



World Health
Organization

Patient Safety

A World Alliance for Safer Health Care

Introduction to Patient Safety Research

Presentation 14 - Identifying Solutions: Randomized Clinical Trial



2: Table of Contents

- **Introduction**
 - [Overview](#)
 - [Study Details](#)
 - [Patient Safety Research Team](#)
- **Background**
 - [Opening Points](#)
 - [Study Rationale](#)
 - [Setting Up a Research Team](#)
- **Methods**
 - [Study Design and Objectives](#)
 - [Study Setting and Population](#)
 - [Data Collection](#)
 - [Data Analysis and Interpretation](#)
- **Results**
 - [Key Findings](#)
 - [Cost Analysis](#)
- **Conclusion**
 - [Main Points](#)
 - [Study Impact](#)
 - [Practical Considerations](#)
- **Author Reflections**
 - [Lessons and Advice](#)
 - [Ideas for Future Research](#)

3: Overview

■ **Methods**

- **In a district rural hospital in Uganda, 850 surgical patients evaluated prospectively over a 3-year period to compare the clinical efficacy of:**
 - Conventional postoperative penicillin therapy with single-dose ampicillin prophylaxis for hernia repair and ectopic pregnancy, and with
 - Single-dose ampicillin-metronidazole prophylaxis for hysterectomy and caesarean section.

■ **Results**

- **High rate of postoperative infection after conventional treatment with penicillin for 7 days was significantly reduced with the new regimen:**
 - From 7.5 to 0% in hernia repair
 - From 10.7 to 2.4% in ectopic pregnancy
 - From 20.0 to 3.4% in hysterectomy
 - From 38.2 to 15.2% in caesarean section.
- **Length of stay and postoperative mortality rates also significantly reduced.**

■ **Conclusion**

- **Single-dose ampicillin prophylaxis with or without metronidazole, although rarely used in developing countries, is more cost effective than standard penicillin treatment.**

4: Introduction: Study Details

■ Full reference

- **Reggiori A et al. Randomized study of antibiotic prophylaxis for general and gynaecological surgery from a single centre in rural Africa. British Journal of Surgery, 1996, 83:356-359**

[Link to Abstract \(HTML\)](#)

[Link to Full Text](#)

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Randomized study of antibiotic prophylaxis for general and gynaecological surgery from a single centre in rural Africa.

[Reggiori A](#), [Ravera M](#), [Cocozza E](#), [Andreato M](#), [Mukasa F](#).

Surgical Department, Hoima Hospital, Kampala, Uganda.

In a district rural hospital in Uganda, 850 surgical patients were evaluated prospectively over a 3-year period to compare the clinical efficacy of conventional postoperative penicillin therapy with single-dose ampicillin prophylaxis for hernia repair and ectopic pregnancy, and with single-dose ampicillin-metronidazole prophylaxis for hysterectomy and caesarean section. The high rate of postoperative infection usually encountered in African hospitals after conventional treatment with penicillin for 7 days was significantly reduced with the new regimen: from 7.5 to 0 per cent in hernia repair and from 10.7 to 2.4 per cent in ectopic pregnancy; from 20.0 to 3.4 per cent in hysterectomy and from 38.2 to 15.2 per cent in caesarean section. Length of hospital stay and postoperative mortality rates were also significantly reduced. Single-dose ampicillin prophylaxis with or without metronidazole, although rarely used in developing countries, is more cost effective than standard penicillin treatment.

