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Application of optimal control to the onchocerciasis transmission model with treatment

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ABSTRACT

In this paper, we present a model for onchocerciasis that considers mass administration of ivermectin, contact prevention controls and vector elimination. The model equilibria are computed and stability analysis carried out in terms of the basic reproduction number R_0. The model is found to exhibit a backward bifurcation so that for R_0 less than unity is not sufficient to eradicate the disease from the population and the need is to lower R_0 to below a certain threshold, R_0^c for effective disease control. The model is fitted to data on individuals with onchocerciasis in Ghana. A sensitivity analysis reveals that the parameters with the most control over the epidemic are the vector death rate and the effective contact rates between susceptible individuals and infected vector and susceptible vector with infected individuals. This suggests that programs aimed controlling vector will be significantly more effective in combating the disease. Optimal control theory is applied to investigate optimal control strategies for controlling onchocerciasis using insect repellent and both insecticide and larvicide as system control variables. We use Pontryagin's Maximum Principle to show the necessary conditions for the optimal control of onchocerciasis. Numerical simulations of the model show that restricted and proper use of control measures might considerably decrease the number of infections in the human population.

1. Introduction

Onchocerciasis is a vector-borne parasitic disease. This is a human disease caused by the filirial (thread like) worms *Onchocerca volvulus* in human hosts and is transmitted by the *Simulium damnosum* [1]. It occurs close to oxygen rich flowing streams and rivers in the inter-tropical zones [2]. This is because the egg, larvae and pupa stages of *Simulium damnosum* are aquatic. Studies show that about 90% of onchocerciasis cases occur in Africa and is predominantly found in West Africa. It is also found in six countries in Latin America and in Yemen in the Arabian Peninsula [3]. Onchocerciasis is a serious public health problem. It is a major constraint to social and economic development [4,5]. It is responsible for ugly skin disease with depigmentation, severe unrelenting itching and blindness [6,7].

In Sub-Sahara Africa, onchocerciasis remains a major health challenge. In Ghana for instance, 3,400,000 in 3204 communities in 66 endemic districts are at risk of acquiring onchocerciasis [8]. Many strategies have been used to eradicate this disease from the population. Mass administration of ivermectin has remained the main strategy in the fight against onchocerciasis. In Sub-Sahara Africa, the struggle to combat onchocerciasis is being led by the African Program of Onchocerciasis Control (APOC). The main control measure for the eradication of onchocerciasis in the countries where the disease is endemic such as Ghana is through community directed treatment with ivermectin. The drugs are distributed by Mectizan™ Donation Program (MDP) by Merck and Co., Inc., [9]. Ivermectin is an antimicrofilarial agent that acts as both the primary and secondary form of prevention for individuals with onchocerciasis. It degenerates intrauterine microfilariae thereby suppressing the release of new microfilariae for up to 3–4 months. However, when the drug wanes the adult worm is still possible to continue producing microfilariae until it dies naturally [10]. Ivermectin shows no or, if any, little macrofilaricidal effects and therefore does not kill the adult worms [11]. For successful control of onchocerciasis, repeated treatment with ivermectin spanning for 10–15 years has to be administered so as to correspond to the life span of adult worm.

One of the purposes of modelling epidemics is to provide a rational basis for policies designed to control the spread of a disease. The inclusion of practical optimal strategies in models allow for the assessment of the intervention of public health authorities. Optimal control is a powerful mathematical tool in decision making that involves

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employing appropriate strategies to eradicate epidemics from the population [12]. The decisions include determining the proportion of the population that should be treated as time evolves in a given epidemic to minimize both the number of infections in the population and the cost of the treatment strategy implementation. Optimal control has been used to study the dynamics of some diseases such as malaria and West Nile virus [13–15]. For instance, in [16,17] optimal control was used to investigate the best strategy for educational campaigns during the outbreak of an epidemic and at the same time minimizing the number of infected humans. It has also been applied in modelling Leukemia [18,19]. However, to the author's best knowledge, optimal control has not been applied to onchocerciasis disease transmission.

In this paper, we develop a mathematical model for onchocerciasis disease transmission with control strategies. The aim is to gain some insights into the best intervention for minimizing and eventual elimination of onchocerciasis from the population. The intervention strategies we incorporate into the model are, personal protection against black-fly, enhanced treatment and insecticide spraying. Three control functions are used, one for vector reduction, one for human protection and another for the reduction of microfilarie in the body following treatment with ivermectin. We characterize the optimal control problem analytically by applying Pontryagin Maximum Principle. We analyse the model analytically and numerically to find out the threshold conditions under which it is optimal to eradicate the disease from the population.

This paper, is organised as follows; in Section 2 we give the formulation of the model and the underlying assumptions. In Section 3 analysis of the model with constant control parameters is provided as well as sensitivity analysis. The optimal control strategies are analysed in Section 4 and numerical simulation results presented in Section 5. Finally, we present the discussion and concluding remarks in Section 6.

