BSH 2020 VIRTUAL
9 -14 NOVEMBER
British Society for Haematology 60 1960–2020
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Impact of changing from co-trimoxazole to alternative pneumocystis pneumonia prophylaxis on the intensity of maintenance chemotherapy in the treatment of children with Acute Lymphoblastic Leukaemia

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INTRODUCTION

•Patients treated for acute lymphoblastic leukaemia (ALL) receive co-trimoxazole prophylaxis against pneumocystis jiroveci pneumonia (PJP) as standard.

• There is some evidence that co-trimoxazole can impact on the oral chemotherapy dose intensity that patients can tolerate due to myelosupression.[1]

•Greater treatment intensity has been correlated with improved event free survival in the treatment of ALL.[2, 3.]

AIM

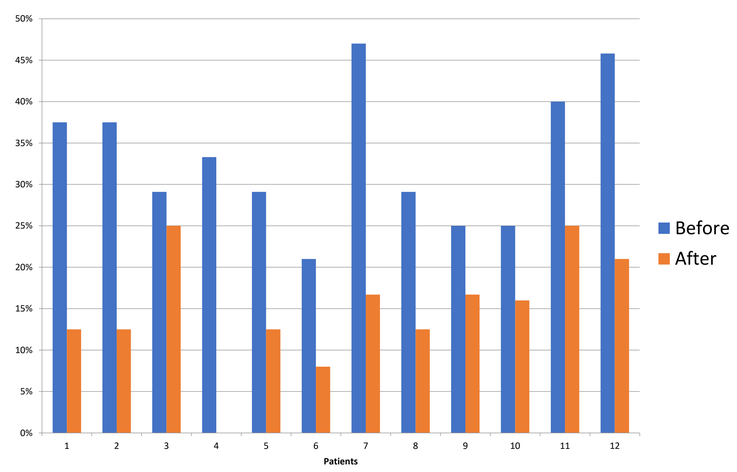
To investigate the impact of changing prophylaxis from co-trimoxazole to an alternative agent on the dose intensity of oral 6-mercaptopurine and methotrexate received by patients in the maintenance phase of ALL therapy.

METHOD

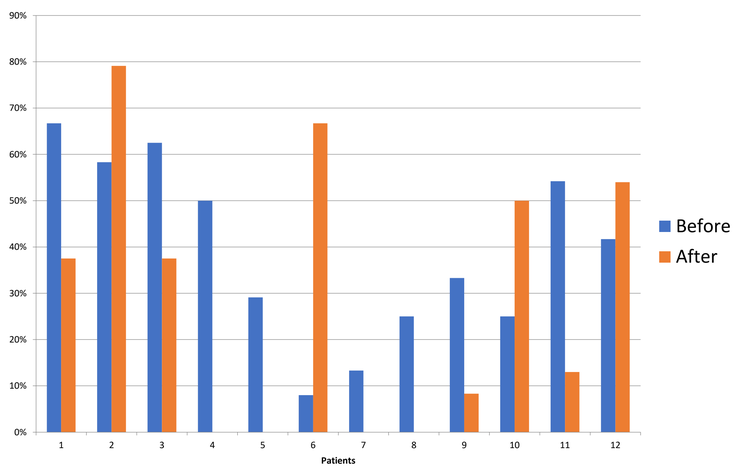
We retrospectively studied patients treated in our centre on a UK ALL protocol over a 5 year period from May 2014 - May 2019 who were switched to alternative PJP prophylaxis. We assessed the treatment intensity tolerated for two cycles of maintenance chemotherapy before and after changing and tolerance of second line agents.

RESULTS

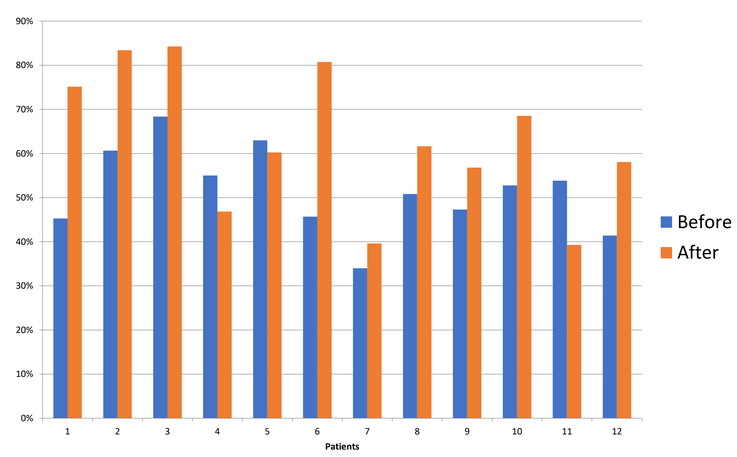
Graph 1: Percentage of weeks off chemotherapy before and after change from co-trimoxazole



