Vingt-sixième Journée Scientifique
Twenty-sixth Scientific Day

2 juin 2016 - 2 June 2016

Résumés des communications
Presentation abstracts

epicentre
ÉPIDÉMIOLOGIE • EPIDEMIOLOGY

MEDECINS SANS FRONTIERES

Paris, 2 juin 2016

Bonjour à tous,

Le renouvellement des pratiques médicales ne consiste pas seulement à introduire de nouvelles techniques. Dans nos contextes d'intervention il repose aussi sur la mise en place de stratégies différentes de prévention, de diagnostic ou de traitement. Les deux premières sessions de la matinée abordent ces aspects ; tout d'abord sur le VIH et la tuberculose dont le diagnostic et le suivi des patients restent un défi opérationnel, puis sur le choléra et les stratégies qui permettent d'en limiter la diffusion. Ce dernier aspect – et plus largement la question des méthodes d'intervention – est une question récurrente en situation épidémique. Le contrôle des foyers africains de rougeole est ainsi régulièrement discuté. De quel contexte parle-t-on précisément, comment expliquer les résurgences régulières de cette maladie, quelles priorités opérationnelles et médicales afficher, qu'en est-il aujourd'hui de l'épidémiologie de la maladie, à quels résultats d'intervention s'attendre ? Nous en discuterons lors de la table ronde en fin de matinée.

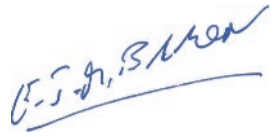
La première session de l'après-midi permet d'apprécier la diversité des champs et des méthodes d'intervention d'Epicentre, un des éléments qui nous distingue d'autres groupes de recherche. En marge des grandes épidémies – nous présentons les résultats d'une étude de séroprévalence de la fièvre Ebola – nous avons également investigué des syndromes toxiques survenus à plus petite échelle en RDC et au Libéria.

Certaines questions de santé ne font pas la une de l'actualité malgré une morbidité et une mortalité parfois très importante. Les morsures de serpents sont un autre exemple qu'Epicentre souhaite contribuer à faire émerger.

Une caractéristique de notre attachement à MSF est notre présence sur les situations de crise. La deuxième session de l'après-midi rapporte des résultats d'enquêtes dans de tels contextes, auprès de migrants et de personnes déplacées.

Enfin la journée se terminera par la présentation d'études de deux nouveaux vaccins contre la fièvre Ebola et les diarrhées à rotavirus. Epicentre a en effet significativement contribué au développement de ces deux vaccins. Leur modèle de développement peut ouvrir une voie vers des produits plus adaptés aux contextes de précarité dans lesquels une grande part de la population mondiale vit toujours.

Je vous souhaite une très bonne journée,



Emmanuel Baron
Directeur Général, Epicentre

Paris, 2 June 2016

Welcome everyone,

Progress in medicine is not limited solely to introducing new techniques. Within the context of our interventions, progress is also based on implementing different strategies for disease prevention, diagnosis or treatment. The first two morning sessions will address these aspects; first for HIV and tuberculosis, for which diagnosis and patient follow-up remain an operational challenge, and second for cholera and strategies for limiting its spread. How to limit the spread of disease - and the question of intervention methods in general - is a recurring question in epidemic situations. This issue is regularly discussed within the context of controlling measles hotspots in Africa. What context are we talking about specifically, how can we explain the regular resurgence of this disease, what should our operational and medical priorities be, what is the current epidemiology of the disease, and what results can we expect from interventions? These questions will be discussed during the round table at the end of the morning session.

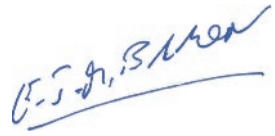
The first afternoon session will highlight the diversity of Epicentre's intervention fields and methods, which is a key element that distinguishes us from other research groups. In addition to widespread epidemics - we will be presenting results from a study of Ebola - we have also studied toxic syndromes that occurred on a smaller scale in the DRC and in Liberia.

Some health issues do not make the headlines, despite at times significant levels of morbidity and mortality. Snakebites are another example of a topic that Epicentre would like to help draw attention to.

Due to our relationship with MSF, we have a presence in crisis situations. The second afternoon session will report the results of studies conducted in these settings, involving migrant populations and displaced persons.

The day will finish with the two presentations of studies of new vaccines against Ebola and rotavirus. Epicentre has made a significant contribution to the development of these two vaccines. The development model for these two vaccines may help facilitate the development of products that are better suited to the unstable contexts in which a large portion of the population worldwide still lives.

