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Full Length Research Paper

Some new results on affinity hemodialysis and T cell recovery

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We provide criteria under which affinity hemodialysis could provide a stable infected equilibrium.

Key words: Affinity hemodialysis, HIV/AIDS envelope protein, stability criteria.

INTRODUCTION

Important studies on HIV/ AIDS include papers of Hazenberge (2000), Duffin and Tullis (2002), Tullis (2004), Tullis et al (2002ab, 2003), Oluyo (2007), Oluyo and Ayeni (2007), Stafford et al (200) and Wang and Li (2006). The hallmark of HIV disease is the gradual loss of CD4+ T cells, which ultimately leaves the immune system unable to defend opportunistic infections. Recent studies Hazenberge (2000) and Tullis (2004) suggest that CD4 + T cells are lost through infection and binding of gp 120 to uninfected CD4 + T cells. The envelope ultimately leads to the death of healthy cells. On the other hand, hemodialysis assists infected T cells to recover. The present study investigates the criteria under which the rate of recovery of infected cells through hemodialysis could lead to the stability of the equilibrium point.

MATHEMATICAL MODEL

We modify the model of Duffin and Tulis (2002) by incorporating recovery through affinity hemodialysis:

Production

$S \xrightarrow{\pi} T$ rate of T-cell production from stem cells.

$T + V \xrightarrow{k_1} T_i$ infection of T cells

$P + T \xleftrightarrow{k_3} PT$ reversible gp 24 binding to normal T-Cells

T_i + hemodialysis $\xrightarrow{\mu} T$ recovery of some T infected cells as a result of hemodialysis

Clearance

$T \xrightarrow{d_1} d_2$ death of normal T cell

$T_i \xrightarrow{} $ death of infected T cells

$V \xrightarrow{c} $ viral clearance rate,

Where T_i is infected T cell, V is virus and P is concentration of gp120.

Arising from above, the relevant mathematical equations are:

$$\frac{dT}{dt} = \pi - d_1 T - k_1 TV + \mu T_i \quad , \quad T(0) = T_0$$

$$\frac{dT_i}{dt} = k_1 TV - d_2 T_i - \mu T_i \quad , \quad T_i(0) = 0$$

$$\frac{dV}{dt} = k_2 T_i - cV \quad , \quad V(0) = 0$$

STABILITY OF THE CRITICAL POINTS

To obtain the critical points, we set In infected free equilibrium

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$$\frac{dT}{dt} = \frac{dT_i}{dt} = \frac{dV}{dt} = 0$$

$$V = T_i = 0$$

So $\pi - d_1 T = 0$ *and* $T = \pi / d_1$

To obtain the infected equilibrium, we obtain

$$0 = k_2 T_i - cV \quad V = \frac{k_2 T_i}{c}$$

Also $0 = k_1 TV - d_2 T_i - \mu T_i$ *and* Substituting for V, we obtain

$$k_1 T \frac{k_2 T_i}{c} - (d_2 + \mu) T_1 = 0$$

$$i.e \quad \frac{k_1 k_2 T}{c} - (d_2 + \mu) T_1 = 0$$

$$T_i \neq 0 \quad T = \frac{(d_2 + \mu) c}{k_1 k_2}$$

Substituting for T and V in

$$0 = \pi - d_1 T - k_2 TV + \mu T_i$$

gives T_i and subsequently V.

So, the un-infected equilibrium is $\pi / d_1, 0, 0$ and the infected equilibrium is

$$\frac{\mu + d_2}{k_1 k_2} c, \frac{\pi}{d_2} - \frac{d_1 (d_2 + \mu) c}{d_2 k_1 k_2}, \frac{k_2}{c} \frac{\pi}{d_2} - \frac{d_1 (d_2 + \mu) c}{d_2 k_1 k_2}$$

Theorem 1

If $\pi / d_1 \neq (\mu + d_2) c / k_1 k_2$ there exist two equilibria.

Let us denote this infected equilibrium by (T_*, T_{i*}, V_*) where each component corresponds to an earlier specified value. We let

$$x = T - T_*, \quad y = T_i - T_{i*}, z = V - V_*$$

Then

$$\frac{dx}{dt} = -(d_1 + k_1 V_*) x + \mu y - k_1$$

$$T_* z \frac{dy}{dt} = k_1 V_* x - (d_2 + \mu) y +$$

$$k_1 T_* z \frac{dz}{dt} = k_2 y - cz$$

Thus

$$\begin{pmatrix} x' \\ y' \\ z' \end{pmatrix} = A \begin{pmatrix} x \\ y \\ z \end{pmatrix}$$

Where;

$$A = \begin{pmatrix} -(d_1 + k_1 V_{*1}) & \mu & -k_1 T_* \\ k_1 V_* & -(d_2 + \mu) & k_1 T_* \\ 0 & k_2 & -c \end{pmatrix}$$

Thus

$$|A - \lambda I| = 0$$

Implies

$$p(\lambda) = \lambda^3 + \lambda^2 (\mu + d_1 + k_1 V_* + c + d_2)$$

$$+ \lambda (c k_1 V_* + d_1 d_2 + d_2 k_1 V_* + \mu k_1 V_*) \qquad 3.1$$

$$+ d_1 d_2 c + k_1 V_* d_2 c + c \mu k_1 V_* = 0$$

Theorem 2

Equation (3.1) has no positive root.