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5: Introduction: Patient Safety Research Team

- **Lead researcher - Dr. Alberto Reggiori, MD**
 - Senior Medical Officer, General Surgery
 - Cittiglio Hospital in Varese, Italy
 - Field of expertise: general, emergency and gynaecological surgery, particularly in developing countries
- **Other team members:**
 - M. Ravera
 - E. Cocozza
 - M. Andreatta
 - F. Mukasa

6: Background: Opening Points

- **Postoperative wound and deep infection remains a major concern in developing countries**
 - In sub-Saharan Africa, records of postoperative infections are rare and few studies are available
 - Nonetheless, infection rates as high as 40-70% have been observed
- **Poor conditions in hospitals may contribute to the high rate of postoperative infection**
 - Poor sterility and hygiene of operating theatres and wards
 - Lack of trained personnel
 - Emergency surgical procedures often performed on patient presenting late in the course of the illness

7: Background: Opening Points (2)

- **Antimicrobial resistance is becoming an increasing problem in these areas, as well as in many other developing countries**
 - **Pencillin is the most commonly used antibiotic in Uganda and African district hospitals**
 - **More appropriate antibiotics not available**
 - **Facilities for microbiological test are rare**
 - **Postoperative follow-up is difficult**
- **Need to provide access to a broader range of antimicrobial prophylaxis to better combat post-operative infection**

8: Background: Study Rationale

- **Short course, single dose antimicrobial prophylaxis has been shown to be effective in reducing incidence of postoperative wound infection**
 - However, all studies have been carried out in developed countries
 - *"We knew that short term antibiotic prophylaxis worked in European hospitals and we wanted to test it in Uganda in a very straightforward way."*
- **Regime of short course, single dose antimicrobial prophylaxis chosen:**
 - Ampicillin: low cost, broad spectrum, sufficient half-life and high wound concentration
 - Metronidazole: anaerobic activity, long half-life
 - Resistance to both is rare in rural Africa

9: Background: Setting Up a Research Team

- **Selecting collaborators**
 - Team composed entirely of medical and paramedical staff from the surgical and maternity units of Hoima Hospital in rural Uganda
- **Funding**
 - Conducted primarily within the regular hospital budget
 - Small amount of additional funding from the Italian Cooperation AVSI used for extra drugs and incentives

10: Methods: Study Design and Objectives

- **Design: randomized clinical trial**
- **Objectives:**
 - **To compare the clinical effectiveness of conventional postoperative penicillin therapy with single-dose ampicillin prophylaxis for hernia repair and ectopic pregnancy**
 - **To compare the clinical effectiveness of conventional postoperative penicillin therapy with single-dose ampicillin-metronidazole prophylaxis for hysterectomy and caesarean section**
 - **To measure the impact of different antimicrobial regimes on factors such as duration of postoperative stay and cost of care**

11: Methods: Study Population and Setting

- **Setting: Hoima Hospital is a 150-bed government institution in rural Uganda sponsored by International Service Volunteers' Association**
 - At the time of the study, 800 major surgical procedures were performed yearly, 35% as emergency surgeries
 - Six Ugandan and two Italian surgeons on staff
 - No microbiological facilities available locally
- **Population**
 - 850 consecutive patients aged over 18 admitted to Hoima Hospital for elective and emergency surgical procedures from 1991 to 1993

12: Methods: Data Collection

- **Patients were divided into two categories according to surgical conditions:**
 - **Group 1 - 479 patients: 229 hernia repairs and 250 surgeries for ectopic pregnancies**
 - **Group 2 - 371 patients: 177 abdominal hysterectomies and 194 caesarean sections**
- **Patients then allocated by random numbers to one of two selected courses of treatment**

13: Methods: Data Collection (2)

- **Group 1:**
 - Half were randomized to receive a single dose of ampicillin 2g intravenously at induction of anaesthesia
 - Remainder received the standard postoperative treatment of intramuscular fortified procaine penicillin: 1-2 megaunits daily for 7 days
- **Group 2:**
 - 192 randomized to receive a single dose of ampicillin 3 g intravenously plus metronidazole 500mg at induction of anaesthesia
 - Remainder received benzylpenicillin 1 megaunit intravenously every 6 hours for one day followed by fortified procaine penicillin 1-2 megaunits daily for 6 days

14: Methods: Data Collection (3)