I hope that you all enjoy the day,



Emmanuel Baron
Managing Director, Epicentre

Journée Scientifique Epicentre/Médecins Sans Frontières - Jeudi 2 juin 2016

8h45 – Accueil et café

9h30 – Introduction générale - Emmanuel Baron

9h45 – VIH et Tuberculose

Modérateur : Fred Eboko, Institut de Recherche pour le Développement

- Diagnostic de la tuberculose dans un contexte de prévalence élevée du VIH. (Helena Huerga)
- Echec virologique, résistance au traitement et besoins en régime de 3ème ligne pour les patients sous 2ème ligne dans 3 programmes VIH au Kenya, Malawi et Mozambique. (Birgit Schramm)
- Mise en place de SAMBA: Test Point-Of-Care Semi-Quantatif de la Charge Virale: Résultats d'un programme décentralisé au Malawi. (Elisabeth Poulet)

10h45 – Choléra

Modérateur : Celestino Obua, Mbarara University of Science and Technology

- Stratégies innovantes de délivrance du vaccin choléra.(Francisco Luquero)
- Amélioration des tests de diagnostic rapide du choléra. (Anne-Laure Page)
- Place de la doxycycline dans la prévention du choléra. (Francesco Grandesso)

11h30 – Pause café

12h00 – Table ronde : Où en sommes-nous dans le contrôle de la rougeole dans les foyers africains ?

Modérateur : Mercedes Tatay, MSF International

- Rougeole en RDC : Leçons des épidémies récentes. (Alexandre Blake)

Participants :
- Matthew Ferrari, Pennsylvania State University
- Jean-Guy Vataux, MSF Centre Opérationnel Paris
- Sandra Cohuet, Epicentre Paris
- Benoît Kebela Ilunga, Ministère de la Santé, RDC

13h00 – Buffet sur place

14h30 – Session générale

Modérateur : Iza Ciglenecki, MSF Centre Opérationnel Genève

- Epidémie de syndrome dystonique en Ituri, RDC. (Florentina Rafael)
- Intoxication aiguë chez des enfants à Monrovia, Libéria. (Mohamad Haidar)
- Traitement des morsures de serpent dans les programmes MSF. (Matthew Coldiron)
- Séroprévalence d'Ebola à Monrovia, Libéria. (Sibylle Gerstl)

15h15 Pause café

15h30 - Urgences

Modérateur : Cristian Casademont, MSF Centre Opérationnel Barcelone

- Estimation de la mortalité parmi des populations déplacées au Sahel. (Brahima Touré)
- Utilisation des méthodes épidémiologiques dans l'estimation des besoins des migrants en France. (Malika Bouhenia)
- Développement d'une échelle d'évaluation en santé mentale: Etude de validation en Palestine et en Colombie. (Augusto Llosa)

16h15 - Nouveaux vaccins

Modérateur : Alejandro Cravioto, Precision Global Health

- Immunogénicité et tolérance d'un vaccin Ebola chez les travailleurs de première ligne. (Aboubacar Soumah)
- Efficacité et tolérance d'un vaccin contre le rotavirus. (Ousmane Guindo)

Intervenant invité : Jean-Marie Okwo-Bele, Organisation Mondiale de la Santé

17h30 - Pot de clôture sur place, 9ème étage Terrasse - Institut du Monde Arabe

Epicentre/Médecins Sans Frontières Scientific Day - Thursday 2 June 2016

8.45 – Welcome and coffee

9.30 – Introductory remarks – Emmanuel Baron

9.45 – HIV and Tuberculosis

Moderator: Fred Eboko, Institut de Recherche pour le Développement

- Diagnosing tuberculosis in a high HIV prevalence setting. (Helena Huerga)
- Virological failure, drug resistance and third-line regimen requirements among patients receiving second-line ART in 3 HIV-programs in Kenya, Malawi and Mozambique. (Birgit Schramm)
- Implementation of SAMBA: Routine Point-of-Care Semi-Quantitative HIV Viral Load: Outcomes from a decentralised HIV program in Malawi. (Elisabeth Poulet)

10.45 – Cholera

Moderator: Celestino Obua, Mbarara University of Science and Technology

- Innovative delivery strategies for oral cholera vaccine. (Francisco Luquero)
- Improving performance of cholera rapid diagnostic tests. (Anne-Laure Page)
- The use of doxycycline to prevent cholera. (Francesco Grandesso)

11.30 – Coffee break

12.00 – Round table discussion: Where are we with measles control in African hotspots ?

Moderator : Mercedes Tatay, MSF International

- Measles in DRC: Lessons from recent epidemics. (Alexandre Blake)

Participants:

- Matthew Ferrari – Pennsylvania State University
- Jean-Guy Vataux, MSF Operational Center Paris- Martin
- Sandra Cohuet, Epicentre Paris
- Benoît Kebela Ilunga, Ministry of Health, DRC

13.00 – Lunch on site

14.30 – General session

Moderator: Iza Ciglenecki, MSF - Operational Center Geneva

- Outbreak of dystonic syndrome in Ituri, DRC. (Florentina Rafael)
- Acute intoxication among children in Monrovia, Liberia. (Mohamad Haidar)
- Treatment of snakebites in MSF programs. (Matthew Coldiron)
- Seroprevalence of Ebola in Monrovia, Liberia. (Sibylle Gerstl)

15.15 – Coffee break

15.30 – Emergencies

Moderator: Cristian Casademont, MSF Operational Center Barcelona

- Estimating mortality among displaced populations in the Sahel. (Brahima Touré)
- Use of epidemiologic methods to estimate needs among migrants in France. (Malika Bouhenia)
- Developing an outcome scale for mental health: A validation study in Palestine and Colombia. (Augusto Llosa)

