

Vingt-huitième Journée Scientifique Twenty-eighth Scientific Day

7 juin 2018 - 7 June 2018

Résumés des communications
Presentation abstracts

epicentre
ÉPIDÉMIOLOGIE • EPIDEMIOLOGY



Paris, 7 Juin 2018

L'atout premier du groupe de recherche qu'est Epicentre est son lien organique à MSF. Au cœur des arcanes s'écrit note histoire commune, celle des individus engagés, des projets, des expériences, des risques pris et des résultats partagés. C'est cette histoire que raconte chaque année notre journée scientifique.

Depuis plusieurs années MSF développe ses modes d'intervention en pédiatrie. De nombreux enfants sont suivis en consultation ou hospitalisés avec une maladie infectieuse au premier plan, souvent accompagnée d'un état de dénutrition. Les équipes soignantes sont alors amenées à s'interroger sur la place de l'antibiothérapie systématique, le risque d'acquisition d'une infection nosocomiale, de surcroît à germes résistants, ou encore l'effet de la supplémentation nutritionnelle des femmes enceintes sur la réponse immunologique de leurs enfants aux vaccins oraux. Ces sujets sont l'objet de la première session.

Le diagnostic étiologique et le traitement des états infectieux sévères reste aussi une question difficile. Aussi MSF et Epicentre se sont-ils lancés avec l'Institut Pasteur dans le développement d'un nouveau test rapide adapté à nos conditions d'exercice. Ce projet, qui n'a pas abouti, sera relaté sous ses différents aspects. Une autre approche sera présentée sur le cas particulier de la tuberculose pédiatrique avec l'objectif de définir une meilleure utilisation des moyens existants.

L'amélioration des pratiques de soins demeure un axe important de nos travaux. La troisième session l'illustrera avec plusieurs évaluations : l'efficacité d'une

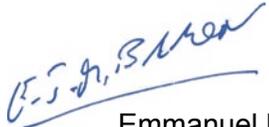
prescription systématique du traitement antituberculeux chez les patients infectés par le VIH, la place dans les programmes de MSF de médicaments récemment développés pour le traitement de l'hépatite C, pour le traitement de la tuberculose résistante, et enfin l'impact de la ciprofloxacine dans la réponse aux épidémies de méningite au Niger.

Après un temps dédié à la session de posters nous reviendrons sur les situations d'urgence dans lesquelles Epicentre a accompagné MSF. Cette ambition s'est par exemple déclinée cette année au Bangladesh, au nord du Cameroun, en Irak et au Yémen. Nous verrons de quelle manière nos travaux ont pu éclairer la décision opérationnelle et soutenir la parole publique de MSF.

Le programme ci-dessous témoigne de notre volonté de placer la recherche au cœur des programmes de soins pour ensuite impacter les politiques nationales. Mais elle n'est pas l'unique arme d'une approche qui peut être pluridisciplinaire. Nous avons réuni quelques collègues qui échangeront à partir de leurs expériences respectives sur la question « Qu'est-ce que la recherche peut changer ? ».

Rien d'évident dans la réponse à tout cela, d'où la nécessité de poursuivre ce débat autour d'un verre en fin de journée.

Je vous souhaite une excellente journée,


Emmanuel Baron
Directeur Général, Epicentre

Paris, June 7, 2018

The greatest asset of the Epicentre research group is its organic relationship with MSF. Behind the scenes, our shared story is written, the story of committed individuals, projects, experiences, risks taken and results shared. This is the story that our scientific day tells each year.

For several years, MSF has been involved in developing pediatric interventions. Many children first visit the doctor or are hospitalized with an infectious disease, often accompanied by malnutrition. The healthcare teams must therefore consider the usefulness of systematic antibiotic treatment, the risk of acquiring a nosocomial infection, possibly with a resistant pathogen, and the effect that supplemental nutrition for mothers during pregnancy can have on the immunological response to oral vaccines.

Etiological diagnosis and treatment of severe infections remain difficult questions as well. Thus, MSF and Epicentre, along with the Institut Pasteur, have begun developing a new rapid diagnostic test that is suitable for use in the areas where we work. Although this project did not reach its objectives, lessons learned will be described. Another approach will be presented with regards to pediatric tuberculosis, for which the objective is to determine how to best use existing methods.

The improvement of healthcare practices remains an important direction for our work. The third session will illustrate this point through several evaluations: the efficacy of systematic administration of antituberculosis

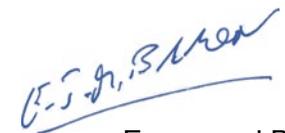
treatment to patients infected with HIV, the place that recently developed medications for hepatitis C have in MSF programs, for the treatment of resistant tuberculosis, and finally the impact of ciprofloxacin in the response to meningitis epidemics in Niger.

After the poster session, we will return to the emergency situations in which Epicentre has supported MSF. This year, for example, this ambition has been realized in Bangladesh, northern Cameroon, Iraq, and Yemen. We will see how our work has helped clarify operational decisions and support MSF's public statements.

