the declaration of Helsinki. *WHO Bul* 2001; 79: 4
13. Lucas AO, Gilles HM, editors. A short textbook of preventive medicine for the tropics. 2nd ed. London (UK): Holder & Stoughton; 1987. p. 161-227.
14. Minossi JG, Picanco HC, Paulucci PR, de Carvalho MA, Vendites S. Inguinal hernia repair in children: importance of combined local anesthesia. *Arg Gastroenterol* 2002; 39: 204-208.
15. Irabor DO. Hernia repair under local or intravenous ketamine in a tropical low socio-economic population. *West Afr J Med* 2005; 24: 143-146.
16. Dalgleish S. Sucrose as analgesia for neonates experiencing mild pain. *Off J Can Assoc Crit Care Nurs* 1999; 10: 18-22.
17. Nze PA, Onyekwulu F. Intraoperative diclofenac for post-adenoidectomy analgesia in small children. *Nig J Clin Pract* 2006; 9: 102-104.
18. Armstrong FD. Analgesia for children with acute abdominal pain: a cautious move to improve pain management. *Pediatrics* 2005; 116: 1018-1019.
19. Somers LJ, Beckett MW, Sedgwick PM, Hulbert DC. Improving the delivery of analgesia to children in pain. *Emerg Med J* 2001; 18: 159-161.
20. Bonanno FG. Ketamine in war/tropical surgery (a final tribute to the racemic mixture). *Injury* 2002; 33: 323-327.

Related topics

Heydarpour F, Amini B, Kalantari S, Rostami A, Heydarpour P. Determination of sensitivity of male Wistar rats to an equal dose of ketamine/xylazine injection at anesthetic dose in a chronic model of hypernatremia in comparison with control group. *Saudi Med J* 2007; 28: 1485-1488.

Erden IA, Artukoglu F, Gozacan A, Ozgen S. Comparison of propofol/fentanyl and ketamine anesthesia in children during extracorporeal shockwave lithotripsy. *Saudi Med J* 2007; 28: 364-368.

Canbay O, Karakas O, Celebi N, Peker L, Coskun F, Aypar U. The preemptive use of diclofenac sodium in combination with ketamine and remifentanyl does not enhance postoperative analgesia after laparoscopic gynecological procedures. *Saudi Med J* 2006; 27: 642-645.