16.15 – New vaccines

Moderator: Alejandro Cravioto, Precision Global Health

- Immunogenicity and safety of an Ebola vaccine among frontline workers. (Aboubacar Soumah)
- Efficacy and safety of a rotavirus vaccine. (Ousmane Guindo)

Keynote speaker: Jean-Marie Okwo-Bele, World Health Organisation

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

Posters

1. Acceptability and utilization of a medium-quantity lipid-based nutrient supplement formulated for pregnant women in rural Niger. Sheila **Isanaka**

2. Childhood tuberculosis in Mbarara National Referral Hospital, Uganda – a description of patients and diagnosis. Elias **Kumbakumba**

3. Treatment outcomes and tolerability of the revised WHO antituberculous drug dosages among children living in high HIV prevalence settings? Margaret **Nansumba**

4. Description of the Viral Load cascade of ART patients using SAMBA, a Point-of-care Viral Load testing method in Chiradzulu district, Malawi. Sarala **Nicholas**

5. Performance of HIV diagnostic algorithms at 6 sites in 5 sub-Saharan African countries. Anne-Laure **Page**

6. Diagnostic accuracy of 8 HIV RDTs and 2 simple confirmatory assays on specimens from 5 sub-Saharan African countries. Anne-Laure **Page**

7. Evaluation of task-shifting SAMBA HIV Viral Load Point-of-Care testing to trained non-health workers in Malawi. Birgit **Schramm**

8. The Regional Anaesthesia for Painful Injuries after Disasters (RAPID) Study: a ran domized controlled trial protocol and analysis of training of Médecins Sans Frontières responders as trial proceduralists. Carrie **Teicher**

HIV and Tuberculosis

Diagnosing tuberculosis in a high HIV prevalence setting

Helena Huerga, Epicentre, Paris

Background

Diagnosis of tuberculosis (TB) remains a challenge in resource-limited countries. XpertMTB/RIF assay (Xpert) and Determine urine TB-LAM test (LAM), are currently available. We evaluated the incremental diagnostic yield of including Xpert and/or LAM test into the clinical-radiological algorithm to diagnose pulmonary TB (PTB) in a HIV prevalent setting.

Methods

Prospective observational study conducted in Homa Bay District Hospital, Kenya. The algorithm with Xpert was evaluated in smear-negative ambulatory patients with symptoms of PTB who received clinical exam, Xpert and chest X-ray. The algorithm with LAM test was evaluated in HIV-positive patients whether hospitalized, with CD4<200cell/µl, BMI<17Kg/m2 or severely ill. LAM test done prior to Xpert. The primary end point was TB treatment initiation and the reference standard was MTB culture (confirmed TB).

Results

In total, 487 smear-negative and 474 HIV-positive patients were included in the evaluation of the Xpert and LAM+Xpert algorithms respectively. Median age was 37 and 35 years, 59.3% and 51.5% were women.
Among 487 smear-negative, 67.1% (320/477) were HIV-positive. Xpert was positive in 11.8% (57/485), culture in 14.7% (69/467). Using the Xpert algorithm, 87.0% (95%CI:76.7-93.9) of confirmed TB patients were started on treatment, as compared to 55.0% (95%CI:41.6-67.9) with the clinical-radiological algorithm alone.
The proportion of culture-negative patients started on TB treatment did not change by adding Xpert (69.4% vs 71.3%,p=0.792).
Among 474 HIV-positive, LAM test was positive in 39.0% (185/474), Xpert in 31.5% (115/365), culture in 32.9% (105/319). Using the LAM algorithm, 80.0% (95%CI:71.1-87.2) of confirmed TB patients were started on treatment as compared to 55.2% (95%CI:45.2-65.0) with the clinical-radiological algorithm alone. Adding Xpert to LAM increased the proportion of confirmed TB cases started on treatment to 92%.

Conclusions

Including Xpert and LAM as initial tests was very useful to start adequately on TB treatment a large majority of patients with confirmed TB smear-negative and HIV-positive patients respectively. Urine LAM test was able to achieve high proportion of advanced HIV infected with confirmed TB started on treatment on the day of admission.

Xpert allows appropriate TB treatment in 90% of smear-negative patients. Urine LAM is useful in HIV-positive patients whether hospitalized, severely ill, with BMI<17 or CD4<200.

Virological failure, drug resistance and third-line regimen requirements among patients receiving second-line ART in 3 HIV-programs in Kenya, Malawi and Mozambique

Birgit Schramm, Epicentre, Paris

Background

The number of patients receiving second-line antiretroviral treatment (ART) is increasing in resource-limited settings. We assessed virological response and second-line drug-resistance in three HIV-programmes to evaluate patient outcomes and support forecasting of effective third-line drugs.

Methods

Between November 2014 and December 2015, patients aged ≥5 years receiving a standard second-line regimen for ≥6 months were recruited in three HIV outpatient-clinics supported by Médecins Sans Frontières in Kenya, Malawi and Mozambique. Viral load (VL) was quantified and resistance-genotyping performed if VL ≥500 HIV RNA copies/ml.