The program below is a testament to our intention of placing research at the heart of healthcare programs and thereby impacting national policies. But this is not the only aspect of what is in reality a multidisciplinary approach. We have assembled a group of colleagues who will discuss their personal experiences regarding the question: "What can research change?"

As the answer to this question is not immediately obvious, the debate will continue over a cocktail at the end of the day.

I hope you have an excellent day.



Emmanuel Baron
Managing Director, Epicentre

Journée Scientifique Epicentre/Médecins Sans Frontières - Jeudi 7 juin 2018

8h45 – Accueil et café

9h30 – Introduction générale - Emmanuel Baron

9h45 – Session 1 : Pédiatrie

Modérateur : James Berkley, Kenya Medical Research Institute

- Bactériémie dans un hôpital pédiatrique au Niger. (Céline Langendorf)
- Antibiotiques de routine dans le traitement de la malnutrition aiguë sévère non compliquée au Niger. (Brigitte Chokote)
- Apport nutritionnel chez les femmes enceintes au Niger. (Sheila Isanaka)

10h30 – Session 2 : Diagnostic

Modérateur : Amadou Sall, Institut Pasteur Dakar

- Diagnostic de la tuberculose chez l'enfant. (Maryline Bonnet)
- Développement d'un test diagnostique pour les infections pédiatriques. (Anne-Laure Page)

11h20 – Pause café

11h40 – Session 3 : Pratique de soins

Modérateur : Els Torreele, Campagne d'Accès aux Médicaments Essentiels

- Traitement de l'hépatite C dans les programmes MSF. (Anne Loarec)
- Introduction de deux nouveaux médicaments contre la tuberculose résistante. (Helena Huerga)
- Prophylaxie antibiotique en réponse à une épidémie de méningite à méningocoques. (Matthew Coldiron)
- Traitement systématique et empirique de la tuberculose chez les patients infectés par le VIH et à un stade avancé. (Conrad Muzooru)

13h00 – Buffet sur place

14h00 – Session posters

15h00 – Session 4 : Urgences

Modérateur : Thierry Allafort-Duverger, MSF-Centre Opérationnel Paris

- Mortalité chez les Rohingyas en 2017. (Sophie Masson)
- Accès aux soins de santé dans le nord du Cameroun. (Etienne Gignoux)
- Santé mentale à Mossoul, Irak. (Jihane Ben Farhat)
- Modélisation de l'épidémie de choléra au Yémen. (Anton Camacho)

16h15 – Table ronde : Qu'est-ce que la recherche peut changer ?

Modératrice : Anne Roca, The Lancet Global Health

Participants :

- James Berkley, Kenya Medical Research Institute
- Bernard Opar, Ministère de la Santé, Ouganda
- Natalie Roberts, MSF - Centre Opérationnel, Paris
- Amadou Sall, Institut Pasteur Dakar

17h00 - Pot de clôture sur place, 9^{ème} étage Terrasse - Institut du Monde Arabe

Epicentre/Médecins Sans Frontières Scientific Day - Thursday 7 June 2018

8.45 – Welcome and coffee

9.30 – Introductory remarks – Emmanuel Baron

9.45 – Session 1: Pediatrics

Moderator: James Berkley, Kenya Medical Research Institute

- Bacterial bloodstream infections in a pediatric hospital in Niger. (Céline Langendorf)
- Routine antibiotics in the treatment of uncomplicated severe acute malnutrition in Niger. (Brigitte Chokote)
- Nutritional support to pregnant women in Niger. (Sheila Isanaka)

10.30 – Session 2: Diagnostic

Moderator: Amadou Sall, Institut Pasteur Dakar

- Diagnostic of tuberculosis in children. (Maryline Bonnet)
- Development of diagnostics for pediatric infections. (Anne-Laure Page)

11.20 – Coffee break

11.40 – Session 3: Delivering care

Moderator: Els Torreele, Campaign for Access to Essential Medicines

- Treating Hepatitis C in MSF programs. (Anne Loarec)
- Introducing two new drugs for resistant tuberculosis. (Helena Huerga)
- Antibiotic prophylaxis as a response to a meningococcal meningitis outbreak. (Matthew Coldiron)
- Systematic and empirical treatment of tuberculosis in HIV advanced infected patients. (Conrad Muzoora)

13.00 – Lunch on site

14:00 – Poster session

15.00 – Session 4: Emergency

Moderator : Thierry Allafort-Duverger, MSF-Operational Center Paris

- Mortality among the Rohingyas in 2017. (Sophie Masson)
- Access to health care in North Cameroon. (Etienne Gignoux)
- Mental health in Mosul, Iraq. (Jihane Ben Farhat)
- Modelling the cholera outbreak in Yemen. (Anton Camacho)

16.15 – Round table: What can research change?

