Structured Treatment Interruption (STI) with Nevirapine (NVP) and Two Nucleoside Reverse Transcriptase Inhibitors (NsRTI): Is Re-suppression Achieved Following Treatment Interruption?

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STRUCTURED TREATMENT INTERRUPTION (STI) WITH NEVIRAPINE (NVP) AND TWO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NsRTI): IS RESUPPRESSION ACHIEVED FOLLOWING TREATMENT INTERRUPTION?

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ABSTRACT

Background: Previous studies have suggested that STI with a protease inhibitor (PI) regimen does not result in resuppression of viral RNA after resumption of therapy. We sought to determine if patients who failed STI on the combination of NVP and two NsRTI had higher rates of resuppression following STI than after resuppression was achieved with resumption of continuous therapy.

Methods: Retrospective chart review of all patients (N = 536) seen 9/96 to 4/00 yielded 135 patients on NVP and dual NsRTI. ART-i was defined as simultaneous cessation of entire regimen for ≥7 days. We stratified patients by initial combination of NVP and NsRTI. The mean duration of therapy was 9.5 years (range 0.4–13.4 years) and the mean age was 36.3 years (range 18–54 years).

Table 1. Study patients

Table 2. Individual patient results

RESULTS

The failure in patient 10 could be attributed to reported noncompliance (no genotype available). Numerous studies have shown that noncompliance greatly reduces the efficacy of NVP regimens through the selection of resistance-conferring mutations. Patient 17 had an impeccable history of compliance and reported good compliance following STI. Therefore, STI cannot be ruled out as the main contributing factor to the selection of the Y181C mutation in this patient. The mean BLVL was significantly higher than the mean VL measured during the ART-i. Because of this difference, Caution must be exercised when drawing conclusions from this result. The mean duration of ART-i was approximately three times the duration of ART. To study the design, we could not accurately measure the duration of BLVL on ART-i. The duration of BLVL should be more appropriate to measure in future prospective trials, as it takes certain patients longer than others to reach BLVL and to have sufficient increase in CD4+ to impact a reduction in rebound VL.

Conclusions: ART-i, mimicking an NVP regimen, resulted in suppression of VL in 21 of 23 interruptions (91.3%). Nonadherence was associated with one failure, while viral isolates resistant to NVP (Y181C) were detected in the other. Resuppression after ART-i was achieved in 21 of 23 interruptions (91.3%). Differences in parental drug exposure and lower levels of NVP and dual NsRTI in our study may have contributed to the increased resuppression rate.

SUMMARY – CONCLUSIONS

• The efficacy of NVP-based regimens was not reduced following interruption of ART after ART interruption in most patients.
• The failure in patient 10 could be attributed to reported noncompliance (no genotype available).
• Numerous studies have shown that noncompliance greatly reduces the efficacy of NVP regimens through the selection of resistance-conferring mutations. Patient 17 had an impeccable history of compliance and reported good compliance following STI. Therefore, STI cannot be ruled out as the main contributing factor to the selection of the Y181C mutation in this patient.
• Both patients failing to resuppress had a high BLVL (10: 96,177;17: 351,288). However, most patients with BLVL ≥100,000 copies/mL (75.0%, N = 4) did resuppress after ART-i.

METHODS

• A retrospective chart review of all patients (N = 536) seen from 9/96 to 4/00 was conducted at Bonnem Inn Internal Medicine (BIM), an urban HIV Clinic.

• The mean duration of ART was approximately three times the duration of ART-i. Due to the study design, we could not accurately measure the duration of BLVL on ART-i. The duration of BLVL should be more appropriate to measure in future prospective trials, as it takes certain patients longer than others to reach BLVL and to have sufficient increase in CD4+ to impact a reduction in rebound VL.

• It is important to note that patients in this study stopped ALL medications simultaneously. Recent discussion has suggested the strategy of sequential interruption, stopping NVPs 48 hours after stopping NRTIs. This may provide the necessary additional inhibition of resistant viral outgrowth during the slow decline of NRTI concentration.

• ART interruptions have been a common part of clinical practice since the development of PIs, with interruption rates ranging from 36.2% to 45.9%. As the need for long-term ART becomes more evident, we should study and examine the effects of STI. We could then utilize this inevitable event as a benefit to the patient, be it through virologic control or temporary relief from AEs.

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• In summary, following ART-i, reintroducing NVP and two NRTIs resulted in the suppression of viral replication to BLVL in most adherent patients. Utilizing sequential interruption of NRTI-based regimens should allow for the design of easier STI protocols. Further examination of this and all aspects of STI is warranted.

REFERENCES

• Dybul M, Yoder C, Belson M, et al: A retrospective chart review of all patients (N = 536) seen from 9/96 to 4/00 was conducted at Bornemann Internal Medicine (BIM), an urban HIV Clinic.

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• The mean BLVL was significantly higher than the mean VL measured during the ART-i. Because of this difference, Caution must be exercised when drawing conclusions from this result. The mean duration of ART-i was approximately three times the duration of ART. To study the design, we could not accurately measure the duration of BLVL on ART-i. The duration of BLVL should be more appropriate to measure in future prospective trials, as it takes certain patients longer than others to reach BLVL and to have sufficient increase in CD4+ to impact a reduction in rebound VL.

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