

Integration of mass drug administration programmes in Nigeria: the challenge of schistosomiasis

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Problem Annual mass drug administration (MDA) with safe oral anthelmintic drugs (praziquantel, ivermectin and albendazole) is the strategy for control of onchocerciasis, lymphatic filariasis (LF) and schistosomiasis. District health officers seek to integrate treatment activities in areas of overlapping disease endemicity, but they are faced with having to merge different programmatic guidelines.

Approach We proceeded through the three stages of integrated MDA implementation: mapping the distribution of the three diseases at district level; tailoring district training and logistics based on the results of the mapping exercises; and implementing community-based annual health education and mass treatment where appropriate. During the process we identified the “know-do” gaps in the MDA guidelines for each disease that prevented successful integration of these programmes.

Local setting An integrated programme launched in 1999 in Plateau and Nasarawa States in central Nigeria, where all three diseases were known to occur.

Relevant changes Current guidelines allowed onchocerciasis and LF activities to be integrated, resulting in rapid mapping throughout the two states, and states-wide provision of over 9.3 million combined ivermectin–albendazole treatments for the two diseases between 2000 and 2004. In contrast, schistosomiasis activities could not be effectively integrated because of the more restrictive guidelines, resulting in less than half of the two states being mapped, and delivery of only 701 419 praziquantel treatments for schistosomiasis since 1999.

Lessons learned Integration of schistosomiasis into other MDA programmes would be helped by amended guidelines leading to simpler mapping, more liberal use of praziquantel and the ability to administer praziquantel simultaneously with ivermectin and albendazole.

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Background

Pablos-Mendez et al., in their October 2005 editorial in the *Bulletin* entitled: Knowledge translation in global health¹ argued that research must be part of a strategic process that moves evidence-based, cost-effective interventions to true practice. Barriers to the implementation of effective interventions lead to what the authors called the “know-do” gap. Research should help us to understand those barriers that prevent bringing what we know to the logical conclusion of action in the field and resultant better health or better health services. The Carter Center-assisted mass treatment programmes in Nigeria² provided an opportunity to demonstrate how differences in mass treatment guidelines and resources create a know-do gap presenting a barrier to the integration of programmes that should logically work together synergistically.

Community-based annual mass drug administration (MDA) with safe and effective oral drugs is the principal strategy for the control of onchocerciasis, lymphatic filariasis (LF) and schistosomiasis.³ Annual treatment with microfilaricide ivermectin (Mectizan, donated by Merck & Co., Inc.) prevents the severe eye and skin manifestations of onchocerciasis. Transmission of LF by mosquitoes can be interrupted in Africa by annual single-dose combination therapy with ivermectin (also donated by Merck & Co.) and albendazole (donated by GlaxoSmithKline).⁴ Schistosomiasis in Africa is usually caused by *Schistosoma mansoni* or *S. haematobium*. School-aged children are the most heavily infected, and the most frequent symptom of urinary schistosomiasis (infection with *S. haematobium*) is blood in the urine. Mass distribution of praziquantel can significantly reduce schistosomiasis morbidity.^{5,6} However, unlike ivermectin and

albendazole, praziquantel is not donated and costs approximately US\$ 0.20 per treatment.

Context of the translation of knowledge: is there a know-do gap in the integration of mass drug administration?

When the Global Alliance to Eliminate LF (GAELF) was launched in 1998, we noted the potential synergy and cost savings to be made in Nigeria from linking the LF activities to those being supported by the African Programme for Onchocerciasis Control (APOC).^{6,7} Both WHO initiatives were based on World Health Assembly-approved strategies of annual MDA and health education; both were working in many of the same countries; both had access to donated drugs; and both used ivermectin. This

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was an excellent opportunity to link the two multicountry WHO programmes in Nigeria. The approach taken was to launch the LF programme from within the mature APOC-supported programme. Albendazole tablets would be given concurrently with the ivermectin tablets already being delivered, together with additional health education.

But we hoped for more than the obvious linkage of onchocerciasis and LF. Efforts to control schistosomiasis were (and are) lagging behind the LF and onchocerciasis initiatives in Nigeria. The Schistosomiasis Control Initiative,⁴ another large regional initiative similar to APOC and GAELF, had not chosen Nigeria as a one of its programme countries. We wondered if linking the LF and onchocerciasis programmes with urinary schistosomiasis control could invigorate this MDA programme as well. A successful know-do programme with three drugs for three diseases in “triendemic areas” might show national and global decision-makers how they could expand integrated helminthic disease control to include schistosomiasis and therefore stimulate new thinking, new policy, new investments and partnerships, and perhaps even a donation of praziquantel.