Moderator: Anne Roca, The Lancet Global Health

- Participants:**
- James Berkley, Kenya Medical Research Institute
 - Bernard Opar, Ministry of Health, Uganda
 - Natalie Roberts, MSF-Operational Center Paris
 - Amadou Sall, Institut Pasteur Dakar

17.00 – Farewell drinks on site, on 9th floor Terrace - Institut du Monde Arabe

Posters

1. Culture conversion and treatment outcomes of a short standardized regimen for multidrug-resistant tuberculosis patients in Mozambique. [Matthieu Bastard](#)
2. Unravelling the dynamics of hepatitis-E infections in displaced populations: implications for reactive vaccination campaigns. [Anton Camacho](#)
3. Prevalence of parasitemia in an area receiving seasonal malaria chemoprevention. [Matthew Coldiron](#)
4. Protective effectiveness of seasonal malaria chemoprevention in Magaria, Niger. [Matthew Coldiron](#)
5. Single-dose oral ciprofloxacin prophylaxis as a meningococcal meningitis outbreak response: results of a cluster-randomized trial. [Matthew Coldiron](#)
6. Field challenges to measles elimination in the Democratic Republic of Congo. [Rebecca Coulborn](#)
7. Reducing the Frequency of Follow up and Task Sharing in the Treatment of Uncomplicated Severe Acute Malnutrition: an evaluation of monthly visits and home-based surveillance for access-limited and high-burden settings. [Sheila Isanaka](#)
8. Community and hospital-acquired invasive bacterial infections in children in Mali: aetiology, antibiotic resistance and clinical outcomes. [Céline Langendorf](#)
9. Cholera diseases burden and circulation of V. cholerae strains in Africa. [Francisco Luquero](#)
10. Cholera spatial clustering and the use of case-area targeted interventions. [Francisco Luquero](#)
11. Cholera vaccine protection: a meta-analysis from efficacy and effectiveness studies. [Francisco Luquero](#)
12. Pneumococcal carriage and serotypes distribution pre- and post- PCV10 vaccination campaign in Adjumani refugee camps, Uganda. [Deborah Nanjebe](#)
13. Evaluation of measles vaccine in extended controlled temperature conditions. [Kevin Tang](#)
14. Enquête de mortalité rétrospective, Zones de Santé de Tshibala et Kalomba, Kasai Central, République Démocratique du Congo (RDC). [Brahima Toure](#)

Session 1: Pediatrics

Moderator: James Berkley,
Kenya Medical Research Institute

Bacterial bloodstream infections in a pediatric hospital in Niger

Céline Langendorf, Epicentre, France

Background

Hospital mortality in the treatment of complicated severe acute malnutrition (SAM) remains important and may be associated with the severity of complications at presentation and healthcare-associated infections (HAI). Data on the incidence of HAIs are scarce, particularly for children in resource-limited settings. Our study aimed to assess the risk of hospital-acquired bacteremia and describe the burden of antibiotic resistance of community and hospital-acquired bacteremia in severely malnourished children hospitalized in a district hospital in Madarounfa, Niger.

Materials/methods

Children 6-59 months of age admitted with complicated SAM were enrolled. Clinical, therapeutic and biological data were collected for each child until discharge. Blood samples were collected on admission and in the case of clinical deterioration >48 hours after admission for culture. Hospital-acquired bacteremia was defined as positive blood culture > 48 hours after admission among children with a negative culture at admission

Results

Between October 2016 and November 2017, 2,225 patients were enrolled and had blood culture on admission. Among them, the prevalence of

community-acquired bacteraemia was 9.3% and a hospital-acquired bacteraemia was confirmed in 1.3%. The most common causative pathogen in community-acquired bacteraemia was non-Typhi Salmonella (59.2%) while it was *Klebsiella pneumoniae* (18.2%) and *Acinetobacter baumannii* (15.2%) in hospital-acquired bacteraemia. Enterobacteria expressing extended-spectrum beta-lactamase were more frequent in hospital-acquired bacteraemia (86.7%) than in community-acquired bacteraemia (10.6%).

Conclusion

We showed high proportion of multidrug-resistant bacteria, specifically in hospital-acquired bloodstream infections. Reinforcement of infection prevention and control procedures should be considered.

Over 1-year period, the incidence of hospital-acquired bloodstream infections among children with SAM was around 1% with high proportion of multidrug-resistant bacteria.

Routine antibiotics in the treatment of uncomplicated severe acute malnutrition in Niger

Brigitte CHOKOTE, Epicentre, Niger

Background

Current guidelines for the treatment of uncomplicated severe acute malnutrition (SAM) recommend the provision of routine antibiotics to reduce mortality, however, the benefit of routine antibiotics to children treated as outpatients remains unclear. From 2012-2014, we conducted a randomized trial to assess the effect routine antibiotics on the nutritional recovery of children with uncomplicated SAM in Madarounfa, Niger. There was no benefit of routine amoxicillin treatment on nutritional recovery or mortality, compared to placebo. Amoxicillin reduced risk of transfer to inpatient care in our trial setting (risk ratio = 0.86, 95% CI: 0.76, 0.98).

Methods

To evaluate the effect of routine antibiotic use in the treatment of uncomplicated SAM in an operational context, we enrolled a prospective cohort in three outpatient treatment sites in Madarounfa, Niger from 2016-2017. Two sites were assigned to provide children with amoxicillin when clinically indicated. Children in the third site received routine amoxicillin on admission. Routine program outcomes, including recovery, default, transfer, non-response and death, were compared between sites and with the original trial population receiving routine amoxicillin.

