

Pharmacotherapeutics of Cancer Chemotherapy: Study of the Treatment Management of Burkitt's Lymphoma in the Pediatric Oncology Unit at the University Hospital of Treichville, Abidjan - Côte d'Ivoire

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Abstract

Burkitt's lymphoma is the most common childhood cancer in sub-Saharan Africa. Its management involves cytotoxic drugs. The aim of this study was to study the pharmacotherapeutics of cancer chemotherapy during the treatment of Burkitt's lymphoma at the Pediatric Oncology Unit of the University Hospital of Treichville, Abidjan. This was a retrospective cross-sectional descriptive study of 46 cases of patients with Burkitt's lymphoma from January 2011 to December 2015.

Concerning medical treatment, patients went through chemotherapy following the Cyclo Burkitt protocol of the Franco-African Group of Pediatric Oncology. The adequacy between this protocol and the patient's medical history situation was sought beforehand. The drugs prescribed were cytotoxic drugs targeting the 3 sites of action of antimetabolites on DNA synthesis, which were associated with corticosteroids. The outcome of 3 cures, a pre-induction cure, an induction cure and a consolidation cure were respectively favorable to 71.74%, 69.70% and 73.91% of patients. A complete remission of 37% was observed after an average of 4.83 months of treatment management.

Regarding the dispensing of antimetabolites, the pharmacy of the University Hospital of Treichville did not realize a nominative dispensation of antimetabolites. Its role was only to ensure the availability of drugs and deliver to the oncology unit.

Adverse effects were dominated by aplasia (43.47%). For the treatment of infections during cancer chemotherapy, the management team used a penicillin-based antibiotic therapy in 27 patients (58.7%) whereas the association penicillins and methotrexate (MTX) is not advisable. This interaction of pharmacokinetic nature is at the origin of the toxicity of the MTX. In fact, 15/27 patients (55.55%) receiving penicillins had medullary aplasia against 5 cases of medullary aplasia in 19 patients without penicillins (26.31%). However, there was no statistical link between the occurrence of aplasia and the co-administration of penicillins and MTX.

In conclusion, the pharmacotherapy of cancer chemotherapy during the treatment of Burkitt's lymphoma in the pediatric oncology unit of the University Hospital of Treichville requires optimization of medical prescription, dispensing as well as therapeutic monitoring.

Keywords: Pharmacotherapeutic; Cancer Chemotherapy; Burkitt's Lymphoma

Abbreviations

BL: Burkitt's lymphoma; CHOP: Cyclophosphamide, doxorubicin (Hydroxydaunorubicin®), vincristine (Oncovin®), Prednisone; COPADM: Cyclophosphamide, Vincristine (Oncovin®), Prednisone, Doxorubicin (Adryamicin®), Methotrexate; COPM: Cyclophosphamide, Vincristine (Oncovin®), Prednisone, Methotrexate). CR: complete remission; CYM: Cytosine arabinoside, Methotrexate; DNA: Deoxyribose Nucleic Acid; GFAOP: Groupe Franco-Africain d'Oncologie Pédiatrique; mini CYCE: Cytosine arabinoside, Etoposide (Vepeside®); MTX: Methotrexate

Introduction

Burkitt's lymphoma (BL) accounts for 35-50% of non-Hodgkin's lymphoma (NHL) in children and 2% in adult LMNH [1]. It is the most common childhood cancer in sub-Saharan Africa [1-4]. In Côte d'Ivoire, Burkitt's lymphoma is the most common malignant tumor [5,6]. Treatment of this type of cancer involves multidrug therapy [7-9]. However, in Côte d'Ivoire, there is very little scientific work done to evaluate the therapeutic protocols in place and the follow-up of patients, whereas anticancer drugs are known for their toxicity [7].

A pharmacotherapeutic approach, which aims at exploiting the properties of medicinal products for individualized therapy, is therefore essential in the management of BL in the pediatric oncology unit of the University Hospital of Treichville.