Information collected

The large-scale integration project is a combined effort by the Federal Ministry of Health and The Carter Center and is situated in Plateau and Nasarawa States, an area which has an estimated population of 4 million inhabitants and comprises 30 administrative districts (local government areas (LGAs)), all of which were mapped for onchocerciasis in the early 1990s. Twelve districts were found to have meso-hyperendemic onchocerciasis (defined as a nodule prevalence of >20%) requiring ivermectin MDA. Full geographical coverage with ivermectin (about 800 000 treatments per year) was reached in 1993 and has since continued with financial support from APOC and the Lions Club’s SightFirst Program. The logistical system for the onchocerciasis MDA in those 12 LGAs served as the

launch point for the urinary schistosomiasis programme in 1999 and the LF programme in 2000. Working through the ministries of health of the state and the LGAs, the partners added each new MDA programme in three phases:

- mapping distribution of the diseases;
- tailoring training and treatment logistics based on results of the mapping; and
- implementing community-based annual health education and MDA where appropriate according to the WHO guidelines.⁶

The results of the LF and schistosomiasis mapping were the key to the decision-making and action plans of the LGAs. Because ivermectin and albendazole are donated, guidelines for the distribution of these medicines are “liberalized”, calling for blanket treatment within the LGAs; this made LF mapping relatively easy. Only one village per LGA (on average there are 100 per LGA) needed to be visited, and in total only 30 villages needed to be visited to completely map the two states for LF. A sample of 100 adult residents in each of the villages visited submitted to a finger-prick blood test that detected LF circulating antigen;⁸ guidelines called for MDA of the whole LGA when one of these 100 tests was positive (i.e. an LF antigen prevalence of $\geq 1\%$). All 30 villages sampled were found to be above this threshold, and LF mapping was completed by the end of 1999.

In contrast, as praziquantel is not donated, mapping guidelines for schistosomiasis are designed to be “restrictive” and “medicine sparing”. Decisions on schistosomiasis treatment are based on assessments at the individual village level. This required visiting over 3000 villages in the two states (100 times the number required by the LF programme). In these village-by-village assessments, the mobile teams use heme reagent dipsticks to test urine for blood in random samples of 30 children (aged 10–14 years) drawn from one randomly selected school. (Guidelines also allow

questionnaires to be used to ask children if they have blood in their urine — as a less expensive alternative for mapping — but in our pilot study of this questionnaire we found its sensitivity to be only 50% that of urine reagent dipsticks (Eigege, unpublished data).) Guidelines also require stratification of villages into three groups:

- those who do not qualify for praziquantel mass treatment (under 20% urine blood prevalence);
- mass treatment of school-aged children (20–49%); and
- community-wide treatment ($\geq 50\%$).

This complex operational treatment recommendation differed considerably from that of “treat or not treat”; used in the onchocerciasis and LF programmes. Lastly, praziquantel is not approved for combined treatment with ivermectin and albendazole. Thus, schistosomiasis treatment had to be temporally separated from MDA activities for the control of LF and onchocerciasis by at least one week.

Thirteen LGAs need MDA and health education for LF only; eight need integrated LF and onchocerciasis activities; five need integrated LF and schistosomiasis activities; and four need all three. All nine LGAs mapped so far for schistosomiasis have villages that were in all three mass praziquantel treatment schemes (not treat, treat school-aged or treat community-wide), and 21 LGAs have yet to be mapped for schistosomiasis.

Not surprisingly, a know-do gap has been identified as to how to link the programmes cost-effectively, and the schistosomiasis programme lags accordingly. Since 1999, distribution activities by community-based volunteers, working with support from ministry of health and Carter Center national staff, have reported only 701 419 praziquantel treatments for schistosomiasis (at a drug cost of over US\$ 100 000, including 150 000 donated tablets). In contrast, the same volunteers have successfully met the challenge of integrating the treatment of onchocerciasis and LF. Since 2000, they have reported a total of 3 731 465 ivermectin/albendazole combination treatments for LF alone, and 5 621 221 ivermectin/albendazole combination treatments for LF and onchocerciasis together (at no drug costs). All LGAs requiring MDA for LF and onchocerciasis are receiving treatment.

Box 1. Benefits of integrated MDA programmes

Community based, annual mass drug administration (MDA) provides an opportunity to improve the health of millions of potential beneficiaries who have the parasitic diseases onchocerciasis, lymphatic filariasis and schistosomiasis. Integrating the MDA programmes for these diseases would be feasible if schistosomiasis guidelines were simplified to be on a par with those for lymphatic filariasis and onchocerciasis.