Results

A total of 1,776 children were included in the two non-routine antibiotic sites and 6,185 children at the single routine antibiotic site. There was no difference in risk of recovery, non-response to treatment, or death between groups between sites, but the risk of transfer was lower at the site providing routine amoxicillin. However when controlling for site, there was no difference in the risk of transfer when comparing children receiving routine amoxicillin compared to children not receiving routine amoxicillin

Conclusions

Data from an operational context were used to extend trial results related to the routine use of antibiotics in the treatment of uncomplicated SAM in Niger. The simplification of treatment protocols may allow important advances in the scaling up of treatment but should consider context-specific factors.

We evaluated the non-routine use of antibiotics in the treatment of uncomplicated SAM in an operational context. Simplification of treatment protocols may facilitate the scaling up of programs but should consider context-specific factors.

Nutritional support to pregnant women in Niger

Sheila Isanaka, Epicentre, France

Background

Recent vaccine trials have shown substantially lower vaccine efficacy in low-income countries than in high- or middle-income countries. Most of the difference in vaccine efficacy between high and low-income countries may be due to lower immunogenicity of oral live vaccines, but the mechanisms underlying lower immunogenicity in developing countries remain poorly understood. To identify potential boosters of immunogenicity, we conducted a nested, cluster randomized study to evaluate the effect of prenatal nutrition supplementation on infant immune response to three doses of oral rotavirus vaccine.

Methods

Fifty-three villages were randomized in a 1:1:1 ratio to receive daily lipid-based nutrient supplements (LNS), multiple micronutrients (MMN) or iron-folic acid (IFA). Pregnant women in participating villages received the assigned supplement at home on a weekly basis from the time of pregnancy identification until delivery. Infants of participating women were randomized in a 1:1 ratio to receive three doses of oral rotavirus vaccine or placebo. Response to the rotavirus vaccine, defined as anti-rotavirus IgA concentration, was assessed at the time of the first dose and 28 days Post-Dose 3.

Results

Immune response among children receiving vaccine vs. placebo, as well among vaccinated children whose mothers received LNS vs. MMN vs. IFA, will be presented.

Conclusions

Evidence supporting the immunogenicity of oral vaccines, and the identification of potential boosters, in an African setting can provide valuable information to increase of impact of vaccination.

Immunogenicity of oral live vaccines is low in developing countries. We examine immune response among children receiving vaccine vs. placebo, as well among vaccinated children whose mothers received nutritional support in pregnancy.

Session 2: Diagnostic

Moderator: Amadou Sall, Institut Pasteur Dakar

Diagnostic of tuberculosis in children

Maryline Bonnet, IRD UMI233 TransVIHMI – UM – INSERM U1175 and Epicentre, Uganda

Background

Childhood tuberculosis (TB) mortality is high, particularly in young untreated children. Child-friendly treatments are available, but childhood TB is often underdiagnosed. Lack of adapted tools and care concentrated at central facilities contribute to this situation. We present Epicentre's work on paediatric TB diagnosis in Mbarara and discuss future orientations.

Methods

One cross-sectional study and two prospective cohorts addressed the issue of specimen collection in children unable to produce sputum, comparing string-test and induced sputum in children with presumptive TB (Study-1) and non-sputum tests (urine-LAM and XpertMTB/RIF on stool) in children with increased risk of severe or disseminated TB (Study 2). Study-3 assessed the outcomes of children with presumptive TB.

Results

String-test performed as well as induced sputum using mycobacterial culture (9/105, 8.6% in each group) and Xpert (3/64, 4.7% vs 4/64, 6.3%, $p=1.0$) but 16.1% of children could not swallow the capsule. Of 235 children in Study-2 (69.8% < 2 years, 31.9% HIV-infected, 66.8% severely malnourished, 28.1% with severe pneumonia), 5.1% were TB confirmed. Sensitivity and specificity of urine-LAM and Xpert on stool were 50.0% and 73.7%, and 50.0% and 99.1%, respectively.

Of 360 children in study-3, 140 (38.9%) were treated for TB but only 13% of them were bacteriologically confirmed. At 3 months, 6.9% children had died: 10.7% on TB treatment vs 4.5% not treated ($p=0.025$). Severe acute malnourished children were more likely to die (aHR 9.86, 95%CI 3.11-31.23).

Conclusions

Few children with presumptive TB from high burden countries were bacteriologically confirmed. Xpert on stool is a promising method, but strengthening of clinical and radiological diagnosis is required. Early TB identification of children with co-morbidities, particularly severe pneumonia is needed. The ongoing TB-Speed project evaluates the impact in term of case detection and reduction of mortality of a diagnostic approach combining XpertMTB/RIF Ultra on stool and nasopharyngeal aspirate, staff training and mentorship on clinical and radiological diagnosis and digital X-ray at peripheral facility level. TB-Speed also evaluates algorithms for TB screening and diagnosis of children with severe pneumonia, HIV-infection and severe acute malnutrition.

