Patient compliance in the treatment of Burkitt's lymphoma in rural Zambia: A retrospective study on 80 Burkitt's lymphoma patients in Katete, Zambia

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ABSTRACT

Background: In African settings the treatment results of Burkitt's lymphoma (BL) seem to be less favourable compared with Western settings. The aim of this retrospective study was to analyse some factors that affect the treatment of BL. **Patients and Methods**: Over a 16 year period, data were extracted of 80 patients. **Results**: Complete remission 5%, very good partial response 35%, partial response 16%, no response 10%, data missing 34%. Of all patients, 56% did have a positive response to treatment. However, 51% of this subgroup of patients did not finish treatment. There was no difference in completion of treatment between patients living in Katete district finishing treatment vs. living outside Katete district (respectively 25% vs. 32%, P = 0.7148). **Conclusion**: There is potential for higher cure rates for BL in tropical settings if full effort is put into compliance since a majority of patients, even while having a good prognosis, abandon treatment. Large distance to hospital makes no difference in completing the chemotherapy course.

Keywords: Burkitt's lymphoma, chemotherapy, compliance

INTRODUCTION

Burkitt's lymphoma (BL) has a peak incidence of 5-9 years and a male predominance.[1,2] Besides the strong association with Epstein-Barr virus (EBV) and malaria,[3,4] there is also a higher frequency of BL in human immunodeficiency virus (HIV) infected patients.[2,5,6] Most patients present with a swelling of the jaw,[7,8] the gastrointestinal tract, kidneys, peritoneum and liver.[9] Chemotherapy is the main treatment for BL.[10] In Western settings, 5-year survival rates up to 80% are seen using a variety of aggressive chemotherapy regimens.[4,11] In tropical settings, treatment results seem to be less favourable.[12-16] The explanation for these disappointing results may be related to hospital factors (such as diagnostic accuracy, availability of drugs, quality of supportive care) and patient factors (such as late presentation, poor compliance, comorbidity).[17-20] The aim of this retrospective study was to analyse some of the hospital and patient related factors that affect the treatment of BL in a rural African setting, with particular attention to the distance that patients had to travel to the hospital.

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PATIENTS AND METHODS

The study was performed in Saint Francis' Hospital, a church sponsored hospital in Katete-district, a rural area in eastern Zambia. This hospital provides basic health care for an estimated 1,75,000 people in the district living at an average distance to the hospital of 25 km (16 miles), and specialist services to a population of over 1 million, living at a distance of up to 300 km (186 miles).

The medical records of patients diagnosed with BL between 1991 and 2006 were analysed. The following characteristics were recorded: demographic, clinical findings, aspiration cytology, histology, treatment details and outcome (complications and survival). When pathology was not available, records of patients were re-examined by two specialists (paediatrician and oncologist) on BL independently to determine their eligibility. The inclusion criteria used were a combination of following information: typical BL tumour location, age group, tumour response to chemotherapy, likeliness of other diagnosis, tumour behaviour, ultrasound results, X-ray results. Only when they both made a positive diagnosis on clinical grounds the patient was included.

A chemotherapy schedule with cyclophosphamide,

vincristine and methotrexate was used [Table 1]. The data was analysed using SPSS version 12.0.1. data editor for Windows.

RESULTS

A total of 80 patients were included over a 16-year period ranging from 1991 to 2006. An average of 5 patients a year was diagnosed with BL in Saint Francis' hospital. A majority of patients was male (1, 5:1 ratio or 59% male vs. 41% female). Average age was 8 years (range 3-50 years, median 7 years, 11.3% data missing). Of the 80 eligible patients, 17 were included on the basis of histology results, 23 by cytology results, 12 by both histology and cytology results and 28 on clinical grounds. There was an 85.7% agreement between the specialists evaluating 'inclusion on clinical grounds'. Locations affected were as follows: 72.5% jaw, 11.2% both jaw and other location, 33.8% other location than jaw. Response rates for the total group were as follows: complete remission 5%, very good partial response 35% ($\geq$50% reduction in total tumour size with chemotherapy), partial response 16% (reduction in total tumour size with chemotherapy >50%), no response 10%, data missing 34%. Of all patients, 56% (partial plus complete response rates) did have a positive response to treatment but the majority of this subgroup (51%) did not complete treatment. There was no difference in completion of treatment between patients living in Katete district finishing treatment vs. living outside Katete district (respectively 25% vs. 32%, $P = 0.7148$, Table 2). It was not our policy to test children with BL for HIV.

DISCUSSION

This study shows that treatment of BL in a rural setting with limited facilities is feasible, but that the results in terms of completion of treatment, follow-up and survival are very disappointing. With 34% missing data, conclusions have to be drawn with great care. Out of all patients diagnosed BL in the Saint Francis Hospital, 56% (partial plus complete response rates) did have a positive response to treatment which is associated with a good prognosis. However, the majority of this subgroup (51%) did not finish treatment. There was no evidence that any of these patients died during treatment or had to stop because of severe side-effects. Therefore, it is likely that the majority of non-finishers can be attributed are abandoners of treatment.