Lessons learned and solutions proposed

We have learned the obvious lessons: similar things are easily combined and dissimilar things are not. It was easy to integrate MDA for LF with that for onchocerciasis, largely because one of the medicines used was the same for both diseases; both medicines are being donated; both can be given simultaneously; and LF spatial targeting is easily accomplished. The know–do gap resulted from the complexity of the guidelines for schistosomiasis control, and we found that as a result, working in areas where there is overlap of all three parasitic infections did not greatly enhance the opportunities for success of all three programmes. It is understandable that schistosomiasis MDA guidelines are “restricted” by the burden of the cost of praziquantel, while guidelines for onchocerciasis and LF are “liberated” because

the necessary drugs are donated (Box 1). The cost of praziquantel will continue to limit the extent to which schistosomiasis activities can be integrated into the larger MDA programme until there is a cheaper or donated source. This problem will not be easily solved. However, the requirement to temporally separate by at least one week praziquantel schistosomiasis treatments from LF and onchocerciasis MDA (due to concerns about drug interactions) has been resolved by a recent clinical trial in Thailand, which found no clinically relevant pharmacokinetic changes or adverse reactions when ivermectin, praziquantel and albendazole were given concurrently compared to when these drugs were given individually.⁹ This study paves the way to “triple therapy” by village volunteers, thereby potentially overcoming a constraint on multiple village treatment rounds that currently hinders the field practice of integrated treatment of onchocerciasis,

LF and schistosomiasis throughout large parts of Africa. ■

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Competing interests: none declared.

Résumé

Intégration des programmes de traitement de masse au Nigéria : le cas difficile de la schistosomiase

Problématique Le traitement annuel de masse au moyen d'anthelminthiques oraux sûrs (praziquantel, ivermectine et albendazole) est la stratégie de choix pour lutter contre l'onchocercose, la filariose lymphatique et la schistosomiase. Les responsables sanitaires de district s'efforcent d'intégrer les activités de traitement dans les zones d'endémie de plusieurs maladies, mais sont confrontés au problème d'avoir à concilier des recommandations programmatiques différentes.

Approche Nous avons suivi les trois étapes de l'intégration des programmes de traitement de masse : cartographie de la distribution des trois maladies au niveau des districts ; adaptation de la formation et de la logistique au niveau des districts en fonction des résultats des exercices de cartographie ; et mise en œuvre d'activités communautaires annuelles d'éducation pour la santé et de traitement de masse selon les besoins. Ce faisant, nous avons constaté, dans les recommandations de traitement concernant chaque maladie, des décalages entre la théorie et son application qui empêchent la bonne intégration de ces programmes.

Contexte local Un programme intégré lancé en 1999 dans les

Etats du Plateau et de Nasarawa dans le centre du Nigéria, où l'on sait que les trois maladies sévissent.

Changements pertinents Les recommandations actuelles ont permis d'intégrer les activités de lutte contre l'onchocercose et la filariose lymphatique, d'où des résultats cartographiques rapides pour ces deux Etats et par la distribution à l'échelle de ceux-ci de plus de 9,3 millions de traitements associés ivermectine-albendazole contre les deux maladies entre 2000 et 2004. En revanche, les activités de lutte contre la schistosomiase n'ont pu être efficacement intégrées en raison de recommandations plus restrictives, ce qui fait que moins de la moitié des deux Etats ont pu être cartographiés et que l'on n'a distribué que 701 419 traitements par le praziquantel depuis 1999.

Enseignements tirés L'intégration de la schistosomiase dans d'autres programmes de chimiothérapie de masse serait facilitée par un aménagement des recommandations qui permettrait de simplifier la cartographie, de généraliser l'utilisation du praziquantel et de pouvoir administrer celui-ci en même temps que l'ivermectine et l'albendazole.

Resumen

Integración de los programas de administración masiva de medicamentos en Nigeria: el reto de la esquistosomiasis

Problema La administración masiva anual de antihelmínticos orales seguros (praziquantel, ivermectina y albendazol) constituye la estrategia de control de la oncocercosis, la filiarisis linfática y la esquistosomiasis. Los funcionarios de salud de distrito procuran integrar las actividades de tratamiento en zonas de superposición de la endemidad de esas enfermedades, pero se encuentran con que tienen que conciliar distintas directrices programáticas.