Epicentre's research on diagnosis of childhood tuberculosis in Mbarara highlights the difficulties of bacteriological confirmation and the need for innovative diagnostic approaches using child friendly tools suitable to low-level health care facilities. This is currently evaluated in TB-Speed.

Development of diagnostics for pediatric infections

Anne-Laure Page, Epicentre, France

Background

Bacterial infections remain the leading cause of child mortality in sub-Saharan Africa. In the absence of simple and rapid diagnostic tests, treatment remains probabilistic and may lead to unnecessary use of antibiotics. We engaged in a collaboration with Institut Pasteur (IP) to bring together biological, clinical and field expertise to develop field-adapted diagnostic tests for pediatric bacterial infections.

After signing an agreement framing the legal, financial and organizational aspects of the collaboration, we launched a call for proposals inviting research units from IP and its international network, in partnership with technological institutions, to submit projects. A steering committee including members from IP, MSF and Epicentre was in charge of selecting the project and following its progress. The selected project, called “Child’s Play”, aimed at developing an automated and integrated molecular assay for the simultaneous detection of the five leading bacterial causes of severe illnesses among children in Africa: *Streptococcus pneumoniae*, *Salmonella spp.*, *Staphylococcus aureus*, *Haemophilus influenzae* and *Escherichia coli*.

The molecular assays showed good analytical sensitivity and specificity using blood samples spiked with bacteria. Integration and automatization in a microfluidic cartridge revealed numerous challenges that were

partly solved during the project. However, when tested on clinical samples from febrile patients collected in Mali and Uganda, less than half of the samples positive by blood culture were detected by the molecular assays. This might reflect lower sensitivity of molecular methods compared to culture when used directly on blood. Considering the limited anticipated clinical impact of such a test, the steering committee decided not to move the project forward.

This collaboration highlighted various legal, institutional, scientific and technological obstacles in the development of diagnostic tests. Although many of them were overcome through collaborative efforts, the project failed to reach sufficient clinical relevance to move to the next challenging step of industrialization.

A collaboration to develop an automated assay for the detection of the leading bacterial causes of pediatric infections revealed numerous legal, institutional and scientific challenges.

Notes

Session 3: Delivering Care

Moderator: Els Torreele,
Campaign for Access to Essential Medicines

Treating Hepatitis C in MSF programs

Anne LOAREC, Epicentre, France

Introduction

Worldwide, 71 million people are infected with hepatitis C (HCV). The introduction of Direct-Acting Antivirals (DAAs) in 2013 radically changed HCV care outcomes, with simpler, cheaper and efficacious treatments. MSF introduced Sofosbuvir into programs in 10 countries beginning in 2013. Here, we present an overview of patients initiated on treatment and an example of a simplified model of care in Cambodia.

Methods

Eligible patients were initiated on DAAs in 9 MSF supported clinics in 7 countries. Longitudinal follow-up data from these patients was entered into a standardized database. Patient characteristics are described using descriptive statistics. To document and describe a simplified model of care, different laboratory and screening possibilities were identified to simplify care. These included Fibroscan®, ultrasound for hepatocarcinoma screening, oesophagus-gastro endoscopy, Sofosbuvir-Daclatasvir as pan-genotypic treatment and simplification of follow-up. In addition, field evaluations were conducted to investigate performance of capillary blood use for HCV RDT (SD Bloline®) and the performance of Genexpert® for viral load in Cambodia, where genotype 6 circulates.

Results

Over 60,000 patients were screened between January 2013 and April 2018. Chronic HCV infection (CHC) was confirmed in 15,500 patients and 9,462 patients were initiated under DAA treatment. Final virological outcome is known for 5,159 patients, with 4,997 patients considered cured (96.9%).

In Cambodia, we describe the different aspects of the simplified model of care. We identified algorithms which decreased the number and types of laboratory tests (e.g. capillary blood for rapid diagnostic tests, point-of-care viral load, removed genotyping) and shifting certain tasks (e.g. refill appointment with pharmacist), thereby allowing for simplification.

Conclusion

We document the feasibility of curing HCV with a simpler cheaper and efficacious regimen and model of care, while maintaining high cure rates and patient safety. Simplification of care is essential for decentralization and scale up of HCV care.

Longitudinal follow-up data from Hepatitis C patients and tests evaluation provided evidence for efficient and simplified model of care in resources limited settings.

Introducing two new drugs for resistant tuberculosis

Helena HUERGA, Epicentre, Senegal

Background

Multidrug-resistant tuberculosis (MDR-TB) remains a serious public health problem. Scarcity of safe, effective drugs contributes to the unfavorable outcomes, reported as 50% globally. The endTB project, funded by UNITAID, aims to expand access to two new anti-TB drugs: bedaquiline and delamanid, and other drugs repurposed for TB, as well as generating evidence about the effectiveness and safety of MDR-TB regimens containing these drugs.

Methods

This multi-centre prospective observational cohort study is conducted in 17 countries and includes patients treated with a bedaquiline - and/or delamanid-containing MDR-TB regimen in an endTB site who consent to participate. The study captures routine programmatic patient data in a standardised electronic medical record. Serious Adverse Events (SAE) are reported to a Pharmacovigilance Unit.

