

Passive Human African Trypanosomiasis in Children in Brazzaville from 2004-2020

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ABSTRACT

Objective: To determine the prevalence of Human African Trypanosomiasis (HAT) in children in Congo-Brazzaville and to look for associated factors.

Patients and Methods: Retrospective descriptive and analytical study of cases of HAT in children in Congo between January 1, 2004 and December 31, 2020, i.e. 17 years.

Results: Out of a total of 3238 people screened as passive, 335 were children and 89 were confirmed sick, i.e. 2.7% of the Total Population Examined (PTE). The mean age was 9.8 ± 5.2 years (10 days-17 years), female (n=48; 53.9%) with a sex ratio of 0.8, from the Ngabé household (n=54; 60.7%), educated (n=44; 49.4%). The most frequently encountered symptoms were fever (n=46; 51.7%), sleep disturbances (n=46; 51.7%) and headache (n=21; 23.6%). CATT was positive in all patients and diluted to 1/32 in 50 cases (56.2%). Lymph node puncture was positive in 49 patients (55.1%) and trypanosomes were isolated from the CTC and the LCS in 28.1% and 41.6%, respectively. The mean cell count in the LCS was 163.9 ± 227.2 (1-1128) and patients were classified as stage 2 in 68 cases (76.4%). DFMO was used in 46 patients (51.7%) and pentamidine in 21 patients (23.6%). The outcome was marked by healing in 77 cases (86.5%). In 7 patients (7.9%), there was a death due to arsenical encephalopathy in 4 cases (57.1%). The female sex (p=0.03), the combination DFMO+Arsobal (p= 0.006) were associated with relapse, while age <5 years (p=0.004) was associated with death.

Conclusion: the prevalence of HAT in Congolese children as well as the lethality was high during the study period. Female sex, Age <5 years remains a poor prognostic factor, as does the combined use of DFMO+Arsobal.

Keywords: Trypanosomiasis; Child; Prevalence; Congo

INTRODUCTION

Human African Trypanosomiasis (HAT), also called sleeping sickness, is a neglected tropical disease about to be eliminated as a public health problem in Africa [1]. It has long afflicted adult rural populations engaged in fishing, farming and hunting. Congo is an endemic country for HAT and five departments continue to report cases periodically. Children residing in endemic areas where they have stayed, regardless of the length of time, are as exposed to the risk like adults.

Goals

Describe the epidemiological, clinical, diagnostic, therapeutic and evolutionary aspects of HAT cases in patients aged 5 days to 17 years.

PATIENTS AND METHODS

This was a retrospective descriptive and analytical study of HAT cases in Congo between January 1, 2004 and December 31, 2020, i.e. 17 years.

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It included patients aged 17 years or less whose diagnosis of HAT had been made according to the algorithm of the national HAT control program, screened only as passive and whose parents had given free and informed consent in order to participate in the study.

Study variables

Epidemiological (age, sex, place of residence, profession), clinics (reason for consultation, signs of examination, stage of the disease), paraclinical (whole blood CATT, dilution CATT, PG, CTC, LCS analysis), therapeutic (type of treatment) and progressive (cure, relapse, death, causes of death).

Data analysis

The data were processed using EPI info 3.3.2 software with the determination of descriptive and analytical statistics for all patients. For all tests, the significance level was set at 5%.

RESULTS

Out of a total of 3238 people screened in liabilities, 89 were children confirmed to be sick, or 2.7% of cases. The mean age was 9.8 ± 5.2 years (10 days-17 years), female (n=48; 53.9%) and male (n=41; 46.1%). -ratio was 0.8. The patients were mainly from the homes of Ngabé (n=54; 60.7%), Mossaka (n=9; 10.1%), and Mpouya (n=6; 6.7%) and educated (n=44; 49.4%). Child fishermen represented 6.7%. There was a peak in cases in 2007 and 2008 (Figure 1). The most frequently encountered symptoms were fever (n=46; 51.7%), sleep disturbances (n=46; 51.7%) as well as headaches (n=21; 23.6%) (Table 1). CATT was positive in all patients and diluted to 1/32 in 50 cases (56.2%). Lymph node puncture was positive in 49 patients (55.1%) and trypanosomes were isolated from the CTC and the LCS in 28.1% and 41.6%, respectively. The mean cell count in the LCS was 163.9 ± 227.2 (1-1128) and patients were classified as stage 2 in 68 cases (76.4%) and stage 1 in 21 cases (23.6%). DFMO (Eflornithine) was used as monotherapy in 46 patients (51.7%), combined with arsobal in 2 patients (2.2%). Pentamidine was used in 21 patients (23.6%). The outcome shows the healing in 77 cases (86.5%), relapse in 5 cases (5.6%). In 7 patients (7.9%) there was a death due to arsenical encephalopathy in 4 cases (57.1%). The female sex (p=0.03), the combination DFMO +Arsobal (p = 0.006) were associated with relapse, while age <5 years (p=0.004) was associated with death (Tables 2 and 3).