This study was conducted with the general objective of studying the pharmacotherapeutics of cancer chemotherapy during the treatment of Burkitt's lymphoma in the pediatric oncology unit of the University Hospital of Treichville.

Material and Methods

This was a retrospective cross-sectional descriptive study of 46 patients treated at the Pediatric Oncology Unit of the University Hospital of Treichville during the period January 2011 to December 2015.

The study population consisted of medical records of patients with BL outpatient or hospitalized from January 2011 to December 2015.

A data collection sheet enabled us to collect information. This information concerned the patient's identity, clinical assessment, diagnosis, extension, pre-therapeutic assessment, cancer treatment received in pre-induction, induction, consolidation and follow up, antibiotic treatments received, monitoring of treatment, improvement and duration of treatment.

The data collected were processed by EXCEL 2007 and Epi Info 7, and the statistical analysis used the chi-square test with significance criterion $p < 0.05$.

Ethical considerations

We received an authorization from the head of the pediatric oncology unit and the head of the Pediatrics Department at University Hospital of Treichville. In addition, the data were collected anonymously.

Results and Discussion

This retrospective study examined the pharmacotherapeutics of cancer chemotherapy in the Burkitt's lymphoma treatment at the Pediatric Oncology Unit of the University Hospital of Treichville involving cases of 46 patients.

The choice of this type of patient is justified by the fact that more than 70% of the activity of the pediatric oncology unit is devoted to the diagnosis and the management of the BL in children [5].

Socio-epidemiological data

Distribution by sex

The study population consisted of 29 male children (63%) and 17 female children (37%), with a sex ratio of 1.70.

The male predominance reported in our study is in agreement with the results of previous studies, in particular those of Kouyaté, *et al.* (2011) [10], Yao, *et al.* (2013) [9] who reported a sex ratio of 1.12 and 1.35 respectively in children with cancer in Côte d'Ivoire.

Distribution by age

Patients' ages ranged from 2 years to 15 years with an average age of 8.12 years. Gngangoran, *et al.* (2012) [11] also reported an average age of 8 years, and Peko, *et al.* 2004, 7.9 years.

Children aged 5 to 10 accounted for 46% of the study population, as was also observed by Yao, *et al.* (2013) [9] and Peko, *et al.* (2004) [12], 78% and 38% respectively.

Distribution by place of residence

Patients in the study were predominantly residing (91.3%) outside Abidjan. Yao, *et al.* (2013) [9] also reported 78% of patients living outside Abidjan, the only city where there is a center for the management of childhood cancer.

Pharmacotherapeutic data

Medical prescription

The diagnosis

Distribution according to the location of the tumor

The main reasons for consultation were abdominal mass (50%) and maxillofacial swelling (41.3%).

This assertion was corroborated by the work of Yao, *et al.* (2013) [9] who observed a predominance of abdominal mass in 41.2% and maxillofacial tumor in 44.1%. Gngangoran, *et al.* (2012) [11] also reported that the main location of suspected punctured masses were maxillofacial and abdominal.

Distribution according to clinical signs at admission

Clinical signs at admission were dominated by malnutrition (64%), abdominal pain (60%), fever (58%) and dehydration (44%). These signs, however, are not specific to cancerous disease.

Distribution according to biological parameters

The patient on admission to the pediatric oncology unit had average hemoglobin of 8.9 g / dl, platelets of $293.10^3 / \text{mm}^3$ of blood, leukocytes of $10.10^3 / \text{mm}^3$ of blood and PNN of $4615 / \text{mm}^3$ of blood. The low value observed in these parameters justified the need for premedication prior to any cancer chemotherapy session.

BL was diagnosed in 100% of patients. An extension report and a pre-therapeutic evaluation were carried out in all the patients. Our results are superior to those obtained by Couithère, *et al.* (2004) [5] where diagnosis to certify was made in 65.2% of cases, and Yao, *et al.* (2013) [9] where 76% of the patients had a pre-therapeutic assessment, in the same unit.