Results

Overall 802 patients were included (median age 41 years, 45% male). Kenya: among 355 participants 18% (65/355) had VL ≥500 copies/ml, 17% ≥1000 copies/ml. Among ≤19 years old, 31% (20/64) had ≥500 copies/ml. Twenty-five-percent of those with ≥500 copies/ml (16/65) had major PI-resistance, 72% major NRTI-resistance, 80% major NNRTI-resistance. Seventeen (26%) needed replacement of ineffective NRTIs, 20 (31%) required switching to a third-line regimen (major PI-resistance), including 3 children needing pediatric formulations. After six months on third-line 77% (10/13) had undetectable VL. Malawi: among 242 participants 17% had VL ≥500 copies/ml and 13% ≥1000 copies/ml. Among ≤19 years old, 29% (10/34) had VL ≥500 copies/ml. Genotyping indicated 3% major PI-resistance, 78% major NRTI-resistance, 84% major NNRTI-resistance. Seven patients required switching to third-line, 12 needed NRTI-replacement. Mozambique: among 205 participants, 28% had VL ≥500 copies/ml, 27% ≥1000 copies/ml. Among ≤19 years, 62% (10/16) had VL ≥500 copies/ml. Twenty patients need a third-line regimen.

Conclusions

Overall virological suppression was good among patients receiving second-line ART. Failure rates were notably higher among children and adolescents, highlighting the need for enhanced monitoring. Resistance data were essential to inform optimal regimen choice. Preliminary results indicate good short-term outcomes of patients on third line ART. Increased access to resistance genotyping and affordable salvage ARVs, including pediatric formulations, is needed.

The number of patients receiving second-line antiretroviral treatment is increasing in resource-limited settings. Better access to resistance genotyping and affordable salvage ARVs, including pediatric formulations, is urgently needed.

Implementation of SAMBA: Routine Point-of-Care Semi-Quantitative HIV Viral Load: Outcomes from a decentralised HIV program in Malawi

Elisabeth Poulet, Epicentre, Paris

Background

Viral load (VL) testing is key for timely provision of intensive adherence counselling or switching treatment regimen of suspect failures. From August 2013, Médecins sans frontières implemented gradually a semi-quantitative (1000 copies threshold) VL test with SAMBA-1, a nearly point-of-care (POC) system in 4 decentralised sites and 1 hospital of Chiradzulu district (Malawi). The protocol recommends 2 follow-up tests before changing ART regimen for those remaining with high VL.

Objective

The objective is to review the VL cascade and identify challenges with VL monitoring and specifically to describe the sequence of VL tests performed in the five sites between August 2013 and December 2015 amongst first line ART-patients.

Results

Over the study period, 13,675 patients had a VL test, among which 1,611 (12%) had a high VL. VL coverage ranged from 60 to 81% depending on timing of POC implementation. Among patients with high VL, 1,146 (71%) had follow-up tests.

Median time between tests was 3.2 months [IQR 2.8-4.6] and clinical review was same day for over 80% of tests in decentralised sites. Among the 1,146, 354 (31%) suppressed at 2nd test and 94 suppressed at 3rd test giving an overall suppression of 39% A total of 381 patients remained with high VL at 3rd test and 259 (68.0%) were switched to 2nd line regimen in a median time of 1.0 month [IQR 0-3]. Second VL test was missing for 465 patients and third one for 317. Among these, over 80% were still followed on 31/12/2015.

Conclusions

Good treatment adherence and VL coverage were observed. Use of POC VL demonstrated short turn-around time for clinical review. Follow-up remains a major challenge which can be addressed by active monitoring and evaluation of the VL cascade and increasing VL literacy amongst healthcare workers and PLHIV.

VL monitoring with POC device is feasible in decentralized setting. However VL follow up testing of suspect failures remains a challenge.

Cholera

Innovative delivery strategies for oral cholera vaccine

Francisco J. Luquero on behalf of the cholera vaccine effectiveness study group

Rapid use of oral cholera vaccines (OCV) have been shown to improve outbreak prevention and control. Heat-stability of OCVs and effectiveness of one dose provide additional opportunities to identify innovative delivery strategies. Here, we discuss additional delivery strategies and estimates of the effectiveness (VE) of one dose of Shanchol® when used in response to epidemics.

A single dose OCV Shanchol® was offered to all persons older than 1 year living in targeted areas or belonging to the identified high-risk groups in Juba, South Sudan and Lusaka, Zambia in response to outbreaks. To estimate short-term direct and total effectiveness of one-dose OCV, we conducted matched case-control and case-cohort studies respectively. We enrolled cholera case-subjects, matched control-individuals and a cohort comprised of a spatially representative sample of the population of Juba and Lusaka.