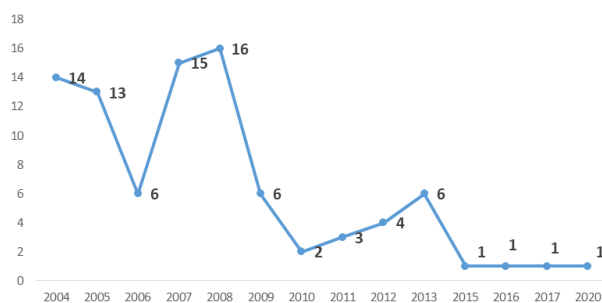


Figure 1: Evolution of passive THA cases de from 2004 to 2020.

Signs	Number(n)	Percentage (%)
Sleeping troubles	46	51.7
Fever	46	51.7
Headache	21	23.6
Weight loss	16	18
Itching	11	12.4
Psychomotor agitations	8	9
Asthenia	8	9
Tremor	3	3.4
Logorrhea	2	2.2
Convulsion	2	2.2

Table 1: Distribution of patients according to clinical signs.

Variables	Evolution		OR	IC95%	P-Value
	Relapse	Healed			
	n(%)	n(%)			
Age range					
<5years	2(40.0)	14(16.7)	3.3	0.5-21.8	0.1
5-9 years	1(20.0)	25(29.8)	0.5	0,06-5,5	0.6
10-14 years	0(0.0)	21(25.0)			0.2
≥ 15 years	2(40.0)	23(28.6)	1.7	0.2-11.2	0.5
Sex					
Male	0(0.0)	41(48.8)			0.03
Female	5(100.0)	43(51.2)			0.03
Signs					
Headache	2(40.0)	19(22.6)	2.2	0.3-14.6	0.3
Asthénia	0(0.0)	8(9.5)			0.4
Fever	1(20.0)	45(53.6)	0.2	0.02-2.02	0.1
Lymphad enopathy	0(0.0)	1(1.2)			0.8
Sleeping troubles	2(40.0)	44(52.4)	0.6	0.09-3.9	0.5

Psychomotor agitations	1(20.0)	7(8.3)	2.7	0.2-28.09	0.3
CATT Dilution					
1/8e	0(0.0)	1(1.2)			0.8
1/16e	1(20.0)	37(44.0)	0.3	0.03-2.9	0.2
1/32e	4(80.0)	46(54.8)	3.3	0.3-30.8	0.2
PG					
Presence of trypanosomes	2(40.0)	47(56.0)	0.5	0.08-3.3	0.4
Absence of trypanosomes	3(60.0)	37(44.0)	1.9	0.3-12.0	0.4
CTC					
Presence of trypanosomes	1(20.0)	24(30.4)	0.6	0.06-5.8	0.6
Absence of trypanosomes	4(80.0)	60(71.4)	1.6	0.1-15.05	0.6
Macroscopy					
Clair hypertensive	0(0.0)	19(46.3)			0.1
Clair normotense	2(100.0)	22(53.7)			0.1
LCS mycology du					
Presence of trypanosomes	2(40,0)	35(41,7)	0,9	0,1-5,8	0,9
Absence of trypanosomes	3(60.0)	49(58.3)	1.07	0.1-6.7	0.9

Phase of the disease					
P1	0(0.0)	21(25.0)			0.2
P2	5(100.0)	63(75.0)			0.2
Protocol					
Pentamidine	0(0.0)	21(25.0)			0.2
DFMO	2(40.0)	44(52.4)	0.6	0.09-3.8	0.5
DFMO+ Arsobal	1(20.0)	1(1.2)	20.7	1.08-395.5	0.006
Arsobal	2(40.0)	8(9.5)	6.3	0.9-43.7	0.03

Table 2: Factors associated to relapse.

Variables	Evolution		OR	IC 95%	P-Value
	Death n(%)	Healed n(%)			
Age range					
<5years	4(57.1)	12(14.6)	7.7	1.5-39.1	0.004
5-9 years	1(14.3)	25(30.5)	0.3	0.04-3.3	0.3
10-14 years	0(0.0)	21(25.6)			0.1
≥ 15 years	2(28.6)	24(29.3)	0.9	0.1-5.3	0.9
Sex					
Male	3(42.9)	38(46.3)	0.8	0.1-4.1	0.8
Female	4(57.1)	44(53.7)	1.1	0.2-5.4	0.8
Signs					
Headache	2(28.6)	19(23.2)	1.3	0.2-7.3	0.7
Asthenia	1(14.3)	7(8.5)	1.7	0.1-17.01	0.6
Fever	3(42.9)	43(52.4)	0.6	0.1-3.2	0.6
Lymphadenopathy	0(0.0)	1(1.2)			0.7
Sleeping troubles	5(71.4)	41(50.0)	2.5	0.4-13.6	0.2
Psychomotor agitations	0(0.0)	8(9.8)			0.3

Parasitology					
Presence of trypanosomes	4(57.1)	33(40.2)	1.9	0.4-9.4	0.3
Absence of trypanosomes	3(42.9)	49(59.8)	0.5	0.1-2.4	0.3
Phase					
P1	1(14.3)	20(24.4)	0.5	0.05-4.5	0.5
P2	6(85.7)	62(75.6)	1.9	0.2-17.05	0.5
Protocol					
Pentamidine	0(0.0)	21(25.0)			0.1
DFMO	6(85.7)	40(48.8)	6.3	0.7-54.6	0.06
DFMO+ Arsobal	0(0.0)	2(2.4)			0.6
Arsobal	1(14.3)	9(11.0)	1.3	0.1-12.5	0.7

Table 3: Factors associated to death.

