Mixture of morphine and clonidine at high and low concentrations: evaluation of physical stability

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Background

- Clonidine, an alpha2-adrenoreceptor agonist, is frequently combined to opioids (i.e., morphine hydrochloride) for the management of chronic pain.
- In the palliative care, the mixture of clonidine and morphine is preconized in front of rapid increasing doses when a tolerance effect is suspected.
- The aim of this study was to evaluate the physical stability of this analgesic combination at high and low concentrations in 14 mL and 48 mL plastic syringes.

Material and methods

- Physical stability of low concentration was evaluated on five syringes of mixture clonidine (Catapressan®0.15 mg/mL, Boehringer Ingelheim, Germany) and morphine (morphine hydrochloride 40mg/mL, Sterop, Belgium) at 0.003 and 0.417mg/L, respectively, in 48mL of NaCl 0.9%.
- The high concentration corresponding at 0.032 mg/mL of clonidine and 4.286 mg/mL of morphine was performed in five syringes of 14 mL NaCl 0.9%.
- All samples were visually examined immediately after the production and after 1 h, 4 h, 8 h, 24h, 48 h and 72h, on black and on white background.
- In addition, the apparition of turbidity was checked by spectrophotometric measurements (Genesys 10 series, USA) at three wavelengths (350, 410 and 550 nm) and pH was monitored with glass electrode pH-meter (Inolab level 1, WTW Weilhem, Germany with biotrode electrode, Hamilton, Bonaduz, Switzerland) throughout the period test.
- The crystal formation has been microscopically verified after centrifugation of each sample.

Résultats

- During the 72 h period, syringes at low and high concentrations have evolved in the same way.
- There were no changes in color or appearance of opacity, turbidity or precipitation.
- Spectrophotometric measurements and pH were not significantly affected.
- The microscopic analysis did not detect any aggregate or crystal formation.

Conclusions

- The mixture of clonidine and morphine hydrochloride at low and high concentrations in plastic syringes is physically stable for at least 72 hours at 4°C and at room temperature.
- These results paved the way for a subsequent study of chemical stability by Ultra Performance Liquid Chromatography.

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Possible conflict of interest : nothing to disclose.