LACK OF EFFECT OF KETAMINE ANALGESIA ON GASTRIC EMPTYING IN MAN

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SUMMARY

The effect of ketamine analgesia on gastric emptying was assessed in five healthy volunteers. Gastric emptying, estimated indirectly by the absorption of orally administered paracetamol, was not significantly delayed following administration of i.m. ketamine when compared with placebo.

Ketamine is a potent analgesic which may have some advantages in the period after operation by avoiding the respiratory and cardiovascular depressant effects of the narcotic analgesic drugs (Sadove et al., 1971). One major side-effect of all narcotic analgesics is a delay in gastric emptying and gastrointestinal transit which may contribute to nausea and vomiting and prevent patients recommencing oral fluids, food and medication in the early period after operation (Nimmo and Wilson, 1975; Nimmo et al., 1978). It is not known if ketamine in analgesic doses produces similar effects.

In the present study, we have investigated the effect of ketamine on gastric emptying in healthy volunteers, using the rate of paracetamol absorption as an index of gastric emptying rate. Paracetamol, a safe analgesic drug, is not absorbed to any extent from the stomach, but is readily absorbed from the upper small intestine. Thus, the rate of gastric emptying determines the rate of absorption of orally administered paracetamol. Simultaneous measurements of paracetamol absorption and gastric emptying have confirmed that measurement of the rate of absorption of orally administered paracetamol is a reliable estimate of gastric emptying (Nimmo et al., 1975, 1979; Clark et al., 1980). Rapid paracetamol absorption indicates rapid gastric emptying, whereas delayed paracetamol absorption reflects delayed gastric emptying.

SUBJECTS AND METHODS

Five healthy volunteers (aged 30–39 yr, weight 65–84 kg) were each studied on two occasions in random order at least 1 week apart, once after i.m. ketamine 0.5 mg kg$^{-1}$ and once after i.m. injection of saline. Ketamine 0.5 mg kg$^{-1}$ i.m. results in analgesic plasma concentrations (>150 ng ml$^{-1}$) from 15 to 45 min after injection without impairment of consciousness (Grant, Nimmo and Clements, 1981). The mean plasma ketamine concentration in six volunteers 20 min after this dose was 190±24 ng ml$^{-1}$ (±SEM).

After an overnight fast, and 20 min after the i.m. injection, the subjects received paracetamol 20 mg kg$^{-1}$ dissolved in 200 ml of orange juice. Venous blood samples were taken from an indwelling cannula before paracetamol administration and at 15, 30, 45, 60, 75, 90 and 120 min afterwards. The plasma was separated and stored at −20 °C until measurement of plasma paracetamol concentrations by high performance liquid chromatography (Howie, Adriaenssens and Prescott, 1977).

Paracetamol absorption was assessed from the plasma concentrations at each sampling time, the peak concentrations and the times to reach peak concentration. Statistical analyses were carried out using Student’s t test.

RESULTS

Paracetamol absorption (and hence gastric emptying) was normal following placebo in all five subjects, with a mean peak paracetamol concentration of 20.3±2.3 μg ml$^{-1}$ (SEM). The mean time of the peak concentration was 36±7.6 min after ingestion (Table I).

After ketamine 0.5 mg kg$^{-1}$ i.m., there was no significant delay in paracetamol absorption, a
TABLE I. Lack of effect of ketamine on paracetamol absorption in five subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean peak plasma paracetamol concn (µg.mL⁻¹ ± SEM)</th>
<th>Mean time of peak concentration (min ± SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>20.3 ± 2.3</td>
<td>36 ± 7.6</td>
</tr>
<tr>
<td>Ketamine</td>
<td>23.8 ± 5.3</td>
<td>63 ± 16</td>
</tr>
</tbody>
</table>

mean peak paracetamol concentration of 23.8 ± 5.3 µg.mL⁻¹ occurring 63 ± 16 min after ingestion. At no sampling time did the concentrations differ significantly from the placebo group (fig. 1).

In only one subject was there any delay in paracetamol absorption following ketamine, with a paracetamol concentration of 7.2 µg.mL⁻¹ 120 min after ingestion. A peak concentration of 17.9 µg.mL⁻¹ was achieved 45 min after placebo.

**DISCUSSION**

Ketamine in analgesic concentrations probably does not influence gastric emptying. Paracetamol absorption was almost identical in all but one of the subjects in the ketamine and control studies. In a similar study, pentazocine 60 mg i.m. given to healthy volunteers 30 min before paracetamol 20 mg kg⁻¹ produced a marked delay in paracetamol absorption in all subjects. The mean peak paracetamol concentration was 10.8 µg.mL⁻¹ at 160 min (control 23.8 µg.mL⁻¹ at 23 min) (Nimmo et al., 1979). Similar delay has been noted following pethidine 150 mg i.m. and diamorphine 10 mg i.m. (Nimmo et al., 1975).

Only one individual in this study experienced any delay in paracetamol absorption. Anxiety and sympathetic overactivity may have contributed to delay in this case (Rees et al., 1980).

Ketamine has been used as a postoperative analgesic which avoids several of the side-effects of narcotic analgesics (Ito and Ichiyanagi, 1974; Slogoff et al., 1974). In this study we have demonstrated that, in an analgesic dose, it has no significant effect on gastric emptying. This finding is consistent with a recent study reporting that ketamine has no effect on gastrointestinal activity in greyhounds (Healy et al., 1981). It may represent another advantage of the drug.

**ACKNOWLEDGEMENTS**

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**REFERENCES**


MANQUE D’EFFET DE L’ANALGESIE INDUITE A L’AIDE DE KETAMINE SUR LE VIDAGE GASTRIQUE CHEZ L’HOMME

RESUME

On a évalué sur cinq volontaires en bonne santé l’effet qu’a l’analgésie induite à l’aide de kéta mine sur le vidage gastrique. Le vidage gastrique, estimé indirectement par l’absorption de paracétamol administré par voie buccale, n’a pas été retardé de façon significative après l’administration intramusculaire de kéta mine, ceci par comparaison à un placébo.

WIRKUNGSLOSIGKEIT VON KETAMIN-ANALGESIE BEI DER MAGENENTLEERUNG BEIM MENSCHEN

ZUSAMMENFASSUNG


AUSENCIA DE EFECTO ALGUNO DE LA ANALGESIA MEDIANTE KETAMINA SOBRE EL VACIADO GASTRICO DEL HOMBRE

SUMARIO

Se evaluó el efecto analgésico de la ketamina en el vaciado gástrico de cinco pacientes sanos. El vaciado gástrico, que se estimó indirectamente por la absorción de paracetamol administrado oralmente, no se retrasó significativamente después de la administración de ketamina intramuscular, cuando se efectuó la comparación con el placebo.