- After operation, each patient assessed daily by two supervisors aware of the type of prophylaxis used
- Further follow-up was performed two weeks after discharge
- Wound infections were graded:
 - Grade 1: superficial infection
 - Grade 2: deep infection
 - Grade 3: infection throughout wound (with or without dehiscence)
- Peritonitis deemed present when clinical signs and symptoms were evident
- Length of stay and postoperative outcome recorded

15: Methods: Data Analysis and Interpretation

- **Analyses performed**
 - Statistical comparison of postoperative infection rates (Chi-square test with Yates' correction and Fisher's exact test)
 - Calculation of differences in postoperative stay (analysis of variance)

16: Results: Key Findings

- **Ampicillin regime significantly reduced the incidence of postoperative infection compared with conventional treatment with penicillin:**
 - From 7.5 to 0% after hernia repair
 - From 10.7 to 2.4% after surgery for ectopic pregnancy
 - From 20 to 3.4% after hysterectomy
 - From 38.2 to 15.2 % after caesarean section
- **Patients receiving ampicillin also experienced significant reductions in:**
 - Length of hospital stay
 - Postoperative mortality rates
 - Post-operative complications for patients with invasive surgeries (hysterectomy and caesarean)

17: Results: Cost Analysis

- **Average cost for an admission day in Hoima Hospital in 1992 was \$3 USD, inclusive of personnel cost, drug, supplies and utilities**
- **Cost savings with new regimes**
 - Ampicillin-metronidazole regimens were cheaper than the full penicillin course
 - Duration of postoperative stay was shorter for both groups of patients receiving ampicillin prophylaxis

18: Conclusion: Main Points

- **Postoperative infection rates in developing countries are often underestimated and undocumented**
- **High postoperative infection rates can be significantly reduced, even in settings with resource constraints**
 - **Antibiotic prophylaxis with ampicillin is effective in reducing the postoperative morbidity rate in clean general surgery and gynaecology operations**
 - **Single-dose ampicillin prophylaxis, though rarely used in developing countries, is more cost effective than standard penicillin treatment**

19: Conclusion: Discussion

- **Short-course, single dose antibiotic prophylaxis may not be optimal if significant contamination is present**
 - Patients with sepsis at the time of surgery were excluded from the study
- **Follow-up compliance was greater the 90% in all groups**
 - However, cash incentives were necessary to achieve follow-up compliance
- **Study limitations**
 - Imperfect balance between groups resulted from the elimination of 12 patients operated on for hernia repair and 8 for caesarean section for whom treatment procedures were not strictly observed
 - Interviewers were not blinded to patient treatment groups

20: Conclusion: Study Impact

- **Practice impact**
 - Care was simpler and results were better
 - Nearby hospitals adopted similar regime changes after learning the results of this study
- **Patient impact**
 - Significant reduction in morbidity, mortality and length of stay at the hospital

21: Conclusion: Practical Considerations

- **Study duration**
 - Three and a half years
- **Cost**
 - Conducted primarily within regular hospital working budget
 - \$500 USD spent on additional drugs and incentives for patients
- **Competencies needed**
 - Utilized clinical expertise of hospital staff
 - One team member was a statistical expert
- **Ethical approval**
 - Approved by hospital authorities

22: Author Reflections: Lessons and Advice

- **What barriers or problematic issues did you encounter when setting up the research and how did you overcome them?**
 - *"We faced challenges changing the behaviour and habits of paramedical staff.*
 - *We convinced them by showing them that the infection rate was really different between the two regimes and that their work could be made easier."*
- **Research is feasible and applicable in other developing countries**
 - *"It is applicable everywhere because it is very simple and the result is to again simplify patient care. No technology or sophisticated items were necessary."*

23: Author Reflections: Ideas for Future Research

- **Message for future researchers from developing countries**
 - *"Try always to find new ways to improve patients care. Don' be satisfied with what you know already and learn from others."*
- **Recommendation for future research project**
 - *"To analyze the importance of the human factor (doctors, nurses, etc) in patients care and to identify the most crucial aspects."*