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Management Sciences for Health

Comparison of Available Antimalarials for treatment of P. *falcipirum*

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P. *falciparum* Antimalarial Drug Comparison

Areas examined

- WHO Standard Treatment Guidelines
- Availability of ACT manufacturers
- Efficacy of Currently available medications
- Cost
- Selection pressure/Fitness Cost of parasite resistance

Treatment for Uncomplicated P. *falciparum*

WHO Standard Treatment Guidelines (2006)

- Artemisinin Combination Therapies (ACT's) are the recommended treatments for uncomplicated P. falcipirum.
- The choice of ACT in a country should be based on the level of resistance of the partner medicine in the combination
- Artemisinin and its derivatives should not be used as mono-therapies for treatment of uncomplicated P. *falciparum* malaria
- Second line malarial treatment.

WHO. 2010. Guidelines for the treatment of Malaria- Second edition

Treatment of Uncomplicated P. *falciparum*

Other WHO guidelines

- ACT's should not be produced singly for uncomplicated P. *falciparum* malaria[1].

- Countries should procure and distribute ACT's in packaging designed to help patients adhere to standard treatment and rational medicine use. Fixed dose combinations are preferred[1].

2.

1. WHO. 2010. Good Procurement Practices for Artemisinin-based Antimalarial Medicines
2. Biomed Central. http://www.biomedcentral.com/1472-6963/8/119/figure/F2. Accessed 3/16/2011

Treatment for P. *falciparum*

WHO recommended treatments

- Artemether- Lumefantrine (AT + LA)
- Artesunate + Mefloquine (AS+MQ)
- Artesunate + sufadoxina-pirimetamina (AS + SP)
- Artesunato- amodiaquine (AS-AQ)
- Dihydorartemisinina-piperaquine (DHA-PPQ)

Currently three of the recommended combinations are used as first line or second line treatments for P. *falciparum* in the Amazon Basin.

  - AT + LA, AS + MQ, AS + SP

WHO. 2010. Guidelines for the treatment of Malaria- Second edition

ACT Pharmaceutical Manufacturers

INN	Formulationa and Strength	# of currently approved providers	WHO pre-qualified	Stringent NDRA registration/ Expert Review panel
Artemether + Lumefantrine (Co-formulated)	20 mg + 120 mg	4	X[1]	
Artesunate + Amodiaquine (Co formulated/Co-packaged)		4	X[1]	
Artesunate	50 mg	2*	X[1]	
Artesunate+ Mefloquina (Co-blistered)	200mg + 250mg	1		X [2]
Artesunato + SP	50 mg + [500mg + 25mg]	1		X [2]
Mefloquina	250 mg	1		X [2]
Sulfadoxine/ Pyrimethamine	500 mg + 25 mg	1		X [2]
Chloroquine Phosphate	150 mg	2		X [2]
Primaquina	15 mg	1		X [2]

*Ningun fabricante contesto el pido de ser proveedor.
Fuente:
1. http://apps.who.int/prequal/query/ProductRegistry.aspx
2. http://www.theglobalfund.org/documents/psm/List_MALARIA.pdf

Artesunate suppliers

- OPS could not find a pharmaceutical company willing to supply AS for the latest OPS order.

- OMS recommended in 2006 that Artemisinin mono-therapies should be removed from the market due to the fear of P. *falcipirum* developing resistance

2010. Global Report on Antimalarial Drug Efficacy and Drug Resistance.

Efficacy of Antimalarial Medications on P. *falciparum* Parasites.

- WHO recommends periodic efficacy studies to assess in vivo response of P. *falciparum* to treatments.

- Assessed by therapeutic efficacy study- gold standard
  - Tx of symptomatic patients infected only with p.f. with a standard dose of an antimalarial drug and subsequent follow-up of parasitaemia and clinical signs over a defined period (28 or 42 days).

- If treatment failure is ≥ 10%, the NMCP should initiate a change to the country treatment policy .