This may be justified by the fact that in 2004 the Pediatric Oncology Unit of the University Hospital of Treichville joined the Franco-African Group of Pediatric Oncology (GFAOP). As a result, chemotherapy is now free; treatment follows established protocols with free access to the various biological analysis.

Distribution according to stage of lymphoma

Children with Burkitt's lymphoma were mostly clinically in stages III (91.3%) and IV (6.53%) of Murphy. Patients in the study conducted by Yao, *et al.* (2013) [9] were 48.8% at stage III and 10.2% at stage IV of Murphy, as well as those of Couithère, *et al.* (2004) [5] where children with Burkitt's lymphoma were 76% in Murphy's Stages III and IV.

The application of the treatment protocol and its adequacy to the patient's need

Drugs prescribed for BL chemotherapy in the pediatric oncology unit at the University Hospital of Treichville were antimetabolites and corticosteroids (prednisone or hydrocortisone). These cytostatics were:

- an alkylating agent, cyclophosphamide, Endoxan®
- an antimetabolite inhibiting the synthesis of nucleic bases (uridine, thymidine), methotrexate (MTX) Methotrexate®
- a mitotic spindle poison, vincristine, Oncovin®
- an anti-metabolite, anti-pyrimidine, arabinoside cytosine, Aracytine®

These drugs, taken according to established protocol, allow targeting the 3 levels of action of antimetabolites on DNA (Upstream of the synthesis, by direct interaction on the DNA and downstream of the synthesis) [7,13]. The protocols in force in this department are those of the French society of pediatric oncology used in the pediatric oncology unit of the University Hospital of Treichville in an adapted form called cyclo Burkitt of the GFAOP. It was based on the consensus recommendations of the GFAOP [14], which was integrated by the pediatric oncology unit of the University Hospital of Treichville in 2004.

A pre-therapeutic assessment was asked of the patient before any prescription of chemotherapy. This assessment made it possible to verify the patient's eligibility for anticancer drugs. Thus, an anticancer treatment was initiated only after assessment of liver, cardiac and renal functions, as well as after a satisfactory haematological state (PNN > 1000 / mm³, platelet > 10000 / mm³). This preparation consisted of a correction of observed deficiencies such as anemia, thrombocytopenia and neutropenia. It consisted of systematic deworming with albendazole or mebendazole, a systematic anti-malarial cure. Moreover, any deficiency observed in a patient was corrected before therapy. Thus, patients received antianemic in case of anemia, a balanced nutrition in case of general poor condition. Also, a mouthwash was prescribed in the maxillary sites and antibiotic therapy was initiated in case of infection.

Furthermore, the dosage of each molecule used was based on body weight. The dosage for intrathecal administration was also based on the age of the patient.

Because of the adequacy of the protocol, intensive chemotherapy was used to treat LB. The treatment management protocol was based on the stage of lymphoma. Almost all of the patients were clinically in Stages III and IV of Murphy, a pre-induction cure based on an alkylating agent, cyclophosphamide was initiated in the 46 study patients (100%).

For 6 of them, the medical team used a second pre-induction because of a poor response to treatment. 33/46 patients (71.74%) had a favorable outcome at the end of this pre-induction cure (Figure 1).