Estimates of the total vaccine protection from Juba are provided in this abstract and preliminary estimates of the direct vaccine protection from Lusaka will be discussed in the oral presentation. For the estimation of total VE we enrolled 34 cholera case-subjects and 898 cohort members in Juba. The unadjusted total single-dose VE was 79.5% (95% CI 59.9-100) and after adjusting for potential confounders, 89.6% (95%CI 75.3-100.0) in Juba study.

The high short-term effectiveness of Shanchol® increases possibilities to conduct timely outbreak response using OCV. This high effectiveness allows for the possibility of more flexible delivery strategies. Flexible dosing intervals combined with use of the vaccine in controlled temperature chain or even out of the cold chain will be critical to ensure that OCVs are offered to the most vulnerable.

High short-term effectiveness of one dose of oral cholera vaccine allows for innovative delivery strategies. Flexible dosing intervals combined with use of the vaccine in controlled temperature chain or even out of the cold chain can help ensure that OCVs are offered to the most vulnerable.

Improving performance of cholera rapid diagnostic tests

Anne-Laure Page on behalf of the Juba cholera vaccine effectiveness study group

Background

Despite the potential role of cholera rapid diagnostic tests (RDT) in outbreak detection and response, the poor diagnostic performance reported has led to mistrust of their results. There is currently no cholera RDT recommended by MSF. An enrichment step was proposed to improve specificity. We describe a prospective diagnostic evaluation of the Crystal VC RDT (Span Diagnostics, India) with or without enrichment step and culture compared to polymerase chain reaction (PCR) during a cholera outbreak in Juba, South Sudan.

Objective

RDTs were performed directly on stool and on alkaline peptone water inoculated with stools and incubated at ambient temperature for 4 to 6 hours. Cholera culture was performed from wet filter paper inoculated with stools. PCR was done from stool inoculated on dry Whatman 903 filter papers, and from wet filter paper supernatant.

Methods

In August and September 2015, 104 consecutive suspected cholera cases were enrolled. *Vibrio cholerae* O1 was detected by PCR in 38 (36.5%). When considering the O1 line only, the direct RDT had 94.7% (95% CI: 82.3-99.4) sensitivity and 80.0% (95% CI: 62.8-88.9) specificity. When including the O139 line as positive, the specificity of the direct RDT dropped to 69.2% (95% CI: 56.6-80.1). The enriched RDT had 84.2% (95% CI: 68.7-94.0) sensitivity and 100% (95% CI: 94.5-100) specificity. Culture on site had 81.6% (65.7-92.3) sensitivity and 98.5% (91.8-100) specificity compared to PCR.

Results

These results confirm the high sensitivity and moderate specificity of Crystal VC performed directly on stool. The addition of an enrichment step greatly improves specificity, while ensuring a sensitivity comparable to that of culture. Further evaluation of all reliable cholera RDTs available could lead to the identification of other simple options for cholera outbreak detection, including tests detecting only *V. cholerae* O1, which remains the sole serogroup causing cholera epidemics worldwide.

The addition of a simple enrichment step increased the performance of the cholera rapid test Crystal VC to a level similar to culture.

The use of doxycycline to prevent cholera

Francesco Grandesso, Epicentre, Paris

Background

In the ongoing cholera epidemic that began in Kenya in early 2015, national health authorities promoted the use of single-dose doxycycline as a preventive measure for all household members of cholera cases. In Nairobi, where more than 3000 cases were reported, doxycycline was not distributed uniformly to all households. We took advantage of this context to assess the association between single-dose doxycycline and the risk of developing diarrhoea among household members of cholera cases.

Methods

A cohort study was conducted retrospectively among households in which at least one laboratory confirmed cholera case was notified. Household members present for at least one day during the index cholera case illness were interviewed to assess whether they took doxycycline and whether they had diarrhoea in the following 11 days. Risk ratios (RR) were estimated using binomial logistic regression. Age, sex, place of residence, food habits, source of drinking water, hygiene habits, and socio-economic status were assessed as potential confounders in a multivariate analysis.

Results

A total of 403 household contacts reported having taken doxycycline; 471 had not. Nine contacts in the doxycycline group and 27 in the non-doxycycline group reported having had diarrhoea (RR 0.40, 95% CI 0.19 – 0.84), 7 and 12 sought for medical care (RR 0.70, 95% CI 0.29 – 1.76) and one and 4 had diarrhoea requiring intravenous rehydration (RR 0.29, 95% CI 0.03 – 2.59), respectively. After adjusting for the number of days spent with the index case and the use of soap for handwashing, the risk ratio was 0.32 (95% CI 0.13 – 0.71) for diarrhoea, 0.54 (95% CI 0.17 – 1.52) for diarrhoea requiring medical care and 0.28 (95% CI 0.01 – 1.88) for diarrhoea requiring intravenous rehydration.

Conclusion

Single-dose doxycycline was associated with a lower risk of developing diarrhoea immediately following the notification of the first case in a household. The somewhat attenuated risk reduction for diarrhoea requiring medical care might be explained by the fact that household members who received doxycycline were encouraged to seek care immediately if they had diarrhoea.