Results

From April 2015 to December 2017, 1,708 patients were included. Median age was 37 years (range: 13-87), 65% were male, 41% had a body mass index below 18.5 Kg/m², 67% had extensively drug-resistant (XDR) or pre-XDR TB.

Of the patients with at least 6 months of follow-up period, 15.9% had at least one SAE in the first 6 months of treatment. Most common SAEs were increased liver enzymes and prolonged QTcF interval, reported in 3.3% and 1.7% of the patients respectively. In total, 5.2% patients had a SAE with fatal outcome.

Of the patients with positive culture at treatment initiation and at least 6 months of follow-up period, 84.8% (95%CI: 81.5-87.6) converted by 6 months. Of those who converted and had at least 12 months of follow-up period, 7.7% (95%CI: 7.2-8.2) reverted by 12 months.

Conclusion

Preliminary analyses show promising results in a large cohort of patients with highly resistant and extensive TB disease treated with bedaquiline or delamanid under programmatic conditions. Safety reporting was adequate with no unexpected safety issues attributed to the new drugs. Culture conversion rates were high although subsequent culture reversion in some patients requires further analyses.

The endTB observational study shows promising safety and treatment results using bedaquiline and delamanid to treat patients with highly resistant and severe forms of TB.

Antibiotic prophylaxis as a response to a meningococcal meningitis outbreak

Matthew COLDIRON, Epicentre, France

Introduction

Vaccine supply against newly-emerged serogroup C meningococcus is limited. New epidemic response strategies are therefore needed in the African meningitis belt. We conducted a three-arm, open-label cluster-randomized trial of single-dose ciprofloxacin prophylaxis as an epidemic response. (ClinicalTrials.gov number NCT02724046).

Methods

Villages notifying a suspected meningitis case were randomly assigned (1:1:1) to standard care, single-dose oral ciprofloxacin for household contacts <24h after case notification, or village-wide distribution of ciprofloxacin <72h after first case notification. Dosing was age-based and directly-observed. The primary outcome was the overall attack rate (AR) after inclusion of the village. A random sample of 400 participants in 20 villages was enrolled to describe any changes in fecal carriage prevalence of ciprofloxacin-resistant Enterobacteriaceae before and after intervention.

Results

Between April 22 and May 18, 2017, 49 villages (total population 71 308) were included and randomly assigned; 17 to the control arm, 17 to household prophylaxis, and 15 to village-wide prophylaxis.

A total of 248 cases were notified. The AR were 451 per 100 000 persons in the control arm; 386 per 100 000 persons in the household prophylaxis arm ($p=0.68$); and 190 per 100 000 persons in the village-wide prophylaxis arm ($p=0.032$). After controlling for whether the village was included after the first rainfall, the adjusted AR ratio between the village-wide prophylaxis arm and the control arm was 0.40 ([0.19–0.87], $p=0.022$). Baseline carriage prevalence of ciprofloxacin-resistant Enterobacteriaceae was 95% in the control arm and the village-wide prophylaxis arm and did not change post-intervention.

Conclusions

Village-wide distribution of single-dose oral ciprofloxacin within 72 hours of case notification reduced overall meningitis AR. This novel strategy is promising as a meningitis epidemic response. Further studies should be carried out in different settings to confirm effectiveness and duration of protection and to investigate the impact on antimicrobial resistance.

New strategies for meningococcal meningitis outbreak response are needed. Village-wide ciprofloxacin prophylaxis is promising but needs further study.

Systematic and empirical treatment of tuberculosis in HIV advanced infected patients

Conrad Muzoora, University of Science and Technology, Uganda

Background

In late presenting HIV+ adults, mortality following ART initiation is high with tuberculosis (TB) or invasive bacterial diseases (IBD) being major causes of mortality. We report the results of the STATIS open-label randomized controlled trial (ANRS 12290) that compared the efficacy and safety of 2 strategies aiming to decrease mortality and IBD in late presenters.

Methods

ART-naïve HIV-1 infected adults with CD4<100 cells/μl were randomly assigned to either ART + extensive TB screening (arm 1) or ART + systematic empirical TB treatment (arm 2). In arm 1, extensive TB screening included Xpert MTB/RIF on sputum, urine lipoarabinomannan (LAM) and chest X-ray at baseline and at any time during follow-up in case of TB symptoms. ART was initiated immediately in patients who did not start TB treatment at baseline (arm 1 patients with negative TB screening) and 2 weeks after starting TB treatment in others (arm 1 patients with positive TB screening and arm 2 patients). The primary outcome was the occurrence of death or IBD at week 24 (W24).