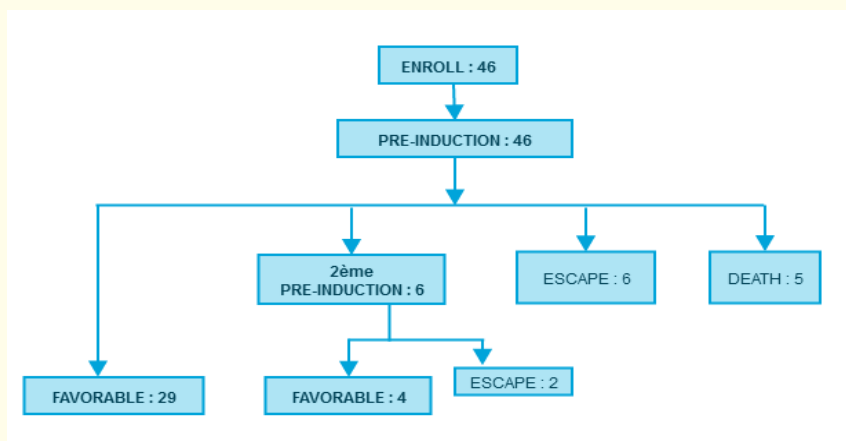


Figure 1: Distribution of patients according to the pre-induction protocol.

As a first line treatment, 28/33 patients with a favorable response to pre-induction, started with a COPM induction cure (Cyclophosphamide, Vincristine (Oncovin®), Prednison, Methotrexate). 2 cycles of COPM were used. Induction with COPM resulted in a favorable outcome in 67.86% (19/28).

A second-line treatment using COPADM (Cyclophosphamide, Vincristine (Oncovin®), Prednison, Doxorubicin (Adryamicin®), Methotrexate) was used in 9 patients, 4 of whom had poor response to COPM, 5 had poor recovery after pre-induction cure. 2 cycles of COPADM were also used giving 44.44% (4/9) favorable response.

The induction cure was generally favorable in 23/33 patients (69.70%) (Figure 2).

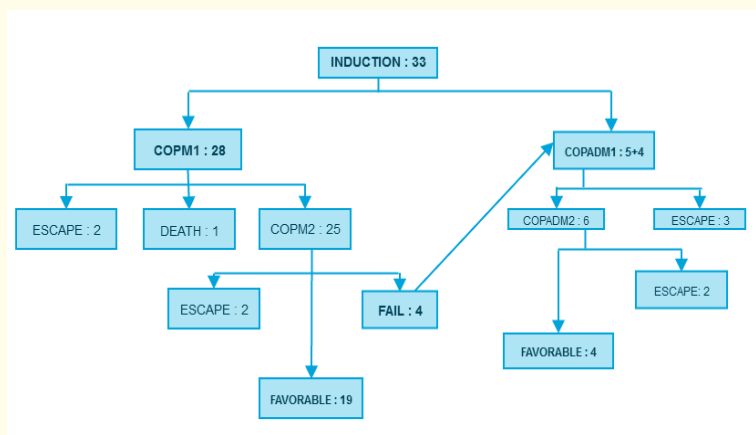


Figure 2: Distribution of patients according to the induction protocol.

A consolidation cure with the CYM protocol (Cytosine arabinoside, Methotrexate) was initiated in 19 of the patients who had a favorable response to the COPM induction cure. 17 of them had a good recovery allowing the utilization of CYM2. The consolidation cure with the CYM gave 78.94% favorable result (15/19);

For the 4 patients who have used the COPADM protocol, the medical team used a mini CYCE protocol (Cytosine arabinoside, Etoposide (Vepeside®)), 2 cycles of mini CYVE were also used, giving 50% favorable result (2/4).

The overall outcome of the consolidation protocol was favorable in 17/23 patients (73.91%) (Figure 3).