Since the participants were interviewed retrospectively, we were not able to confirm whether the diarrhoeal episodes of household contacts were actually cholera. Although diarrhoeal episodes requiring intravenous rehydration may be more specifically associated with cholera, the low number of cases reported did not allow us to draw a solid conclusion. This study, nevertheless, encourages continuing research on this preventive approach.

The use of a single dose of doxycycline may be effective in preventing cholera and other diarrhoeal diseases among household members of cholera case.

Round table

Where are we with measles control in African hotspots?

Moderator: Mercedes Tatay, MSF International

Participants:
- Matthew Ferrari, Pennsylvania State University
- Jean-Guy Vataux, MSF Operational Center Paris
- Sandra Cohuet, Epicentre Paris
- Benoît Kebela Ilunga, Ministry of Health, DRC

Notes

General session

Outbreak of dystonic syndrome in Ituri, DRC

Florentina Rafael, Epicentre, Paris

Background

An outbreak of a dystonic syndrome occurred from December 2014 to September 2015 in the contiguous Health Zones of Adja, Ariwara and Laybo (Democratic Republic of Congo). A total of 1029 persons reported acute dystonic reactions affecting the muscles of the face, eyes, neck, tongue, and/or upper limbs, some with Parkinsonism and oculogyric crises. Initial toxicological analyses revealed the presence of haloperidol in patients' urine, and initial investigations showed that tablets sold as diazepam at local pharmacies were found to contain haloperidol. We investigated the risk factors associated with this dystonic syndrome, and whether other molecules were involved.

Methods

A prospective case-control study was carried out from 26 June to 30 July 2015. Dystonic syndrome patients were enrolled at the MSF reference treatment centre for dystonic syndrome patients. Two healthy controls were matched to each case by age, sex and village of residence. Cases and controls were interviewed with a standardized questionnaire regarding their medication intake (names of drugs and description of colour, size and shape of tablets) and health seeking behaviour.
Urine samples were collected from all cases and a randomly selected sub-group of controls. If cases or controls had leftover medication, one tablet was collected for analysis. A sample of common medications was bought in local pharmacies. Toxicological analyses were carried by Toxipharm Laboratory (Garches, France). Matched odds ratios (OR) were estimated using conditional logistic regression.

Results

Thirty-six cases and 71 controls were enrolled (20 in control sub-group). Haloperidol was detected in the urine of all 36 cases and in 4/20 controls with samples (OR 16.5, 95% CI 2.1-120.6). Tablets described as "white-big-round", associated with paracetamol, and the tablets described as "yellow-small-round", associated to diazepam, were both strongly associated with the occurrence of the dystonic syndrome (OR 20.1 and 9.8, respectively). The analysis of medication collected from participants and bought in pharmacies, revealed the presence of haloperidol in tablets with the inscription "AGOG" and marketed as diazepam. Of 15 samples of paracetamol tested, haloperidol was not found in tablets.

Conclusion

This study confirms that the epidemic of the dystonic syndrome was caused by haloperidol. The only source detected in the three Health Zones was tablets of diazepam sold under the name of Agog Pharma.

A dystonic syndrome epidemic in a rural area of the Democratic Republic of Congo was due to the intoxication of haloperidol through the consumption of tablets sold as diazepam.

Acute Intoxication among Children in Monrovia, Liberia

Mohamad Haidar, Epicentre, Paris

Background

In July 2015 an increased admission of patients presenting multi-organ symptoms majorly involving liver was observed at MSF paediatric hospital in Monrovia. Patient history including paracetamol, herbal treatments and other conventional medicine suggested toxicity. The objective of the study is to identify the potential toxicant and describe its toxidrome.

Methods

A hospital-based matched case-control study included patients admitted between September 2015 and January 2016. A sample size of 30 cases and 60 asymptomatic matched controls (two hospital and two community controls for each case ideally) were needed to reach the desired power of 80%. Intoxication cases were identified as all children presenting respiratory distress, normal SPO2 and either hepatomegaly, hypoglycaemia or absence of fever. A case-series analysis was conducted including a line-listing of all suspected intoxication patients with two different organ symptoms between July and December 2015.

Results

The line-list included 77 patients with 60% being under the age of one year. 45% of the patients admitted died during hospitalization. Respiratory distress (94%), hepatomegaly (74%), high anion gap (67%), severe elevation in AST (50%) and ALT (43%) enzyme levels were the major signs present; highlighting hepatotoxicity.

We enrolled 30 cases, 53 hospital and 48 community controls in the case-control investigation. Significantly, altered consciousness, convulsions, and difficulty breathing were higher among cases than controls (60 vs.36% p-value: 0.001 & 48%vs.24% p-value: 0.001 & 77%vs.53% p-value: 0.004; respectively). In the multivariate analysis, paracetamol associated significantly with toxicity resulting an aOR=5.3 (95%CI: 1.6-17.3) for paracetamol supra-therapeutic doses, aOR=6.3 (95%CI: 1.8-21.9) for paracetamol dose>=500mg/day and aOR=32.5 (95%CI: 2.0-533.4) for paracetamol dose>=1000mg/day.