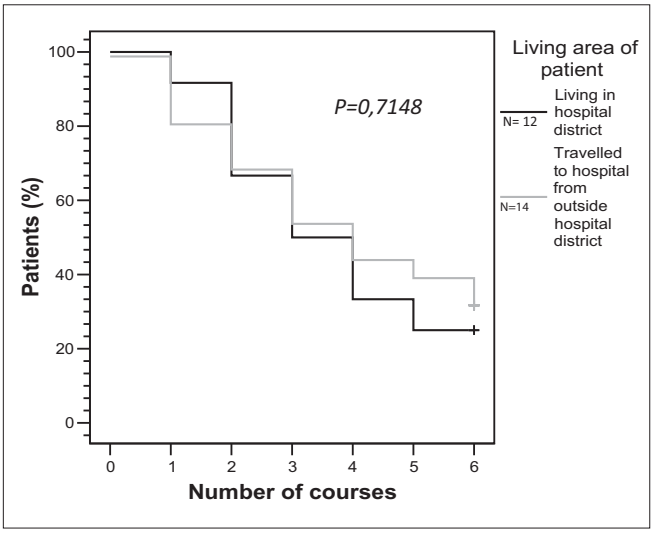
Despite a regular supply of drugs, only one quarter to one third of the patients completed the full course of cytotoxic drugs. While it is difficult to explain from a retrospective study, there are likely multiple factors involved with issues of compliance in this setting. One probable explanation, namely distance between home and hospital, was not found to be correlated with the chances of completion of treatment in our study. This finding is in concordance with the results of a recent study on compliance in HIV therapy in Zambia.[21] It maybe that there is already a selection *before* people will travel to hospital. Some people do not realize the medical urgency or do not have the money to travel to a hospital. Thus, patients who *do* arrive from far at the hospital clinic are probably already selected by means of education, wealth and personal circumstances in comparison to the patients who did come to the hospital. This research shows the 'large distance to hospital' seems partly non-physical and this 'distance' needs to be shortened by means of health education. Lack of understanding by the parents of the importance of completion of treatment is a main factor, particularly if the initial response has been dramatic. Investigators in Johannesburg[17] showed the impact of differences in

Table 1: Treatment protocol for Burkitt's lymphoma described in Primary Surgery by Maurice King using cyclophosphamide, vincristine and methotrexate[10]

Medicine	Dose	When
Cyclophosphamide	1 to 1,5 g/m^2	Day 1
Vincristine	1.4 mg/m^2	Day 1
Methotrexate	15 mg/m^2 (PO)	Daily for 4 days

Subsequent courses are started on the 21st day following the start of first treatment, A generally accepted minimum of 6 courses is needed to complete treatment

Table 2: Patient compliance to treatment schedule. Kaplan-Meier plot which shows no significant difference in completion of chemotherapy schedule between patients living inside the hospital district vs. patients living outside the hospital district.



educational background on therapy adherence. They found that less than 50% of black parents with lower socio-economic and educational status understood the nature of the child's leukemia. Only 53% of those children attended on the first appointed day of treatment. This percentage makes a clear statement on the importance of clinical information and education. Caretakers of patients need good clinical information, cause if they do not understand what is going on they will not come to clinic or stay adherent to therapy. Doctors working in a tropical setting should be aware of this phenomenon and should anticipate on giving additional information to patients/caretakers with no or little education. Doctors should explain the child's illness and urge the patient or caretaker to stay the full length of treatment. It can be good to be aware of structural problems like other children at home to be taken care of, a field of crops to harvest, etc. Adverse side-effects of treatment can convince a caretaker who is not medically educated that staying in the hospital is not beneficial for the child.

Accommodation is an issue to address when discussing strategies to improve adherence to treatment when living far from hospital. Two models are challenged here, both with their advantages and disadvantages. The first one is accommodation in-hospital full length of therapy; the second one is in-hospital care only on days receiving chemotherapy. When staying full length of therapy a patient can be monitored properly for adherence to treatment and possible side-effects. Main argument against this model is that an expansible bed in a - probably - over capacitated hospital is taken for months. The second option is a less costly one and it is thinkable a more manageable option for caretakers when thinking about the field of crops and the other children at home. But for patients living far from hospital and in view of the results of this research, there also will be more moments to decide whether to return to hospital at all, more costs on travelling, in the back of cars, loaded busses or walking miles, and this all, with a sick child. A solution in between the two mentioned maybe is accommodation nearby hospital. The patient is in-hospital during courses and in between courses the bed is available for others while the patient stays near hospital. It is an interesting option which needs more investigating.

This research shows only some explanations for low compliance rates, but there will be additional ones that need to be investigated, while compliance is a very complex process and is influenced by many factors. More research about the causes of non-compliance can help raise compliance percentages even more. That research should not only investigate patient factors like the exact reasons for patients or caretakers to abandon treatment, but also hospital factors like providing information and motivation procedure (health workers seem to underestimate the influence of their attitude towards patients and caretakers on compliance[18,19] and the scale of non-availability of medicines).

CONCLUSIONS

This study shows that it is possible to apply a multidrug chemotherapy schedule in a rural African setting. There is potential for higher cure rates for Burkitt's lymphoma in tropical settings if full effort is put into compliance since a vast majority of patients, even while having a good prognosis, abandon treatment. Having to travel a large distance to hospital makes no difference in finishing the complete chemotherapy course. More research is needed to improve compliance.

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