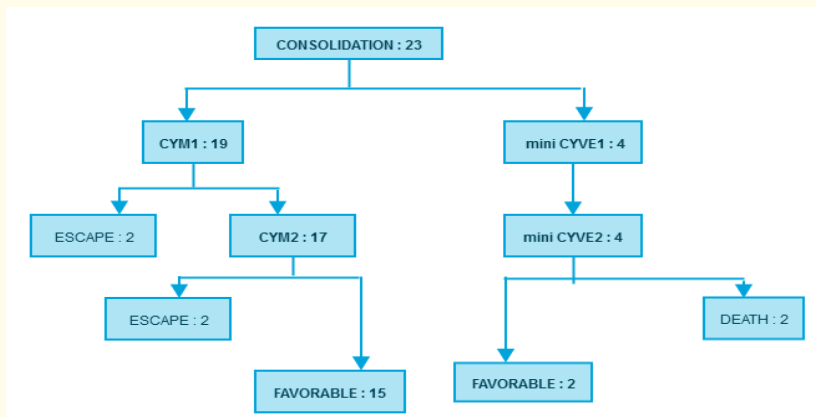


Figure 3: Distribution of patients according to the consolidation protocol

There were no monitoring cures given to the study population, patients with Stage IV of Murphy being escaped or deceased.

At the end of these 3 treatments, overall complete remission (CR) was reported in 37% of patients out of the 46 cases examined, due to large number of patients who were lost in sight 46% (21/46) during the follow-up period.

In the same unit of pediatric oncology, Couitchère., *et al.* (2004) [5] in a study carried out from 1996 to 2000 on 204 patients treated with a protocol comprising 4 antimitotics, cyclophosphamide, vincristine, adriamycin and actinomycin D; and a corticosteroid, prednisone, reported CR rate of 5%. Also in the same unit, the work of Yao., *et al.* (2013) [9] reported from 1995 to 2004, a CR rate of 6.6% with the same protocol applied to 331 patients. This protocol, in its mechanism of action allows an action downstream of the synthesis of the DNA with also, certainly a reinforced action on the DNA, but is devoid of an action upstream of the synthesis of the DNA, Site of action that would have allowed the protocol to target the 3 levels of action of antimitotics on DNA [7,13].

The cyclo Burkitt protocol has an action that targets the 3 different levels of action of antimitotics, which could justify these best results (37% of CR against 5% and 6.6%).

Elsewhere, in Africa (Senegal and Cameroon), Harif and Moreira (2011) [15] reported higher rates of CR in multicentre studies using the Cyclo Burkitt protocol of the GFAOP, 53% with 187 patients in 2001 and 64% in 2010 on a population of 332 patients. This difference could be explained by the fact that our study was retrospective and covered only 46 patients.

In china and other European countries, rituximab, a monoclonal antibody is efficient in the treatment of BL since 1988 [16]. Indeed, in China, Wu., *et al.* (2016) [17] reported 94.2% CR in patients whose chemotherapy protocol was accompanied with rituximab. Coiffier., *et al.* (2010) [18] also reported 63% CR in patients using CHOP protocol (cyclophosphamide, doxorubicin (hydroxydaunorubicin®), vincristine (oncovon®) and prednisone) and 75% CR in patients treated with protocol Rituximab-CHOP rates maintained for 10 years.

The association of Rituximab to the Cyclo Burkitt protocol of the GFAOP would allow a more interesting CR rate, however the Rituximab is not financially affordable in Africa.

In addition, the use of rituximab is controversial because of its hepatic and cardiovascular toxicity, requiring preventive measures [17].

Other Medications

For the other drugs, penicillin were used in 27 patients (58.7%). as follows: 18 patients for amoxicillin, combined amoxicillin and clavulanic acid used by 8 patients and 1 patient used ampicillin.

The use of penicillins was justified by the occurrence of respiratory or digestive infections in patients during chemotherapy or during premedication. However, there are potential drug interactions when penicillins are used in co-administration with antimitotics (Ronchera., *et al.* 1993). This association is discouraged [19]. The interaction of association MTX-Penicillin is pharmacokinetic. It leads to an inhibition of the renal tubular secretion of MTX, by competition in the membrane transport. This leads to a decrease in the renal excretion capacity of MTX, the mechanism most frequently encountered in MTX overdose. This interaction increases the toxicity of MTX [20]. This toxicity is mainly manifested by medullary aplasia, infections, fibrosis (hepatic and pulmonary), severe cutaneo-mucosa, neurotoxicity (peripheral and/or central) and acute renal failure [8].