Conclusion

Research suggests paracetamol toxicity is a common cause of morbidity and mortality in developed countries. The strong association between paracetamol supra-therapeutic doses and toxicity highlight it as a public health issue in developing countries.

The investigation suggests that the majority of cases present an intrinsic hepatotoxicity with liver injury confirming paracetamol supra-therapeutic dosage to be the major potential toxicant.

Treatment of snakebites in MSF programs

Matthew Coldiron, Epicentre, Paris

Venomous snakes are widely distributed, but most snakebites occur in rural areas of the tropics. Although data are notoriously poor, in Africa, there are an estimated 1 million snakebites, 500 000 envenomings, and up to 30 000 deaths annually.

The venom of any single snake may contain more than 100 different toxins and enzymes, so the clinical result for victims can differ as well. Three major families of toxicities exist: local cytotoxicity (tissue necrosis), neurotoxicity (paralysis), and hematotoxicity (pro-coagulant and anti-coagulant).

Snakebite patients with evidence of envenoming should be promptly treated with antivenom. The choice of antivenom depends on the local epidemiology of snakebites and the availability of antivenoms. If given with minimal delay, antivenoms can drastically reduce mortality associated with snakebite, particularly for hematotoxic envenomings, which typically cause death many hours or days after the snakebite.

Antivenom production is onerous and has changed little since the 19th century. In brief, venom is harvested from snakes and small amounts are injected into a mammal (usually horses). After several months, the equine serum is collected and purified, and anti-venom specific antibodies are collected, and sometimes digested into fragments. Some commercially available antivenoms are species-specific, others are polyvalent.

FAV-Africa (Sanofi Pasteur) is a polyspecific antivenom which covers 10 different species of snake. It has been the primary antivenom used by MSF across Africa for many years. Its production ended in 2013, and the last doses produced expire in June 2016. Several new antivenoms have entered the market in recent years, but with insufficient data supporting their safety and efficacy. In several settings, MSF is facing challenges over the choice of antivenom (or antivenoms) to use to replace FAV-Africa. Epicentre is conducting studies in the Central African Republic and South Sudan to evaluate and document the use of new products.

Snakebite is a major health problem in rural Africa. Although there are several antivenoms available, there is insufficient data to support their safety and efficacy

Emergencies

Estimating mortality among displaced populations in the Sahel

Brahima Touré, Epicentre, Paris

Background

The intensification of Boko Haram attacks in the Sahel belt since 2014 have led to substantial displacements of the population in the area. In support of MSF's humanitarian assistance programs, population surveys were conducted in the town of Maiduguri (Nigeria) and in 5 locations in the Diffa region (Niger) to obtain mortality estimates over the course of 2015 among the host population, refugees, and returnees. In addition, the nutritional status and the measles vaccination coverage among children aged between 6 and 59 months were estimated.

Methods

A cross-sectional retrospective survey was performed in Maiduguri from June to July 2015 and from January to April 2016, including 21 414 individuals in Maiduguri and 51 081 individuals in the Diffa region (including the town of Diffa, Chetimari-Gagamari, Assaga, Yébi and Toumour), selected by random spatial sampling.

Results

In the town of Maiduguri, the crude mortality rate (CMR) was 0.30 deaths/10 000 persons/day [95%CI: 0.27 – 0.35] and 28.5% of the deaths were violence-related. The prevalence of severe acute malnutrition (SAM) was estimated at 1.3% [95%CI = 0.93 – 1.76].

In the Diffa region, the CMR varied from 0.30 deaths/10 000 persons/day [IC95%: 0.25 – 0.36] in Chetimari-Gagamari to 0.60 deaths/10 000 persons/day [IC95%: 0.53 – 0.68] in Yébi. Among the 841 recorded deaths in the Diffa region, 14.4% were violence-related; violence-related deaths varied from 10.1% in Assaga to 15.2% in Yébi.

The prevalence of SAM varied from 0.5% [95%CI = 0.22 – 1.0] in Yébi to 3% [IC95% = 2.3 – 3.9] in Toumour. Measles vaccination coverage confirmed by documentation was 11.7% in Toumour, 15.4% in Yébi, 42.4% in Diffa, 51.4% in Chetimari-Gagamari and 88.1% à Assaga.

These are the first crude mortality estimates available for the displaced populations in the region that is prone to Boko Haram attacks. The CMR and the prevalence of SAM observed were below the emergency and alert thresholds. However, the proportion of deaths caused by violence continue to be a matter of great concern in Maiduguri and the Diffa region.

Use of epidemiologic methods to estimate needs among migrants in France

Malika Bouhenia, Epicentre, Paris

Background

During 2015, >1 million refugees arrived in the European Union to seek asylum. At the end of 2015, in Calais, northern France, 30 km from the United Kingdom, around 6000 refugees were living in unsatisfactory conditions in an open camp called the “jungle” and trying to reach England. MSF began providing medical and psychological care in the “jungle” in September 2015. On their journey, refugees are exposed to diseases related to their living conditions and to violence in countries hostile to their reception. We aimed to determine the health status of refugees and the violence they have endured.