Results

1047 participants were included (arm 1: 525; arm 2: 522). Baseline characteristics were: 58% male, mean age 36 years, body mass index 20.1 kg/m², CD4 36 cells/μl, plasma HIV RNA 5.4 log₁₀ copies/ml. At W24,

39 patients (3.8%) were lost to follow-up (arm 1: 21; arm 2: 18), while there were 69 deaths (arm 1: 36; arm 2: 33) and 29 IBD (arm 1: 14; arm 2: 15). The W24 hazard ratio of events between arm 2 vs. arm 1 was 0.93 (95%CI 0.61-1.42) for death or IBD, 0.92 (0.57-1.48) for death alone, 1.14 (0.54-2.40) for IBD alone and 2.70 (1.80-4.04) for grade 3-4 drug-related toxicity.

Conclusions

We found that systematic TB treatment is not superior to extensive TB screening using Xpert MTB/RIF and urine LAM and targeted TB treatment to decrease the risk of mortality or IBD in ART-naïve adults with CD4<100/μl.

The STATIS trial compared the efficacy and safety of 2 strategies aiming to decrease mortality and invasive bacterial disease in late presenting HIV+ adults: initiation of TB treatment after extensive TB screening vs systematic empirical TB treatment. Systematic empirical TB treatment was not superior to extensive TB screening.

Notes

Session 4: Emergency

Moderator: Thierry Allafort-Duverger,
MSF-Operational Center Paris

Mortality among the Rohingyas, displaced in Bangladesh, 2017

Sophie MASSON, Epicentre, France

Background

On August 25, 2017, a counter-insurgency military operation in Rakhine State, Myanmar, led to the displacement of approximately 626,000 Rohingya civilians into Bangladesh in under three months. To inform humanitarian assistance, Médecins Sans Frontières (MSF)/Epicentre performed a survey to estimate retrospective mortality, and set-up a prospective mortality surveillance system among the population of Balukhali 2 and Tasnemarkhola settlements, in Cox's Bazar District, Bangladesh.

Methods

In November 2017, MSF/Epicentre conducted a retrospective survey with systematic sampling among a population of 135,980 Rohingyas (1,529 families included) who had recently arrived in the two targeted settlements in Bangladesh. The recall period for mortality extended from May 27- November 12, 2017, spanning roughly equal periods before and after August 25, 2017. Heads of family described the family structure, and provided the date, location and cause of death for family members who died during the recall period. Following the survey, a prospective mortality community-based surveillance was implemented using a weekly systematic sampling (1/4 households interviewed every week) and a recall period of one week.

Results

Before the crisis, the crude mortality rate (CMR) (expressed as deaths/10,000/day), was 0.6[95% CI: 0.4-0.8], and the under 5 mortality rate

(U5MR) 0.5[0.2-1.1]. Following the crisis mortality rates were 4.6[4.1-5.2] and 3.8[2.8-5.2] respectively. Violence caused respectively 77.4% and 57.5% of these deaths. Over this later period of time, 88.1% of the deaths reported occurred in Myanmar or during the exodus and 86.1% during the first month of the crisis. During this first month, coinciding with the pic of displacement, the CMR was 10.2[8.9-11.6], and the U5MR 7.4[5.2-10.6], with 85.3% of the deaths reported as due to intentional violence.

Following the survey, the prospective surveillance showed a rapid decline of the mortality to reach a CMR of 0.1[0.0-0.2] and an U5MR of 0.4[0.0-0.9] end of December.

Conclusions

This survey provided epidemiological evidence of high rates of mortality due to violence among the displaced Rohingyas in Myanmar, while the prospective surveillance in the camps in Bangladesh showed a mortality comparable to the mortality among this population prior to the displacement and the events.

In November 2017, MSF/Epicentre conducted a retrospective mortality survey among recently settled Rohingyas in Tasnemarkhola and Balukhali 2 settlements in Bangladesh. This survey provided epidemiological evidence of high rates of mortality due to violence in Myanmar.

Access to health care in North Cameroon

Etienne GIGNOUX, Epicentre, Switzerland

Background

Field access has been considerably limited in the Far North region of Cameroon due to the ongoing conflict. Médecins Sans Frontières (MSF) wanted to estimate difficulties in accessing health care, access to food and mortality rates of the populations in the Logone-et-Chari and Mayo-Sava departments.

Methods

We estimated access to health care and mortality rates through cell phone interviews. We selected 30 villages (clusters) in each department. Local Community Health Workers (CHWs) collected all household phone numbers in the selected villages from which we randomly selected nineteen. To compare telephone interviews to face-to-face interviews for estimation of access to health care and mortality rates we applied the two methods in parallel in the town of Mora. To evaluate access to food, push messages were sent by the 3 main mobile network operators in Cameroon. We interviewed by phone all identified legal health care facilities in the area to estimate their attendances and the services offered before the conflict and at the date of the survey.

Results

We reached 43% of the 3,423 numbers called. Over 600,000 push messages were sent and only 2,255 were returned. We called 43 health facilities and reached 34. In The town of Mora, telephone interviews showed a Crude Mortality Rate (CMR) at 0.30 (CI 95%: 0.16-0.43) and home

visits reported a CMR at 0.16 (0.05-0.27), most other indicators showed comparable results except household composition (more IDPs by telephone).