In our study, 15 patients out of 27 (55.55%) receiving penicillins had medullary aplasia against 5 cases of medullary aplasia in 19 patients without penicillins (26.31%). However, there was no statistical link between the occurrence of aplasia and the co-administration of penicillins and MTX.

In the case of a curative treatment, an aminoglycoside or a cephalosporin would be better in co-administration with antimitotics [19].

In the case of preventive treatment of infections, cephalosporins (ceftriaxone or cefotaxime) and aminoglycosides (gentamicin or amikacin) have been prescribed following medullary aplasia. It was an intravenous bi-antibiotic therapy [7,14].

Pharmaceutical dispensing

The Pediatric Oncology Unit of the University Hospital of Treichville is endowed with pharmaceutical products donated by its various donors. These pharmaceutical products are held by the hospital pharmacy of the University Hospital of Treichville which make them available for the pediatric unit within the limits of their available stock. This fact obliges the unit to use only the available drugs, parents of the patients in most cases are unable to buy other drugs at the hospital pharmacy, and pharmacy of office.

The pharmacist dispenser, within the hospital pharmacy of the University Hospital of Treichville did not carry out operations related to the dispensation of antimitotics. Therefore, he had no contact with the patient, no access to the doctor's prescription for his analysis. He did not prepared the doses to be administrated; he did not deliver drugs directly to the patient. It's role was only to hold the drugs and make them available to the unit. The management of the pharmaceutical products was handled by a nurse of the unit who give them out to the medical team.

There is no pharmacist in the unit. In addition, the drugs needs of the pediatric oncology unit at University Hospital of Treichville are met only by voluntary donations. These products are delivered to the unit in accordance with the protocols in place, as a result of the GFAOP agreement. Stock shortages often occur. It therefore obliges the oncology unit team to postpone certain cures, which is detrimental to the patient.

It is therefore advisable that a pharmacist join the Pediatric Oncology Unit at University Hospital of Treichville. Indeed, the treatment management team has to be multidisciplinary, including pharmacist, health professional, drug specialist, and specialist of prescription's analysis for the interaction's detection of and taking part in the global management of the patients [21].

In addition, antimitotics are highly reactive substances [22,23] whose reconstitution constitutes a public health issue in terms of protection of personnel, the environment and safety of the patient themselves, by the quality of the preparation administered [24]. Preparations at the Pediatric Oncology Unit at the University Hospital of Treichville are done by nurses. These preparations are not carried out in a suitable environment, that is to say in a specific room with proper ventilation, either under a vertical laminar flow hood or in an insulator [25]. As for the staff responsible for administration of cytostatics to the patient, they must wear personal protective equipment [25]. These various rules are not respected in the pediatric oncology unit of the University Hospital of Treichville because of a lack of knowledge of the serious health risks of nurses who prepare, transport and administrate them to patients and those who carry out certain tasks like cleaning and waste disposal (carers, cleaning staff).

Therapeutic Follow-up

During cancer chemotherapy, therapeutic follow-up involves conducting clinical and biological examinations to detect the expected and unexpected toxicity of antimitotics, and to report adverse events that occur. This follow-up concerns heartbeat, respiratory rate, blood pressure, temperature, diuresis, NFS, haemostasis, ionogram, serum calcium, phosphoric acid, uricemia [7].

This procedure was applied at the pediatric oncology unit at the University Hospital of Treichville and revealed the following; aplasia in 43.47% of study patients, fever in 36.95%, cough in 36.95%, and Mucositis in 19.56%. These adverse effects have common effects on anti-cancer chemotherapy [7,26].

The incidence of aplasia was greater in patients treated with penicillins (15/27) than in patients not treated with penicillins (5/19). The recommended use of penicillins with MTX would certainly have favored the toxicity of the MTX responsible for the occurrence of aplasia and mucositis [7], although no direct link could be established between these events and Concomitant use of penicillins / MTX ($p = 0.93$). A proper dosage of methotrexate should be applied in order to better adjust the dose of its antidote, folinic acid.