2. Mathematical model

2.1. Model formulation

We consider a habitat with two interacting populations. The two populations are humans (as hosts) and the black–flies (as vectors). The total human population is partitioned into six compartments: the susceptible human compartment; S_H, referring to individuals not infected with onchocerciasis but are at risk of infection, the exposed compartment; E_H, referring to the individuals that have been exposed to onchocerciaisis through bites but not infectious, the infectious compartment; I_H, referring to individuals with onchocerciaisis infection, the susceptible human on ivermectin treatment compartment; S_T, the exposed human on ivermectin treatment compartment; E_T, and the infectious human on ivermectin treatment compartment; I_T. The black–fly population is partitioned into three compartments: susceptible vector; S_V, referring to black–flies that have never been in contact with infected human and have not picked up microfilariae but are at risk of picking up microfilariae during blood meal from an infected human, the exposed vector compartment; E_V, referring to vector that has picked up microfilariae from an infective human during blood meal but does not transmit the infection and the infective vector compartment; I_V, referring to the vector with the infective L3 larvae stage.

Individuals and the vector move from one compartment to another as their disease status evolve. The total human and vector populations at any given time, t, are respectively given by;

$$N = S_H(t) + E_H(t) + I_H(t) + S_T(t) + E_T(t) + I_T(t) \text{ and } V = S_V(t) + E_V(t) + I_V(t). \quad (1)$$

We assume that the transmission of onchocerciaisis in susceptible hosts is only through contact with infectious vector. We also assume that susceptible vector becomes infectious as a result of contact with infectious hosts during blood meal. The population under study is assumed to be large enough to be modelled deterministically. The constant recruitments of new susceptible human and susceptible vector are given by b_1 and b_2 respectively. Assuming β is the black–fly biting rate, that is, the average number of bites per black–fly per unit, the rate of infection per susceptible black-fly can be represented by

$$\lambda_v(t) = \frac{q\beta(I_H + \kappa I_T)}{N}, \quad (2)$$

where q is the transmission probability from infectious human to black-flies and κ is the modification parameter which measures the relative ability of individuals in class I_T to cause new infections relative to those in compartment I_H. We assume here that the individuals under treatment have a slightly lower probability to initiate new infections, thus, $0 \le \kappa \le 1$. Assuming that the total number of bites made by black-flies equals to the number of bites received by humans, then the average number of bites per human per unit time is $\frac{\beta V}{N}$. Assuming that the transmission probability per bite from infectious black-flies to human is p, the rate of infection per susceptible human is given by

$$\lambda_h(t) = \frac{p\beta V}{N}\frac{I_V}{V} = \frac{p\beta I_V}{N}. \quad (3)$$

We then introduce $\beta_h = p\beta$ and $\beta_v = q\beta$ parameters to simplify the infection rates per susceptible human and vector respectively. The individuals in class E_H progress to the infectious class I_H at the rate γ. Individuals on ivermectin treatment in class S_T acquire infection at the rate $\delta\lambda_h$. Here, $\delta \in [0, 1]$, defines the reduced effect of infection of the susceptible individuals on ivermectin as a result of treatment. Individuals in class E_T progress to infectious class on ivermectin I_T at the rate $\rho\gamma$, where $\rho \in [0, 1]$ is the reduced effect of progression to class I_T as a result of treatment. The uptake rate of the mass administration of ivermectin for individuals in class S_H, E_H and I_H are given by α_1, α_2 and α_3 respectively. We assume relapse due to waning of the drug at the rate φ_1, φ_2 and φ_3 for individuals in class S_H, E_H and I_H respectively. We also assume natural mortality rates given by μ_h and μ_v for the human and vector populations respectively.

We then include vector control strategies. Personal protection efforts through wearing insect repellents such as N,N-Diethyl-meta-toluamide (DEET) on exposed skin, wearing long sleeves and long pants during the day when black-flies bite, and wearing permethrin-treated clothing minimizes or eliminates black-fly-human contacts [20]. Insecticide spraying with larvicide and adulticide ensures that the breeding sites of the black-flies are minimized. We thus define some linear control functions $u_i(t)$ such that $u_i(t) = 1$, $i = 1, 2, 3$. It is important to note that controls are fully effective when $u_i(t) = 1$ and not effective control when $u_i(t) = 0$. The forces of infection λ_h and λ_v corresponding to human population and vector population respectively are reduced by factor $(1 - u_1)$, where $u_1(t)$ measures the level of successful exposure prevention efforts. The control $u_1(t)$ represents the use of alternative prevention measures to minimize or eliminate the black-fly-human contacts. Such measures include the use of insect repellents, wearing protective coats and long sleeves and wearing permethrin-treated clothing amongst other. The mass administration of ivermectin as a control is modelled by u_2. The factor u_2 can be viewed as the coverage of ivermectin, i.e, the percentage of individuals in which the treatment with ivermectin is effective. The factor $u_3(t)$, represents the level of insecticide use for the elimination of black–flies from the breeding sites u_3. This implies that the reproduction rate of the black–fly population is reduced by a factor of $(1 - u_3(t))$. We assume that, insecticide spraying increases the mortality rate of the black-flies at a rate proportional to the control factor $u_3(t)$. It is further assumed that the per capita mortality rate of the vector is $r_0u_3(t)$, where $0 \le r_0 \le 1$ is the proportion of effective insecticide spraying.

2.2. Model assumptions

(i) There is a constant recruitment to the susceptible human