Published in final edited form as:

Trans R Soc Trop Med Hyg. 2011 July ; 105(7): 361–363. doi:10.1016/j.trstmh.2011.04.003.

Cure rate is not a valid indicator for assessing drug efficacy and impact of preventive chemotherapy interventions against schistosomiasis and soil-transmitted helminthiasis

Antonio Montresor

Department of Control of Neglected Tropical Diseases, World Health Organization, 20 Avenue Appia, CH-1211 Geneva, Switzerland

Abstract

Every year, in endemic countries, several million individuals are given anthelmintic drugs in the context of preventive chemotherapy programmes for morbidity control of schistosomiasis and soil-transmitted helminthiasis. The capacity of accurately evaluating the efficacy of the drugs used as well as the health impact produced by treatment is of utmost importance for the appropriate planning and implementation of these interventions. The cure rate is an indicator of drug efficacy that was originally developed for assessing the clinical efficacy of antibiotics on selected bacterial diseases. Over time, this indicator has also been widely applied to anthelmintic drugs and consequently used to monitor and evaluate preventive chemotherapy interventions. In the author's opinion, however, measurement of cure rate provides information of limited usefulness in the context of helminth control programmes. The present article analyses the peculiarities of helminth infections and those of the drugs used in preventive chemotherapy, explaining the reasons why the cure rate is not an adequate indicator in this specific public health context.

Keywords

anthelmintic drug; schistosomiasis; soil-transmitted helminthiasis; cure rate; preventive chemotherapy

1 Introduction

Currently, most of the evaluations of anthelmintic drug efficacy on Soil Transmitted Helminth (STH)¹ and schistosomiasis² are based on the analysis of cure rate (CR) calculated as the percent of infected individuals at baseline that results free from infection after treatment. CR is an efficient indicator of drug efficacy against bacterial diseases and researchers in the field of helminthiasis adopted CR for analogy, however in my opinion, this indicator is less efficient for helminth infections.

Tel.: +41 22 791 3322; montresora@who.int.

Conflict of interests The author has no conflicts of interest concerning the work reported in this paper.

Ethical approval: Not required

2 Peculiarities of schistosomiasis and STH

The schistosomes and STH do not replicate in the human host, if few parasites survive treatment, they remain few. This is different from most of the other communicable diseases, in which, if few infectious agents survive treatment, they replicate, restoring the initial pathology.³

Another peculiarity is that morbidity associated with STH and schistosomes is proportional to the number of parasites. When several hundreds of parasites infect the host, morbidity is severe; a drastic reduction of the number of parasites results in an improvement in morbidity because the few surviving worms cause only minimal harm.³

A third characteristic is that, the numbers of worms per person are not distributed evenly: most individuals have infections of light or moderate intensity, while few harbor infections of high intensity.⁴

The main objective of PC against schistosomes and STH is therefore to eliminate the infections of moderate and heavy intensity, with the aim of preventing morbidity.³

3 Why the CR is not a valid indicator for assessing drug efficacy and impact of PC interventions

As consequence of the characteristics of schistosomes and STH and the peculiarities of PC detailed above, the author has identified the following reasons that limit the usefulness of CR as a tool to monitor drug efficacy as well as the impact of PC against these diseases.

3.1 CR is influenced by the intensity of infection at baseline

In endemic areas, some of the individuals with schistosomiasis or STH are infected by few worms and some with hundreds of worms. It is intuitively easier to cure an individual infected with few worms; therefore CR after treatment will result to be more satisfactory in areas where high-intensity infections are rarer.¹

It is therefore inappropriate to compare CR calculated in areas with different proportion of infections of high/low intensity: as an example albendazole results having a relatively low CR (45%) on hookworms when the mean pre-treatment infection intensity is high (1120 eggs per gram of faeces [epg]),⁵ or high CR (83%) when faecal egg count at baseline are lower (hookworms 174 epg).⁶

3.2 CR is influenced by the sensitivity of the parasitological method used to recover eggs from stool

The more sensitive is the parasitological method used to recover eggs in stool, the lower will be the CR.

The sensitivity of a parasitological technique is a function of the intensity of infection⁷ and of the intrinsic capacity of the technique to recover parasite eggs from specimens. The number of negative readings (and consequently the CR after treatment) is, by definition,

lower when a sensitive technique is used. The use of the Kato-Katz technique that, compared to other methods, lacks sensitivity at low intensity of infections⁸ will result in better CR.

3.3 CR cannot be considered as a proxy for "morbidity reduction", the objective of PC

The CR measures the number of infected individuals who are completely cured after treatment. For this reason, a drug that reduces by 90% the number of worms infecting a given individual, results in having the same CR (0%) of a completely inactive drug. However, while in the first case the effect on morbidity will be massive, in the second it will be irrelevant.