Métodos Seguimos las tres etapas de aplicación integrada de la administración masiva de medicamentos (AMM): mapeo de la distribución de las tres enfermedades a nivel de distrito; planificación de la formación y la logística de distrito a partir de los resultados de los trabajos de mapeo; y aplicación de educación sanitaria y tratamiento masivo anuales basados en la comunidad en caso necesario. Durante el proceso identificamos las brechas «teórico-prácticas» de las directrices de AMM para

cada enfermedad que impedían una integración eficaz de esos programas.

Contexto local Un programa integrado lanzado en 1999 en los Estados de Plateau y Nasarawa en el centro de Nigeria, donde se sabía que se daban las tres enfermedades.

Cambios destacables Las directrices existentes permitieron integrar las actividades contra la oncocercosis y la filariasis linfática, lo que se tradujo en un rápido mapeo en los dos Estados, y en el suministro en el conjunto de esos territorios de más de 9,3 millones de tratamientos combinados de ivermectina-albendazol contra las dos enfermedades entre 2000 y 2004. Sin embargo,

las actividades contra la esquistosomiasis no pudieron integrarse eficazmente debido al carácter más restrictivo de las directrices, lo que se tradujo en un mapeo de menos de la mitad de los dos Estados, y el suministro de sólo 701 419 tratamientos de praziquantel contra la esquistosomiasis desde 1999.

Enseñanzas resultantes La integración de la esquistosomiasis en otros programas de AMM se vería facilitada si se modificaran las directrices para poder simplificar el mapeo, usar de forma más flexible el praziquantel, y administrar simultáneamente este producto junto con la ivermectina y el albendazol.

ملخص

إدماج برامج المعالجة الجموعية بالأدوية في نيجيريا: التحدي في داء البلهارسيات

التغيرات المتعلقة بالبحث: إن الدلائل الإرشادية المتاحة في الوقت الحاضر تسمح بدمج الأنشطة الخاصة بكل من داء كلابيات الذئب وداء الفيلاريات للمفمية، مما يؤدي إلى رسم سريع للخرائط في جميع أنحاء الولاياتين، مع تقديم ما يزيد على 9.3 مليون عبوة مزدوجة من الإيفرمكتين والألبندازول لمعالجة المرضين معاً وذلك في جميع أنحاء الولاياتين في الفترة بين عامي 2000 و2004. وبالمقابل لم يكن إدماج أنشطة معالجة داء البلهارسيات ممكناً بشكل فعال بسبب الدلائل الإرشادية الأكثر تقييداً والتي أدت إلى رسم الخرائط لما يقل عن نصف الولاياتين فقط، مع تقديم ما يقل عن 701 419 من عبوات البرازيكوانتيل لمكافحة داء البلهارسيات منذ عام 1999.

الدروس المستفادة: يمكن المساعدة في إدماج البلهارسيا ضمن برامج المعالجة الجموعية بالأدوية المضادة للديدان بتعديل الدلائل الإرشادية لتؤدي إلى رسم أبسط للخرائط، وحرية أكثر لاستخدام البرازيكوانتيل، وقدرة أكثر على إعطاء البرازيكوانتيل مع الإيفرمكتين والألبندازول معاً.

المشكلة: إن استراتيجية مكافحة داء كلابيات الذئب وداء الفيلاريات للمفمية وداء البلهارسيات تتمثل بالمعالجة الجموعية بالأدوية الفموية الآمنة المضادة للديدان (البرازيكوانتيل والإيفرمكتين والألبندازول). ويحاول الموظفون الصحيون في مستوى المنطقة إدماج أنشطة المعالجة في المناطق الموطونة بأدواء متعددة، إلا أنهم يواجهون بوجوب دمج دلائل إرشادية متعددة لعدة برامج معاً.

الأسلوب: أتبعنا ثلاث مراحل لتنفيذ إدماج المعالجة الجموعية بالأدوية، وهي: رسم خرائط لتوزع هذه الأمراض الثلاث على مستوى المناطق، وتصميم مواد تدريبية ولوجستية (إمدادية) بناءً على النتائج التي توصلنا إليها أثناء رسم الخرائط، وتنفيذ أنشطة التنقيف الصحي والمعالجة الجموعية المرتركة على المجتمع في الأماكن الملائمة. وقد كشفنا أثناء التنفيذ العملي الفجوة بين المعارف والعمل ضمن الدلائل الإرشادية للمعالجة الجموعية بالأدوية لكل مرض على حدة وهي الفجوة التي تمنع الإدماج الناجح لهذه البرامج.

الموقع المحلي: بدئ بالبرنامج في عام 1999 في ولايات بلاتو وناساراوا في وسط نيجيريا، حيث تنتشر هذه الأمراض الثلاثة معاً.

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