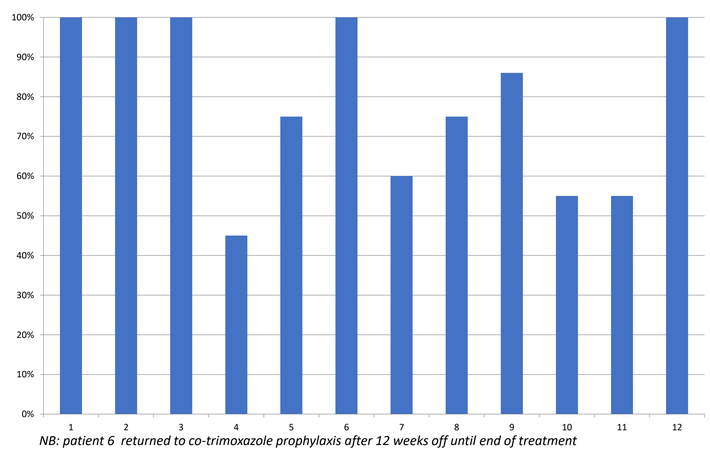
Graph 2: Percentage of weeks on full dose chemotherapy before and after change



Graph 3: Average percentage of full maintenance dose before and after change from co-trimoxazole



Graph 4: Final dose of chemotherapy (mode dose percentage in the final cycle of treatment)



NB: patient 6 returned to co-trimoxazole prophylaxis after 12 weeks off until end of treatment

RESULTS

•14 patients changed from co-trimoxazole because they did not tolerate full dose oral chemotherapy due to myelosuppression. 12 had sufficient data to include in study. 2 patients on interim guidelines UK ALL and 12 on UK ALL 2011.

•After changing :
➢ In all patients there was a reduction in the time spent off chemotherapy (Graph 1)
➢Only 4 patients had increase number of weeks of 100% dose (Graph 2)
➢Overall there was an increase in the amount of chemotherapy delivered (Graph 3)
➢5 of the 12 patients finished able to tolerate full dose oral chemotherapy (Graph 4)

•7/14 of the patients did not tolerate dapsone as a second-line agent, 4 of these patients had methaemaglobinaemia.

•One patient developed PJP infection on dapsone.

LIMITATIONS

•This study was retrospective limiting our ability to control certain variables such as threshold for when to change PJP prophylaxis and variance between individual practice of clinicians.

•Prior clinical knowledge of a patients treatment response has an impact on future clinical decision making which can impact upon chemotherapy dosing independent of the effect of changing PJP prophylaxis.

CONCLUSIONS

For some patients experiencing dose-limiting myelosuppression in the maintenance phase of ALL treatment, changing from co-trimoxazole to alternative PJP prophylaxis may improve delivery of higher intensity oral chemotherapy.

Only half the patients on dapsone were able to tolerate dapsone due to side effects.

This study was limited by its retrospective nature and we plan to follow this study up with a prospective study.

REFERENCES

1**LLevinson et al.** Pneumocystis jiroveci pneumonia prophylaxis during maintenance therapy influences methotrexate/6-mercaptopurine dosing but not event-free survival for childhood acute lymphoblastic leukemia. *European Journal of Haematology. 2012;88(1):78-86.*

2 **Relling MV et al**. Prognostic importance of 6-mercaptopurine dose intensity in acute lymphoblastic leukemia. *Blood (1999) 93 (9): 2817–2823*

3 **Schmiegelow K et al.** Prognostic significance of methotrexate and 6-mercaptopurine dosage during maintenance chemotherapy for childhood acute lymphoblastic leukemia Pediatr Hematol Oncol 1992 Apr-Jun;9(2):following 198

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