Paraesthesia after Local Anesthetics: An Analysis of Reports to the FDA Adverse Event Reporting System

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Background. The hypothesis on neurotoxicity of local anesthetics is controversial. The incidence of paraesthesia increased following the introduction of articaine 4% and frequently dental anesthesia is involved.
Aim. To provide the contribution of spontaneous adverse events reporting analysis on association between paraesthesia and local anesthetics, focusing on those used in dentistry.
Methods. Association between local anesthetics (ATC: N01B) and paraesthesia was analyzed by the case/non-case of spontaneous adverse events recorded in FDA_AERS (Food And Drug Adverse Event Reporting System) between 2004 and 2011. Cases were represented by the reports of reactions included in the MedDRA high-level term 'Paraesthesias and dysaesthesias' for a given local anesthetic; non-cases were all other reports of the same drug. For each anesthetic, the association between such drug and paraesthesia was calculated by using the reporting odds ratio (ROR) with the relevant 95% Confidence Intervals (95CI). Association was considered statistically significant when: number of cases >3, ROR >1 and lower limit of 95CI >1. To estimate the influence of this association in dentistry, two sensitive analyses were performed: (i) analysis restricted to anesthetics used in dentistry (lidocaine 2%, bupivacaine 2%, articaine 4%, prilocaine 4% and mepivacaine 2% and 3%), (ii) analysis focused on the specific adverse reaction "Paraesthesia Oral".
Results. Overall, 528 reports of "Paraesthesias and dysaesthesias" were retrieved, corresponding to 573 drug reaction pairs, with 247 lidocaine 2%, 99 bupivacaine 2%, 85 articaine 4%, 30 prilocaine 4%, 112 others. The association between drug and adverse reaction was significant for articaine 4% (ROR=18.38; 95CI=13.95-24.21), and prilocaine 4% (2.66; 1.82-3.90). These associations were confirmed in the sensitive analysis. Indeed, analyzing only anesthetics used in dentistry, articaine 4% and prilocaine 4% were significantly associated to paraesthesia. The analysis of the specific term "Oral Paraesthesia" retrieved 90 drug-reaction pairs (37 articaine 4%, 19 lidocaine 2%, 14 prilocaine 4%, 7 bupivacaine 2%, 13 others), and a statistical significant association for articaine 4% (58.77; 37.82-91.31) and prilocaine 4% (8.73; 4.89-15.57).
Conclusion. Our study underlined a stronger association between paraesthesia and articaine 4% or prilocaine 4%, rather than other local anesthetics. Data are in agreement with different studies that reported nerve damage after receiving an inferior alveolar nerve block with articaine 4% or prilocaine 4% in dentistry. The exact mechanism and the incidence of association remain still unknown. These safety disproportionality signals should stimulate more specific studies to confirm or reject the causality relationship between the 4% anesthetic solutions and paraesthesia, and to quantify the magnitude of the hazard. In conclusion, health-care professionals, and in specific dentists, should consider risks and complications of articaine/prilocaine administration.