Pharmacokinetic analysis of pralidoxime after its intramuscular injection alone or in combination with atropine-avizafone in healthy volunteers

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Résumé en anglais	**BACKGROUND AND PURPOSE** Treatment of organophosphate poisoning with pralidoxime needs to be improved. Here we have studied the pharmacokinetics of pralidoxime after its intramuscular injection alone or in combination with avizafone and atropine using an auto-injector device. **EXPERIMENTAL APPROACH** The study was conducted in an open, randomized, single-dose, two-way, cross-over design. At each period, each subject received either intramuscular injections of pralidoxime (700 mg), or two injections of the combination: pralidoxime (350 mg), atropine (2 mg), avizafone (20 mg). Pralidoxime concentrations were quantified using a validated LC/MS-MS method. Two approaches were used to analyse these data: (i) a non-compartmental approach; and (ii) a compartmental modelling approach. **KEY RESULTS** The injection of pralidoxime combination with atropine and avizafone provided a higher pralidoxime maximal concentration than that obtained after the injection of pralidoxime alone (out of bioequivalence range), while pralidoxime AUC values were equivalent. Pralidoxime concentrations reached their maximal value earlier after the injection of the combination. According to Akaike and to goodness of fit criteria, the best model describing the pharmacokinetics of pralidoxime was a two-compartment with a zero-order absorption model. When avizafone and atropine were injected with pralidoxime, the best model describing pralidoxime pharmacokinetics becomes a two-compartment with a first-order absorption model. **CONCLUSIONS AND IMPLICATIONS** The two approaches, non-compartmental and compartmental, showed that the administration of avizafone and atropine with pralidoxime results in a faster absorption into the general circulation and higher maximal concentrations, compared with the administration of pralidoxime alone.
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