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**Intravenous Access in Distressed Children:  
Effects of midazolam and nitrous oxide on  
success rate, hormone and metabolic stress  
responses**

**AKADEMISK AVHANDLING**

som för avläggande av medicine doktorsexamen vid Karolinska  
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## Abstract

### Background and Aims:

Intravenous (IV) access has demonstrated high levels of pain and distress in children. A stress full IV access should be avoided, primarily by the children, but also for the parents and staff. When testing children with suspected endocrine and metabolic disorders there is a substantial risk that a stressful IV access influences the hormone releases and metabolic response.

The aims of this thesis were to facilitate painful procedures and IV access in children at a paediatric outpatient clinic. To study the feasibility, effects and stress response of Nitrous Oxide (N<sub>2</sub>O) compared to Midazolam and EMLA alone in children with endocrine disorders and obesity

### Material and Methods:

Children with anxiety or previous difficulties establishing IV access were included (n=140).

50 children were openly randomised to EMLA (n=25) or EMLA+ N<sub>2</sub>O (n=25).

90 children (60 obese and 30 growth retarded) were double blinded randomised to; midazolam, 0.3mg/kg, max 15 mg, (n=30), 50% N<sub>2</sub>O (n=30), and to 10% N<sub>2</sub>O (n=30).

A subgroup of 20 anxious children undergoing repeatedly painful procedures was also included. These children underwent two procedures with EMLA and EMLA+N<sub>2</sub>O, the order of priority being randomised.

*Measurments: Number of attempts*; defined both as the number required to succeed in setting up double IV lines, and as a successful IV line procedure with 2 attempts for two iv lines vs >2 attempts, *IV access time*; defined as time from start of setting up the IV lines until two IV lines were established. *Recovery time*; defined as the time from establishment of the IV lines until regained alertness. *Total procedure time*; defined as IV access time plus recovery time. *Evaluations*; children's, parents' and nurses' satisfaction of the IV line procedure, *Pain*; evaluated by the child. *Sedation levels*; assessed using the Observer's Assessment of Alertness/Sedation Score.

*Blood samples* were obtained during 30 minutes at four time points after achieving venous access and, if possible, after 24 hours. 1; 0–1 min, 2; 5–6 min, 3; 14–15 min, and 4; 29–30 min. Analyses were compared between treatments and treatments over time.

60 children (40 obese and 20 growth retarded), served as controls.

### Results:

Comparing all study children together with IV access problems, a significant difference in number of attempts between the treatments groups were seen (P<0.001) with differences between midazolam compared with 50% N<sub>2</sub>O and EMLA compared with midazolam, 10%, 50% N<sub>2</sub>O. The percentage of successfully IV line procedures were 70% using 50% N<sub>2</sub>O.

The children's evaluations were significantly more positive for 50% N<sub>2</sub>O during IV access and painful procedures.

50% N<sub>2</sub>O was more efficient measured as total procedure time (P<0.001) and especially in obese children an unfavourable long procedure time was observed after midazolam.

Significantly lower cortisol levels were detected when midazolam was used compared to both 50% and 10% N<sub>2</sub>O and to unstressed controls. Glucose levels among growth retarded children increased from 0 to 30 min, whereas the opposite was found in obese children regardless of treatment. The growth hormone levels decreased with time in the midazolam group compared to 50% and 10% N<sub>2</sub>O, where the effect of time was reversed.

### Conclusion:

50% N<sub>2</sub>O in combination with EMLA, was in all aspects superior to midazolam for facilitation of IV access for distressed children. The IV access procedure was more efficient, with a shorter total procedure time and an increased number of successful IV lines.

Midazolam should only be used exceptionally in obese children due to the long recovery time.

Treatment with N<sub>2</sub>O and midazolam influence the results of hormone analyses in the form of different levels and trends in glucose and stress hormones.

Keywords: children, adolescents, intravenous access, pain, distress, stress response, hormone, metabolic