Methods

We conducted a cross-sectional population-based survey in Nov/Dec 2015; the study population included everyone residing in the “jungle”. We used spatial simple random sampling. We collected data on demographics, countries crossed, health status, violence, and life plans.

Results

425 (94.9%) of 462 residents approached participated. Overall, 95.0% were male, 33.3% were Sudanese, and median (IQR) age was 25 (21-30) years. Half of the participants were educated to secondary or tertiary level. Most had fled conflict in their country, with most having left in Sept 2015. The median (IQR) time taken to reach Calais was 100 (41-498) days. 61.0% reported having encountered a total of 331 health problems. Overall, 65.6% (95%CI 60.3-70.6) had experienced at least one violent event: 30.8% (95%CI 25.11-37.2) in Libya and 25.3% (95%CI 19.9-31.6) in Calais. 81.5% of refugees wanted to go to England, of whom 51.5% (95%CI 45.4-57.6) had a family member there.

Conclusion

Data from these analyses suggest that MSF should continue to be involved in medical care of refugees in Europe countries and could help to strengthen advocacy in countries where MSF is already involved.

This first quantitative survey of refugees in Europe shows that refugees, who mostly came from conflict areas, still had to cope with violence and problem of access to health in the countries they crossed and in France.

Developing an outcome scale for mental health: A validation study in Palestine and Colombia

Augusto Llosa, Epicentre, Paris

The Mental Health Outcomes Scale (MHOS) is under development as a multidimensional score, which takes the patient's perspective into account. When coupled with the therapist's assessment through the Clinical Global Impression (CGI) scale, MHOS could help evaluate interventions. Here we present results from validation studies in two contexts.

Thirteen adult and 14 children's items were identified across several languages and contexts through literature review, community focus and expert consensus groups. Each item, quantified on a five point scale for a 2-week recall period was scored by adding difficulties and subtracting coping items uniformly. MHOS was translated/back-translated from English and pilot tested in Cauca, Colombia and Hebron, occupied Palestinian territories. Reliability was assessed by re-interviewing the subject and close family member, convergent validity by comparison to clinical appraisal through CGI.

The studies enrolled 150 (Cauca) and 152 (Hebron) participants between December 2013 and August 2014. MHOS showed high internal consistency (α = 0.8), test-retest (ICC= 0.9 and 0.7) and inter-rater reliability (ICC = 0.7 and 0.8) in Cauca and Hebron respectively.

Correlation with function and symptom scores of CGI and the Symptom Rating Scale scores were lower, rs = 0.2-0.6 for both for adults and children in both contexts. Concordance between the two evaluation systems was modest to low (rs = 0.3 and 0.5 in Cauca; 0.5 and 0.3 Hebron, for children and adults, respectively) due to the great variability in MHOS scores among both CGI outcome groups.

When coded simply, the Spanish and Arabic versions of MHOS showed good repeatability and consistency across raters but limited concordance with therapist ratings. Comparison to other instruments and alternative scoring algorithms may result in convergence of findings, but it is also possible that therapists and patients may have somewhat differing constructs of well-being.

Development of outcome scales for mental health programs can help to improve their delivery as well as providing essential feedback to staff.

New vaccines

Efficacy and safety of a rotavirus vaccine

Ousmane Guindo for the ROSE study team

Prevention of rotavirus disease through vaccination is a public health priority. In 2009, the World Health Organization recommended rotavirus vaccination be introduced in all countries to reduce disease burden and mortality among young children.

Two live oral attenuated rotavirus vaccines are globally licensed and WHO prequalified for the prevention of rotavirus gastroenteritis. Safety and efficacy of these vaccines has been established in high- and middle-income countries, but vaccination in sub-Saharan Africa, where there is the largest burden of rotavirus-related mortality, presents certain logistical and financial challenges.

BRV-PV is a low-cost and heat-stable rotavirus vaccine manufactured by the Serum Institute of India, Limited whose introduction may help minimize the burden on already-strained national immunization programs throughout sub-Saharan Africa.

We conducted a double-blind, placebo-controlled randomized phase III event-driven trial in Niger to assess the efficacy and safety of BRV-PV against severe rotavirus gastroenteritis in infants in Niger. Infants were randomized in a 1:1 ratio to receive three doses of BRV-PRV or placebo at approximately 6, 10, and 14 weeks of age.

Cases of gastroenteritis and adverse events were captured through facility and home-based surveillance from 28 days post Dose 3 (gastroenteritis) and from the moment the first dose until 2 years of age. As an event-driven trial, the primary efficacy analysis is planned when 117 cases of severe rotavirus gastroenteritis. Vaccine efficacy against severe rotavirus gastroenteritis and risk of serious adverse events, including hospitalization, intussusception and death will be presented.

Evidence supporting the efficacy and safety of BRV-PV vaccine in an African setting would support the pre-qualification of and increased access to rotavirus vaccine across Africa.

Results of a phase III trial on the efficacy and safety of a low-cost, heat-stable oral rotavirus vaccine against severe rotavirus gastroenteritis are presented. Efficacy and safety results are presented.

Notes

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