DISCUSSION

Human African trypanosomiasis, also known as "sleeping sickness", is a parasitic infection that is almost always fatal if left untreated. However, thanks to sustained and coordinated efforts over the past 25 years, the number of reported cases is lower than ever (<1000 in 2018) [1]. It is a neglected tropical disease currently in the process of being eliminated as a public health problem with a significant drop in cases in both adults and children residing in endemic areas in Figure 1.

The overall prevalence of HAT in children remains high and concentrated in households that continue to report cases. These are very often children accompanying parents during hunting or fishing activities as notified in the DRC, the most endemic country [2]. For children in general, the rate is generally less than half of that observed in adults, which is explained by less exposure to flies during daily activities [3]. The distribution by sex depends on the behaviour and activities that are carried out in a particular epidemiological context. In areas of transitional vegetation in forest and wooded savannah, where infection is linked to agricultural work or activities around water points, the prevalence is similar in both sexes with a slight female predominance as in our study [3,4]. The predominance of cases originating from Ngabé is explained by the fact that this focus is closer to a large active focus in the DRC, thus facilitating cross-border movements. We also note that the infection mainly strikes in remote rural communities where the health

infrastructure is rudimentary and it is possible that a number of cases are neither recognized nor notified [5]. Neurological signs and symptoms, and in particular sleep disturbances, are characteristics of the second phase as reported in the present study. However, most symptoms of the two phases are interwoven, making it difficult to distinguish between the two phases based solely on the clinical picture. Febrile episodes are more intense and more frequent during the first phase than during the second phase [6]. Somnographic studies conducted in Congo by Buguet and Damba show that the disease disrupts the circadian rhythm of the sleep-wake cycle and causes sleep fragmentation rather than the often described inversion [7]. Our study found the rarity of lymphadenopathy in small children than in adults. Indeed, the presence of trypanosomes in the cervical lymph nodes is less common in preschool children than in older children and adults [8].

The diagnosis of trypanosomiasis is facilitated by serological tests, but parasitological proof must always be made [9]. CATT performed on dilutions of plasma or serum is more specific than CATT for blood and is often used before parasitological examination because it allows having fewer false positives as was the case in our study. Trypanosomes were seen after examination of lymph node juice in older children in 55.1%. Due to its simplicity and low cost, this technique is widely used with a sensitivity of around 59% (43%-77%) [10]. However, other examinations such as the mini-column due to its validity would have allowed to isolate the trypanosomes if it had been carried out as notified in the DRC [11].

Phase diagnosis, that is, determining the stage of the disease is necessary to complete the diagnosis of HAT and is crucial in determining the correct treatment. More than half of the children were seen at the stage of brain polarization. More infants are seen in the second phase of the disease, most likely due to late diagnosis (the second phase occurs after 300 to 500 days in the case of Tb gambiense HAT) and the immaturity of the blood brain barrier [12, 13]. During the study period, treatment for the Gambian form of HAT relied on four drugs (eflornithine, melarsoprol, nifurtimox and pentamidine). Second or third-line alternatives, namely melarsoprol or eflornithine as monotherapy were only rarely used. On melarsoprol, encephalopathic syndrome was still observed in 5% to 10% of patients treated with melarsoprol with a fatal outcome in 10% to 50% of those who developed encephalopathy, and in some foci cases increasingly refractory to the disease were noted melarsoprol [14,15]. In 7 patients (7.9%), death due to arsenical encephalopathy, was noted in 4 cases (57.1%), and 5.6% relapse. Relapses are often due either to insufficient doses of molecules used, or to errors in the phase diagnosis, as was the case in a 16-year-old adolescent in Congo [16]. Female sex ($P=0.03$), the association DFMO+Arsobal ($p=0.006$) were associated with relapse, while age <5 years ($p=0.004$) was associated with death. In most patients, melarsoprol clears the parasites from the blood and lymph within 24 hours. However, in several foci in Angola, the Democratic Republic of the Congo, southern Sudan and Uganda, the rate of treatment failure can be up to 30% in treated subjects with a fatal outcome in 10% to 70% of them [16-18].

CONCLUSION

Human African trypanosomiasis in children remains an epidemiological reality in Congo with a high prevalence. Children from Ngabé are the most affected and pay the heaviest price with arsenical drugs. The advent of Fexinidazole could have a positive impact on reducing HAT-related mortality in pediatric settings.

CONFLICT OF INTEREST

The authors report that they have no conflict of interest with this study.

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