Literature also reported that antimitotics are emetogenic [7]. However, no case of vomiting was reported in the patient files submitted to our study. Indeed, metopimazine was systematically associated with all cures. On the other hand, the use of corticosteroids in the cancer chemotherapy protocol was aimed, on the one hand, at potentiating the antimitotic effect and on the other hand at preventing certain side effects, among others the emetic effect [7]. This preventive action would appear to be sufficient since no case of nausea and/or vomiting has been mentioned in the various patient files. Also, no cases of alopecia have been mentioned in the various files whereas most alkylants have this undesirable effect in common.

Patients outcomes were marked by a significant number of patients lost to follow-up (46%) and deaths (17%). Our results are clearly improved compared to those of Couithère, *et al.* (2004) [5] and Yao A., *et al.* (2013) [9] in the same unit for which the trend was marked by a significant number of 52% and 50% respectively; And deaths respectively of 36% and 40, 6%.

The high proportion of children living outside Abidjan, the only place with a specialized unit for the care of childhood cancer in Côte d'Ivoire; the low income of families and the use of traditional medicine, often in the first instance, could explain the advanced stages of the disease which affects the reduced number of patients in CR and the many lost to follow-up. To this could be added the duration of the care of 4.83 months on average for a patient, depriving parents of their activities mostly rural dwellers. Yao, *et al.* (2003) [9] found that 1 in 2 patients (52.6%) of their study could not pay for the drugs. Similar effects of financial constraints have been described in a Nigeria study [27].

Conclusion

The aim of this study was to study the pharmacotherapeutics of cancer chemotherapy of Burkitt's lymphoma at the Pediatric Oncology Unit of the University Hospital of Treichville.

It emerges that the treatment regimen used in this department for the management of Burkitt's lymphoma is the cyclo Burkitt protocol of the GFAOP. This protocol, which targets the three levels of action of antimitotics on DNA, makes it possible to obtain remission rates that are generally satisfactory.

However, the absence of an individualized drug dispensing, and of a pharmacist in the unit, is a limit to the quality of care, the dispensing of cytostatics, highly reactive products, being done by a nurse. The therapeutic follow-up was jeopardized by the appearance of adverse effects, harmful drug interactions and a significant number of lost to follow-up patients.

Based on the observations above, pharmacotherapeutic optimization, a rigorous approach that will contribute towards correct utilization of drug, is essential to improve the quality of patient care at the pediatric oncology unit of the University Hospital of Treichville.

Conflict of Interest

The authors declare no conflicts of interest.

Bibliography

1. Rafaramino F, *et al.* "Burkitt's lymphoma in children of Madagascar. Anatomico-clinical forms, therapeutic and evolutive aspects". *Bulletin De La Societe De Pathologie Exotique* 94.5 (2001): 389-393.
2. Missaoui N, *et al.* "Childhood cancer frequency in the center of Tunisia". *Asian Pacific Journal of Cancer Prevention* 12.2 (2011): 537-542.
3. Segbena AY, *et al.* "Le lymphome de Burkitt au Togo. Aspects épidémiologique, clinique, thérapeutique et évolutif". *Médecine d'Afrique Noire* 44.3 (1997): 141-145.
4. Stefan DC, *et al.* "Hope for African children with cancer: African pediatric oncology group". *Pediatric Blood and Cancer* 59.2 (2012): 349.