Table 1. Description of variables and constants.

Terms	Description	Values
π	Rate of production of T cells	dT_0/day
d_1	Natural death rate of healthy T cells	0.01/day
k_1	Viral infection rate (CD4+Tcells)	0.00027/virus day
μ	Infected T cell recovery rate	μ/day
d_2	Death rate of infected T cells	0.39/day
k_2	Viral production for T cell	850/day
c	Clearance rate of the virus	3/day
S	Stem cell	
T	Uninfected activated CD4+T cell	
T_i	Infected CD4+T cells	
V	Virus produced by T cells and macrophages	
PConcentration of pg 120		

Theorem 3

Equation (3.1) has three negative roots or one negative root and two complex roots.

Theorem 4

The infected equilibrium is globally asymptotically stable.

Routh – Hurwitz criteria (Wang and Li, 2006). All zeros of $\lambda^3 + \alpha\lambda^2 + \beta\lambda + \gamma = 0$ have negative real parts if and only if $\alpha\beta - \gamma > 0$.

Therefore, all zeros of (3.1) have negative real parts if and only if

$$(\mu + d_1 + k_1 V_* + c + d_2)(ck_1V_* + d_1d_2 + d_2k_1V_* + \mu k_1V_*) - (d_1 d_2 c + k_1V_* d_2c + c\,\mu\, k_1 V_*) > 0$$

That is,

$$(d_1 + k_1V_* + d_2)(ck_1V_* + d_1d_2 + d_2k_1V_* + \mu k_1V_*) + \mu(d_1 d_2 + d_2k_1V_* + \mu k_1 V_*) + c(ck_1 V_* + \mu k_1 V_*) > 0$$

Proof of theorems

Clearly all coefficients and the constants of $p(\lambda)$ are positive. The proof of the theorems 2 to 4 involved using the Descartes rule of signs: The number of positive zeros of a polynomial with real coefficients is either equal to the number of variations in sign of the polynomial or is less than this by an even number.Table 1

Proof of theorem 1

The infection – freeequilibrium isgiven by

$$\pi / d_1, 0, 0, \text{ if } \quad T_i \neq 0,\ V \neq 0,$$

then $T = (\mu + d_2)c / k_1k_2$. Hence the other equilibrium is

$$\frac{(\mu + d_2)}{k_1 k_2}^{c}, \frac{\pi}{d_1} - d_1 \frac{(d_2 + \mu)}{d_1 k_2 k_1}^{c}, \frac{k_2}{c}\frac{\pi}{d_2} - \frac{d_1(d_2 + \mu)}{d_2 k_1 k_2}$$

Proof of theorem 2

The number of variations in sign is zero. Hence by Descartes' rule of signs the polynomial equation has no positive root.

Proof of theorem 3

From p(λ) in (3.1), we obtain

$$p(-\lambda) = \lambda^3 - \lambda^2(\mu + d_1 + k_1V_* + c + d_2) + \lambda(ck_1V_* + d_1d_2 + d_2k_1V_* + \mu k_1V_*) - (d_1d_2c + k_1V_* d_2c) + c\mu k_1V_*) = 0$$

So the number of changes in sign is 3. Hence by Descartes' rule of signs, p(λ) has either three negative roots or one negative root and two complex roots.

Proof of theorem 4

Since all the parameters are positive, the inequality holds.
By theorem 3 and Routh – Hurwitz criteria (3.1) has;

(i) Either three negative roots or
(ii) One negative root and two complex roots whose real parts are equal and negative. So in either case the equilibrium is globally asymptotically stable.

RESULT AND DISCUSSION

The main purpose of this paper is to verify, beyond earlier papers, the effect of affinity hemodialysis on HIV/AIDS as a potential treatment option for HIV patients resistant to drugs. A key factor in this analysis is μ. When μ is zero, the possibility of a quasi-steady infected equilibrium does not exist. Thus a stable infected equilibrium does not arise. This paper shows, further, that affinity hemodialysis is a potentially useful adjunctive therapy which can be employed to treat HIV-infected patients either directly or in conjunction with drug therapy (Tullis, 2004)

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