3.4 CR does not take into consideration that PC is applied periodically

The CR, measured by definition at a single point after treatment, makes no allowance for the long-term nature of PC, which also achieves cure of target individuals as a result of its periodical application.

The following two examples, one from Viet Nam and the other from Cambodia, refer to PC interventions conducted with drugs with a low CR, and show that reduction in prevalence of infection was in fact achieved after a number of rounds of PC:

Figure 1 presents the impact produced by the administration of albendazole on hookworm infections (CR = 59-81%)¹ to 52,000 women in Yen Bay Province, Viet Nam.⁹ The parasitological data were collected from a sample of 360 women. After the first round of PC the prevalence of hookworm infection passed from 75% to 60% (20% reduction or CR) while the prevalence of hookworm infections of high intensity passed from 15% to 2% (-87%). The second round produced a reduction of prevalence from 60% to 22% (64% reduction) and a complete elimination of infections of high intensity.

Figure 2 presents the effect of the annual distribution of praziquantel on schistosomiasis mekongi (CR = 60%)¹⁰ in a population of 80 000 individuals conducted for 10 years in Cambodia. The data were collected in a sample of over 1500 individuals. In this case, the number of infections has progressively been reduced until no infection was identified by survey in 2006.¹¹

4 Conclusions

In the author's opinion, the examples presented in this article show that the CR has a limited capacity to provide conclusive information on efficacy of anthelmintic drugs in different areas (because differences in the baseline situation influence the results) or with different laboratory techniques (because the CR results depend strongly on the sensitivity of the parasitological method used). In addition, the CR is not suitable to assess the impact produced by PC as it does not measure the main objective of such intervention (i.e. the reduction of morbidity consequent to a reduced intensity of infection). This opinion is confirmed by the excellent performances obtained by PC interventions with drugs for which the CR is considered low. For all these reasons, in the author's view, the role of CR in the context of helminth control programmes should be reconsidered.

Funding

None.

References

1. Keiser J, Utzinger J. Efficacy of current drugs against soil-transmitted helminth infections: systematic review and meta-analysis. *JAMA*. 2008; 299:1937–48. [PubMed: 18430913]
2. Saconato H, Atallah A. Interventions for treating schistosomiasis mansoni. *Cochrane Database Syst Rev*. 2000 CD000528.
3. Crompton, DW., Savioli, L. Handbook of helminthiasis for public health. Boca Raton, London, New York: 2006.
4. Anderson, RM., May, RM. Infectious diseases of humans Dynamics and control. Oxford University Press; Oxford, New York, London: 1991.
5. Flohr C, Tuyen LN, Lewis S, et al. Low efficacy of mebendazole against hookworm in Vietnam: two randomized controlled trials. *Am J Trop Med Hyg*. 2007; 76:732–6. [PubMed: 17426180]
6. Sacko M, De Clercq D, Behnke JM, Gilbert FS, Dorny P, Vercruysse J. Comparison of the efficacy of mebendazole, albendazole and pyrantel in treatment of human hookworm infections in the southern region of Mali, West Africa. *Trans R Soc Trop Med Hyg*. 1999; 93:195–203. [PubMed: 10450449]
7. Bergquist R, Johansen MV, Utzinger J. Diagnostic dilemmas in helminthology: what tools to use and when? *Trends Parasitol*. 2009; 25:151–6. [PubMed: 19269899]
8. Glinz D, Silue KD, Knopp S, Lohourignon LK, Yao KP, Steinmann P, et al. Comparing diagnostic accuracy of Kato-Katz, Koga agar plate, ether-concentration, and FLOTAC for *Schistosoma mansoni* and soil-transmitted helminths. *PLoS Negl Trop Dis*. 2010; 4:e754. [PubMed: 20651931]
9. Casey GJ, Phuc TQ, MacGregor L, Montresor A, Mihrshahi S, Thach TD, et al. A free weekly iron-folic acid supplementation and regular deworming program is associated with improved hemoglobin and iron status indicators in Vietnamese women. *BMC Public Health*. 2009; 9:261. [PubMed: 19630954]
10. Jordan, P., Webbe, G. Schistosomiasis Epidemiology, treatment and control. William Heinemann Medical Books; London: 1982.
11. Sinuon M, Tsuyuoka R, Socheat D, Odermatt P, Ohmae H, Matsuda H, et al. Control of *Schistosoma mekongi* in Cambodia: results of eight years of control activities in the two endemic provinces. *Trans R Soc Trop Med Hyg*. 2007; 101:34–9. [PubMed: 17028047]

Figure 1.

Reduction of total prevalence of hookworm infections and prevalence of infection light and high intensity during the one year implementation of a preventive chemotherapy campaign in Yen Bai Province, Vietnam.

Figure 2.
Reduction of prevalence of *Schistosoma mekongi* infections during the preventive chemotherapy campaign conducted for 10 years in Stung Treng and Kratie provinces, Cambodia.