Phone interviews showed a CMR at 0.63 (0.29 – 0.97) per 10,000-person per day in Logone-et-Chari, and 0.30 (0.07 – 0.50) per 10,000-person per day in Mayo-Sava. Among 86 deaths, 13 were attributed to violence (15%), with terrorist attacks being explicitly mentioned for seven deaths. Among 29 health centres 5 reported to have been attacked and vandalized; 3 remained temporarily closed; Only 4 reported not being affected.

Conclusion

Telephone interviews are feasible in areas with limited access, although a particular attention should be put on the initial collection of phone numbers. The use of text messages to collect data was not satisfactory and for this purpose is not recommendable. Mortality in Logone-et-Chari and Mayo-Sava was not alarming although a considerable number of deaths were directly related to the conflict.

Insecurity limits the access to the population. In North Cameroon we used cell phone survey to estimate health access and mortality rate. Results were satisfactory even if some limitations were present. Health facilities had been heavily impacted by the conflict, population mortality rates were not alarming although a substantial proportion of deaths were directly related to the conflict.

Mental Health in Mosul, Iraq

Jihane BEN FARHAT, Epicentre, France

Background

Between October 2016 and July 2017, Mosul, Iraq's second largest city, was under siege, leading to mass displacement of its population. Médecins Sans Frontières (MSF) provides primary health care and mental health services to displaced Iraqis fleeing the war and currently living in camps in Kurdistan Regional Governorate (KRG). The proportion of children in need of specialized psychological support, as reported by MSF child psychologists, highlighted a high need for mental health services. Furthermore, mental health conditions or diagnoses by psychologists evidenced the presence of cumulative stressors. The aim of this study was to quantify and describe war related stressors, and the prevalence of children in need of psychological support.

Methods

The survey was conducted in Hasan Sham U2 camp in KRG in December 2017 to assess mental health status and stressors. Households were the primary sampling unit, selected randomly from the numbers provided by camp management. All questionnaires were administered in each selected household: the Childhood War and Trauma Questionnaire (CWTQ) among the older child, the SDQ 7-16 and PsyCa 3-6 among all eligible children in household.

Results

In total, 477 children were screened, accounting for almost one third of the children in the camp. Twenty nine percent of 329 children screened using the SDQ (95% Confidence Interval (CI):23.9-33.7) and 70.9% of 148 children screened using the PsyCa3-6 (95% CI: 63.0-77.8) had a positive test result. Of 240 CWTQ administered, 10,0% of the households reported the death of the father and 5.7% the death of a child, with no statistically significant differences between the area of origin ($p>0.2$). Eighty percent of households from West Mosul and 66% of those from other areas ($p<0.001$) had experienced at least one recent violent event.

Conclusion

This study conducted after a mass displacement of the Mosul population supports the notion that displaced population have faced traumatic events before fleeing their region, and that a high proportion of these displaced children were in need of mental health support.

This study conducted among families fleeing a violent context, underscores the importance of including mental health services for children as part of a comprehensive package of support for displaced populations.

Modelling the cholera outbreak in Yemen

Anton CAMACHO, Epicentre, France

Background

In war-torn Yemen, reports of confirmed cholera started in late September 2016. Cholera continues to plague Yemen today in what has become the largest documented cholera epidemic of modern times. We aim to describe key epidemiological features of this epidemic, including the drivers that triggered the massive surge of cholera cases in May 2017.

Methods

The Health Authorities of Yemen set up a national cholera surveillance system to collect information on suspected cholera cases presenting at health-facilities and MSF cholera treatment centres. We first conducted descriptive analyses at national and governorate levels.

We reconstructed the changes in cholera transmission over time by estimating the instantaneous reproduction number, R_t . Finally, we estimated the association between rainfall and the daily cholera incidence during the increasing phase of the second epidemic wave, from April 15 to June 24 2017, by fitting a spatiotemporal regression model.

Results

From 28 September 2016 to 12 March 2018, 1,103,683 suspected cholera cases (attack rate 3.69%) and 2,385 deaths (case fatality risk 0.22%) were reported countrywide. The epidemic comprised of two distinct waves with a surge in transmission in May 2017, corresponding to a median $R_t > 2$ in 13 of 23 Governorates. Microbiological analyses suggested that the same *V. cholerae* O1 Ogawa strain circulated in both waves. We found a positive, non-linear, association between the weekly rainfall and cholera incidence in the following 10 days, with weekly rainfall of 25 mm being associated with a 1.42-fold (95% CI: [1.31 – 1.55]) increase in cholera risk compared to a week without rain.

Conclusion

Our analysis suggests that the small first cholera epidemic wave seeded cholera across Yemen during the dry season. When the rains returned in April 2017, they triggered widespread cholera transmission that led to the large second wave.

We modelled the plausible drivers of cholera transmission during the course of the outbreak in Yemen. We found a strong association between rainfall and the massive surge of cholera cases in May 2017.

Notes

Round table

What can research change?

Moderator: Anne Roca, The Lancet Global Health

Participants:

- James Berkley, Kenya Medical Research Institute
- Bernard Opar, Ministry of Health, Uganda
- Natalie Roberts, MSF-Operational Center Paris
- Amadou Sall, Institut Pasteur Dakar



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