

TITLE:

A STUDY TO DEVELOP AN ALTERNATE SAMPLING STRATEGY TO MEASURE RIFAMPICIN CONCENTRATION – TO FACILITATE THIS SERVICE IN RESOURCE LIMITED SETTINGS.

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BACKGROUND:

Rifampicin, the cornerstone of anti-tuberculosis therapy, is known to have high interindividual variability. The therapeutic range for rifampicin plasma concentration for C_{max} is 8-24 ug/ml and in a study done in our department it was reported that 77% of children failed to achieve the recommended concentration with the doses used in the National TB Elimination Programme (1).

Peripheral clinics which treat TB, do not have the infrastructure for monitoring plasma rifampicin concentrations. We looked into the use of DPS [Dried Plasma Spots] to predict rifampicin concentration, which has the advantage of lesser sample and biohazard, easier storage, transport without the need of cold chain, possibility of guiding patient care even from a distance.

AIM & OBJECTIVES:

To develop and validate an alternate sampling strategy using DPS for measurement of rifampicin concentration in comparison with plasma rifampicin concentration as reference standard.

METHODS:

Patients diagnosed with tuberculosis and on anti TB treatment, were recruited in the study. 2 ml of blood was withdrawn two hours after the administration of rifampicin, plasma separated and stored at -80°C. The plasma was used both to measure rifampicin concentrations by HPLC [High Performance Liquid Chromatography] method and secondly to spot 40 ul on the Whatman™ filter paper (DPS). A newly developed and validated HPLC method was used to measure DPS rifampicin concentration. Plasma was used to avoid the influence of haematocrit on the accuracy of this assay. The correlation between plasma and DPS rifampicin concentration was estimated and possibility to predict plasma rifampicin concentration using DPS was studied.

RESULTS:

A total of 61 patients were recruited and the data of 41 patients were used to develop an equation to predict the plasma rifampicin concentrations from the Dried Plasma Concentration (PREDICTED PLASMA = 1.16 + 1.15(DPS) with an Intraclass correlation coefficient (ICC) consistency of 0.97 CI (0.93-0.98) and this equation was validated on another set 20 patients with ICC agreement of 0.96 CI (0.89 – 0.98). Bland Altman plot showed 95 % of the values from the predicted plasma concentration were within 2 Standard Deviation.

CONCLUSION AND RECOMMENDATIONS:

Dried plasma spot can be an effective alternative to predicting the plasma rifampicin concentration in resource limited settings.

REFERENCES

1. Isoniazid and rifampicin concentrations in children with tuberculosis, on either daily or intermittent regimen – implications for the revised RNTCP 2012 doses, in India. 2017. International Journal of Antimicrobial Agents

KEY WORDS: Rifampicin, Dried plasma spot, alternate sampling