Evidence For Action on HIV treatment and care systems

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Case Study
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Tablets are more acceptable and give fewer problems than syrups among young HIV-infected children in resource-limited settings in the ARROW trial

Background & Summary

The provision of anti-retrovirals (ARVs) for children is complicated by syrup formulations, which have a number of important limitations. Children are often treated with partial adult tablets, which are crushed and given with food or liquid, a practice that can result in inaccurate dosing. Syrups are usually more expensive than tablets, harder to transport and store which makes confidentiality difficult to maintain; and difficult for carers to administer. Therefore, provided correct doses can be given, tablets are often more appropriate for children in resource-limited settings. The ARROW trial studied the acceptability of syrups and scored tablets (ARVs) as a sub-study among children substituting syrups with tablets.

ARROW (www.arrowtrial.org), which commenced in March 2007, is an ongoing 5 year open label randomised clinical trial in 1207 HIV infected children in Uganda and Zimbabwe, investigating monitoring practice and first line antiretroviral therapy strategies. This sub-study within ARROW highlighted that scored tablets compared to syrups can be used in young children with few problems, and also that most children and their carers prefer them. It identified that fewer difficulties were expected and much less experienced with the use of tablets. Furthermore, a pharmacokinetic study showed that these tablets (dosed according to WHO weight band tables) provided correct plasma drug levels for children.

Methods

Children were enrolled in Uganda / Zimbabwe during 2007/08. At enrolment, 406 (34%) children with a median age of 1.8 years (IQR 1.1, 2.5) received syrups of individual drugs (NNRTI + 2 of ZDV, ABC, 3TC), of whom 236 (58%) substituted scored tablets (also individual drugs) between May 2008 and December 2009 at a median age of 2.8 years (IQR 2.4,3.3). At substitution, baseline questionnaires administered to carers elicited their experience with syrups and expectations of tablets; eight weeks later follow-up questionnaires asked their experience with tablets.

Results

Questionnaires from 186 (79%) children changing formulation were analysed (exclusions: on tablets < 8 weeks n=17; missing forms n=33). Median age of children was 2.9 years (IQR 2.4, 3.4), and most carers dissolved/crushed the tablets in liquid. At baseline, 77% of carers reported problems with syrups, commonly related to the number, weight and transportation of bottles. Difficulties with tablets were expected by 53% of carers before switching from liquids however only 27% reported any problems after 8 weeks on tablets. Most frequently expected and experienced problems were taste, swallowing and vomiting. At baseline, 69% of carers expected to prefer tablets and 24% thought their child would. After 8 weeks, 93% of carers preferred tablets and 56% reported that their child did.

Conclusions

Carers anticipated fewer difficulties using tablets than syrups, and experienced even less. After eight weeks of use most children reportedly preferred tablets and none had switched back to syrups. These results show that scored tablets can be used in young children with few problems, and also that most children and their carers prefer them.

Box 1: Average number of bottles of syrups per child per visit versus average bottles of tablets per child per visit

Tablets are more acceptable and give fewer problems than syrups for young children

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HIV-infected children depend upon adults for their HIV-related care. It has been suggested that less amount of drug taken by children in terms of frequency and volume may improve adherence to ART. Anti HIV drugs can be given as syrups and tablets in children. Syrups are notably more expensive to make, store and transport. This may be even more difficult in a resource limited setting, for both the individuals involved in care who may experience fatigue; and the governments in terms of sustainability. For the children attending the ARROW trial clinics, carers have been seen carrying bigger bags to transport the syrups. These increase as the children get bigger. Although there are challenges in giving tablets, the tablets offered are smaller in size and are easily crushable. The amount of volume of water or other liquid used to dissolve them before swallowing does not compare with volume of syrup given. The syrup is more likely to spill, reducing the dose which results in poor adherence. With these findings one can advocate for tablets in a smaller child which is beneficial to both carer and clinician.

What is the potential impact of this?

The younger children in the ARROW trial are now able to safely use the scored tablets which are likely to improve adherence to their treatment. It has made transportation and administration of ARVs given by the primary carers easier. In addition, evaluating adherence to ARVs by counting returned drugs is much easier with tablets than liquids for health care workers.

The result of this sub-study was presented at the World AIDS Conference and International HIV paediatric workshop in Vienna in July 2010. The information from this sub-study should support development of solid based scored formulations by generic and innovator companies alike and should be noted by Drug Regulatory Authorities. As carers and children face far fewer difficulties with tablets, this will probably influence the future policy on age at which paediatric formulations such as tablets can be used in children.

The actual impact is to highlight that tablets are more acceptable and give fewer problems than syrups among young HIV-infected children in resource limited settings as shown within the ARROW trial. The potential impact is to help advocate for production of more tablet paediatric formulations for younger children especially by the pharmaceutical companies which are less expensive therefore making the drugs more available.

Who has been involved?

The ARROW trial is collaboration between:

- Medical Research Council/ Uganda Virus Research Institute, Entebbe, Uganda
- Joint Clinical Research Centre (JCRC), Kampala, Uganda
- Paediatric Infectious Diseases Clinic (PIDC), Kampala, Uganda
- University of Zimbabwe College of health sciences, Harare, Zimbabwe
- Medical Research Council Clinical Trials Unit (MRC CTU), UK
- GlaxoSmithKline (GSK)

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Evidence For Action on HIV treatment and care systems

About Evidence for Action

Evidence for Action is an international research consortium with partners in India, Malawi, Uganda, UK and Zambia, examining issues surrounding HIV treatment and care systems.

The research is organised in four key themes:

1. What "package" of HIV treatment and care services should be provided in different settings?
2. What delivery systems should be used in different contexts?
3. How best should HIV treatment and care be integrated into existing health and social systems?
4. How can new knowledge related to the first three questions be rapidly translated into improved policy and programming?

Partners:

International HIV/AIDS Alliance, UK

Lighthouse Trust, Malawi

London School of Hygiene and Tropical Medicine, UK

Medical Research Council Uganda Research Unit on AIDS, Uganda

Medical Research Council Clinical Trials Unit / University College London, UK

National AIDS Research Institute, India

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