5. Couitchère L., *et al.* "Bilan de cinq années d'activité de l'unité d'oncologie pédiatrique du CHU de Treichville à Abidjan, Côte-d'Ivoire". *Archives de Pédiatrie* 11.3 (2004): 257-260.
6. Effi AB., *et al.* "Descriptive epidemiology of cancers in Cote d'Ivoire". *Bull Cancer* 100.2 (2013): 119-125.
7. Heron JF. "Cancérologie générale". Faculté de Médecine de Caen – France, Polycopié 9 (2003).
8. Reutenauer S., *et al.* "Surdosage au méthotrexate: complications, prise en charge et prevention". *Revue Réanimation* 18.7 (2009): 654-658.
9. Yao A J J., *et al.* "Childhood cancer in Côte d'Ivoire, 1995 - 2004 – challenges and hopes". *South African Medical Journal* 103.2 (2013): 113-115.
10. Kouyate M., *et al.* "Aspects histo-épidémiologiques des Cancers solides du rein De l'enfant en Cote D'ivoire". *African Journal of Urology* 17.4 (2011): 153-156.
11. Gnanngoran Victor Yao., *et al.* "Pediatric lymphomas diagnosis after needle biopsy in Abidjan: Value of cytology versus MYC translocation examination". *Annales de Pathologie* 32.1 (2012): 14-18.
12. Peko J F., *et al.* "Les tumeurs solides malignes de l'enfant à Brazzaville: aspects épidémiologique et anatomo-pathologique". *Bulletin De La Societe De Pathologie Exotique* 97.2 (2004): 117-118.
13. Pr Baillet. "Cancérologie - Service de radiothérapie". *Faculté de Médecine Pierre et Marie Curie* (2015).
14. Service de Pédiatrie CHU de Treichville Abidjan Côte d'Ivoire. Protocoles et CAT en oncologie pédiatrique. Polycopié (2001).
15. Harif M and Moreira C. "Le lymphome B, expérience du groupe franco-africain d'oncologie pédiatrique". *Paris, Mai* (2011).
16. Vannier JP., *et al.* "Traitement des lymphomes B étendus de l'enfant: étude de la Société Française d'Oncologie Pédiatrique". *Bull Cancer* 75 (1988): 61-68.
17. Wu J., *et al.* "Rituximab plus chemotherapy as first-line treatment in Chinese patients with diffuse large B-cell lymphoma in routine practice: a prospective, multicentre, non-interventional study". *BMC cancer* 16 (2016): 537.
18. Coiffier B., *et al.* "Long-term outcome of patients in the LNH-98.5 trial, the first randomized study comparing rituximab-CHOP to standard CHOP chemotherapy in DLBCL patients: a study by the Groupe d'Etudes des Lymphomes de l'Adulte". *Blood* 116.12 (2010): 2040-2045.
19. Vidal 2016
20. Ronchera C., *et al.* "Pharmacokinetic interaction between high dose methotrexate and amoxycillin". *Therapeutic Drug Monitoring* 15.5 (1993): 375-379.
21. Brunie V., *et al.* "Le rôle du pharmacien dans l'éducation thérapeutique du patient". *Journal de Pharmacie Clinique* 29.2 (2010): 90-92.
22. Falck K., *et al.* "Mutagenicity in urine of nurses handling cytostatic drugs". *Lancet* 1.8128 (1979): 1250-1251.

23. Hirst M., *et al.* "Occupational exposure to cyclophosphamide". *Lancet* 1.8370 (1984): 186-188.
24. "Centre International de Recherche sur le Cancer. Monographs on the evaluation of the carcinogenic risk of chemicals to man. Chemicals, industrial processes and industries associated with cancer in human". *Lyon* 4 (1982): 292.
25. Boiano JM., *et al.* "Adherence to safe handling guidelines by health care workers who administer antineoplastic drugs". *Journal of Occupational and Environmental Hygiene* 11.11 (2014): 728-740.
26. Talbert M., *et al.* "Le guide pharmaco Clinique" (2009): 202-245.
27. Meremikwu MM., *et al.* "Socioeconomic constraints to effective management of Burkitt's lymphoma in south-eastern Nigeria". *Tropical Medicine and International Health* 10.1 (2005): 92-98.

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