2010. Global Report on Antimalarial Drug Efficacy and Drug Resistance

Efficacy of Anti-malarial Medications against P. *falciparum*

Artemether- Lumefantrine					
Country	Study Years	Number of Studies	Median % of treatment failure	Minimum % of treatment failure	Maximum % of treatment failure
Brazil	2005-2007	2	0.0	0.0	0.0
Ecuador	2005-2006	1	0.0	0.0	0.0
Guyana	2004-2008	2	1.6	0.0	3.2
Suriname	2003-2006	3	2.0	1.9	4.7
Venezuela	2004-2005	1	0.0	0.0	0.0

All numbers are expressed as a percentage of treatment failures after a minimum of 28 days.
WHO. 2010. Global Report on Antimalarial Drug Efficacy and Resistance: 2000- 2010.

Efficacy of Anti-malarial Medications against P. *falciparum*

Artesunate- Mefloquine					
Country	Study Years	Number of Studies	Median % of treatment failure	Minimum % of treatment failure	Maximum % of treatment failure
Brazil	2005-2007	3	0.0	0.0	0.0
Colombia	2007-2008	1	0.0	0.0	0.0
Guyana	2004-2005	1	1.2	1.2	1.2
Perú	2003-2006	3	0.0	0.0	0.0
Suriname	2002-2003	2	4.1	2.4	5.8
Venezuela	2004-2005	1	0.0	0.0	0.0

All numbers are expressed as a percentage of treatment failures after a minimum of 28 days.
WHO. 2010. Global Report on Antimalarial Drug Efficacy and Resistance: 2000- 2010.

Efficacy of Anti-malarial Medications against P. *falciparum*

Artesunate- Sulfadoxine- Pirimethamine					
Country	Study Years	Number of Studies	Median % of treatment failure	Minimum % of treatment failure	Maximum % of treatment failure
Colombia	2001-2006	2	8.3	5.7	10.8
Ecuador	2004	1	0.0	0.0	0.0
Perú	2001	1	1.1	1.1	1.1

All numbers are expressed as a percentage of treatment failures after a minimum of 28 days.
WHO. 2010. Global Report on Antimalarial Drug Efficacy and Resistance: 2000- 2010.

Efficacy of Common ACT Pairs

- SP- Median Treatment failure- Medium
  - 2% to 10.7%
- Mefloquine- Median Treatment Failure- Low
  - 2.4% to 7.3%
- Amodiaquine- Median treatment failure High
  - was 28.8% to 53.1%

All numbers are expressed as a percentage of treatment failures after a minimum of 28 days.
WHO. 2010. Global Report on Antimalarial Drug Efficacy and Resistance: 2000- 2010.

