Poster

[P26-3] P26-3: Central nervous system drugs (2)

Chair: Chiyo Imamura, Japan

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[P26-3-4] Inflammation increased serum clozapine concentrations: two cases reports

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Background

Cytokine release decreases the expression of several cytochrome P450 (CYPs) isoenzymes, increasing serum clozapine concentrations, which is equivalent to a drug-drug interaction (DDI) with an inhibitor of clozapine metabolism.

Methods

These are the two first cases described in Chinese patients (Case 1: a 57-year-old female non-smoker with severe dermatitis and Case 2: a 47-year-old male non-smoker with influenza and secondary infection). early morning total clozapine concentration/dose (C/D) ratios were measured. DDI between inflammation and clozapine was established. Independent sample Man-Whitney U tests were performed to compare total C/D ratios.

Results

In both cases, the Drug Interaction Probability Scale established the presence of a probable drug-drug interaction. In both cases, the clozapine and the total clozapine concentration-to-dose (C/D) ratios followed a temporal pattern (normal-high-normal), consistent with an inhibition of clozapine metabolism during peak inflammation. In the first case, the total clozapine C/D ratio (8 with no/low inflammation: median of 3.10 and 2 at peak inflammation: median of 3.90) provided a significant difference (P=0.044). In the second patient, because of the smaller sample size and reduced statistical power (4 with no infection: a median of 1.59 and 2 at peak infection: 3.46), the increase did not reach significance (P=0.13). In the first case, the median baseline clozapine C/D ratio increased from 2.00 to a peak of 2.89 by a factor of 1.45. To compensate for the inhibition of clozapine metabolism, the dose correction factor was 0.69 (1/1.45) or a decrease in dose of approximately one third. In the second case, the median baseline clozapine C/D ratio increased from 1.15 to a peak of 2.94, by a factor of 2.56.

Conclusions

The second case suggests that, as in Caucasians, in Chinese patients it may be a good idea to cut the clozapine dose during a severe inflammation/infection unless TDM is available to individualize dose changes. The first case suggests that severe dermatitis may require lower correction factors, but we have no experience with other cases of dermatitis in Chinese patients. Our cases contribute to the literature suggesting that dose modifications are needed in patients taking clozapine during infections and/or inflammations.