Critical Review: An Evaluation of Nitrous Oxide Analgesia During Transcutaneous Pacing by Kaplan, Heller, McPherson, and Paris

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In the paper, Evaluation of Nitrous Oxide Analgesia during Transcutaneous Pacing, by Kaplan et al., which appeared in the second issue of Prehospital and Disaster Medicine, there are several points made by the authors which require careful consideration before they are put into effect by the corps of EMTs and paramedics.

The search continues for a solution to the outstanding problem of discomfort and pain related to transcutaneous pacing (TCP), which presently constitutes a constraint on the application of TCP as a life support intervention. This paper reports a laboratory evaluation of the inhalation of 50:50 $\text{N}_2\text{O}/\text{O}_2$ ($\text{N}_2\text{O}$) as an analgesic, and proposes extrapolation of the results into the prehospital environment.

The study is important on two counts. First, it utilizes methods taken from analgesimetry, a technique widely applied but often with defective rigor in anesthesia, obstetrics, dentistry, and clinical pharmacology; and, second, by virtue of its position in a cohort of progressive studies, it may serve as a potential template for future investigations. The paper merits critical consideration on both counts. This commentary first will address general considerations and then specific aspects, in manuscript order.

The study exhibits, and the paper concedes, overt omissions in the rigor of design; firstly, in the application of the reference analgesimetry model and secondly, in the logic of the extrapolation to the clinical setting. In addition, however, there are covert omissions in the rigor of method of both data acquisition and processing. The entire study would be enhanced by the provision first of more explicit information on rationale, criteria, and technique of management of material, method, procedure, and protocol, which would both improve rigor and facilitate audit and evaluation of the study. In addition, if more detailed data were presented, it would help to identify internal errors and facilitate analysis and validation of the results.

The abstract and introduction are excellent. They provide a concise and lucid account of the investigative hypothesis and protocol. The methods invite consideration of the following comments, cataloguing errors, and omissions.

There is no statement of approval from ethical and experimental committees; perhaps this was implicit in the form of consent.

No rationale or criteria are given for the selection of the pacemaker-electrode combination in each subject; this is germane to the exclusion of correlation bias. There is no specific evidence of exclusion of confound-
The effect of \( N_2O \) on TVP thresh-

valve system introduces a placebo-

effect there might be a further

on TCP threshold is not; if there is

fraction); was ventilation "con-

trolled"? Cardiac output would be

raised both by pacing and the

experimentation model; this would

slow the rate of "induction."

Pharmacodynamically, \( N_2O \)

itself affects ventilation and car-
diatic output but the effect is still
dynamic at five minutes. In obstet-
rics, analgesia is obtained in 90 sec-
onds. No rationale is given for the
selection of the 30 seconds TCP
"challenge time." Was this dictated
by empirical, ethical, or cardiology-
ical constraints? If not, why was
extended TCP tolerance time not
subjected to measurement rather
than subjective "guesstimation,"
and extended to a "median pre-
hospital run time," as the authors
suggest?

Criteria for premature termination
of pacing are omitted. The
range given for PVAS (pain visual
analog score) extends only to 8
which seems paradoxical. The last
sentence of the methods section
seems far from exact! The results
are presented discursively, non-
algorithmically, and, despite the
small sample, with only summary
information, omitting supportive
detailed and tabulated data, thus
frustrating both internal and
external correlation analysis.

There is an obfuscating lack of
coherence of treatment between
the methods and results, for exam-
ple: "Electrical capture was docu-
mented for each of the room air
trials," omitting comment on cap-
ture verification in the \( N_2O \) trials;
or is this at variance with the ran-
donization protocol? "Prolon-
tation time" appears in the results
without reference or definition.

Such data, as are given, merit
comment. Of the 18 subjects
remaining after exclusion, 15
expressed subjective preference in
favor of \( N_2O \), for which signifi-
cance is omitted. The only signifi-
cant difference between the air
and the \( N_2O \) trial group is at
\( p<0.05. \) The pacing time (TCP tol-
erance time) trials report means at
22.4 and 23.8 seconds, with respec-
tive standard deviation of 10.2 and
9.6. These data are not normally
distributed and the \( t \) test is invalid.
In addition, a Chi-square test is
invalid when cells contain very low
counts, as appears to be the case
here.

In the subset of six subjects,
favoring \( N_2O \) but not achieving a
TCP tolerance time of 30 seconds,
large variability was noted, repro-
ducing scatter noted in one pilot
study (reference 10). Data are
omitted on scatter for the other
subsets. Capture threshold is
reported as \( 107\pm37 \) mA (sic \( ? \) s.d.),
implying a range of at least 70 to
144 mA. Insufficient data are pro-
vided to determine correlation
between threshold and either dis-
comfort rating or TCP tolerance
time.

These laboratory results must
be considered equivocal and inde-
terminate. Thus, subject to the
considerations above, the study
valuably could be repeated, aug-
mented, and extended. In the lab-
atory and the field, non-invasive
saturation oximetry measurements
should be incorporated. Para-
doxically, in the critically ill, hy-
pothetical consideration of \( N_2O \)
kinetics and dynamics favor both
rapid onset and synergy with other
modes of analgesia.

Finally, a question: if pacers with
a pulse duration of 20 msec consis-
tently evoke more pain than a
pace with a pulse duration (PD)
of 40 msec (not used in this study
and operating in different mode),
then, subject to technical and clin-
ical feasibility, might this not sug-
gest an alternative vector for
research and development?