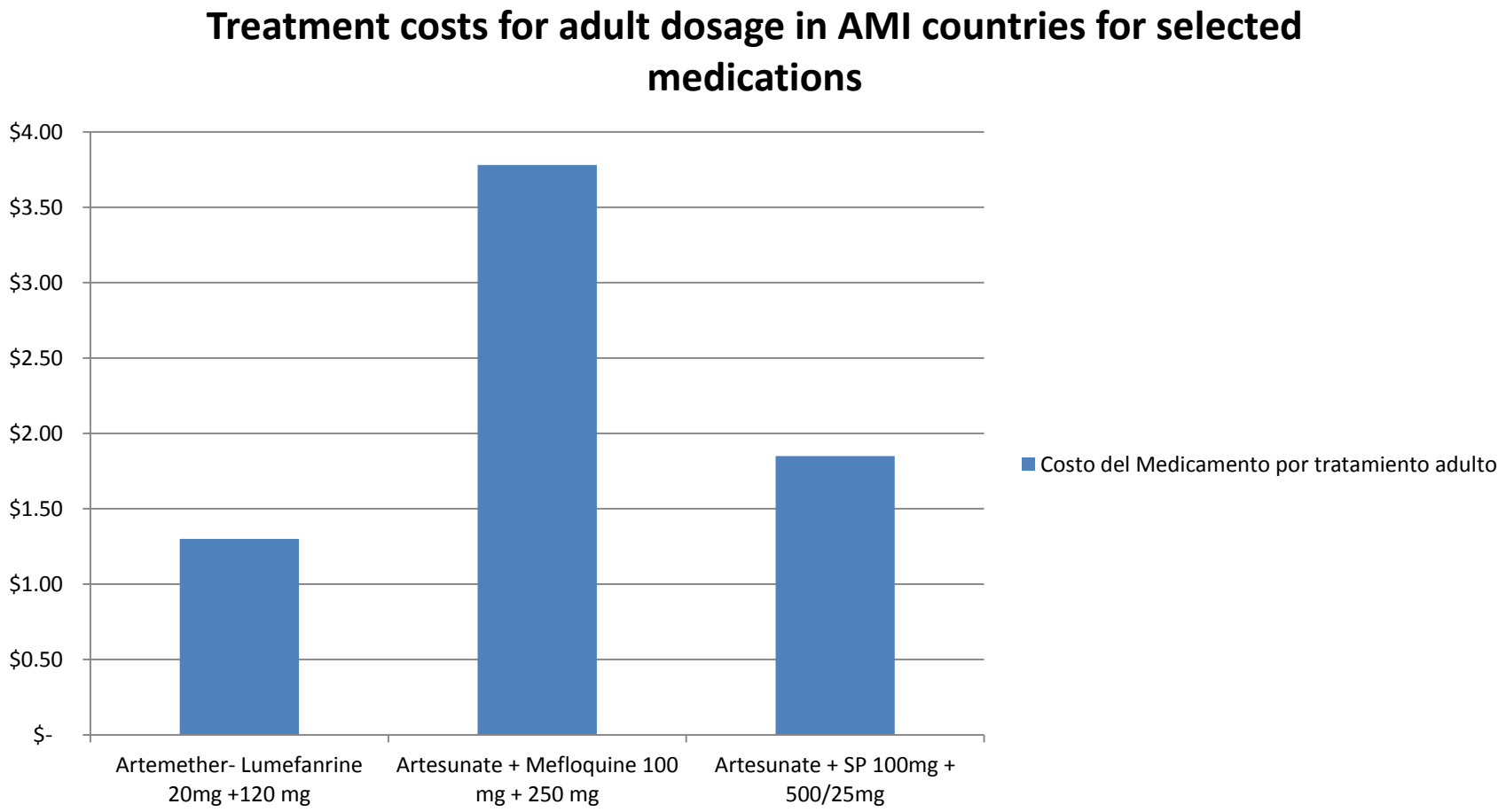
Cost of Different Malaria Treatments

Tabla 1: El Costo de Diferentes Tratamiento de un caso de malaria por los adultos.

Drug	Strength	Dosage	P. falcipirum	
			Prices offered to PAHO	Drug Indicator Guide (MSH)
Artemether- Lumefantrine (AL)	20mg +120mg	24 tabs [b]	$ 1.30[d]	$ 1.37 [f]
Artesunate- Amodiaquine (AS + AQ)	50mg + 153 mg	12 tabs [b]		$ 0.93 [f]
Artesunate [a]+ Mefloquina (AS + MQ)	100mg + 250 mg	6 tabs Artesunate + 6 tabs Mefloquina [b]		$ 3.78 [f]
Artesunate [a]+ Sulfadoxine-Pyramethamine (SP)	100mg + 500/25mg	6 tabs artesunate + 3 tabs SP [b]	$ 1.85 [e]	$ 1.07 [f]
Dihidroartemisinina-Piperaquine (DHA-PPQ)	40mg + 320mg	9 tabs[b]		$ 6.66 [f]
Cloroquina (CQ)	150mg tab	10 tabs [c]	$ 0.93 [d]	$ 0.19 [f]

a - PAHO solicited bids in Oct. 2010 for these medications and did not receive any offers.
b- WHO good procurement procedures for ACT's
c- Drugs.com
d- Offers obtained by PAHO during the solicitation from Oct. 2010
e- Prices paid by PAHO in 2010
f- Prices are from Management Sciences for Health 's International Drug Price Indicator Guide

Cost of Antimalarial Treatments in South America



Selection pressure and Fitness Cost

Selection Pressure-

1. It is most affected by:
   A. Poor drug quality
   B. Poor adherence
   C. Incorrect dosage
   D. Incorrect medication.
2. No conclusive data to determine if cycling medications is beneficial.

Okeke, et.al., 2005. Antimicrobial resistance in developing countries. Part II: strategies for containment. The Lancet.

Questions?

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