# NITROGLYCERIN INFUSION FOR THE PREVENTION OF DECOMPRESSION SICKNESS

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## ABSTRACT

**INTRODUCTION**: Rapid decompression of nitrogen-saturated crewmen from a disabled submarine will likely require recompression treatment of multiple survivors, overwhelming resources. Nitric Oxide (NO) appears to decrease bubble formation and intravenous (IV) nitroglycerin (NTG) reduced bubble burden in sedated swine following dropout decompression from 40 meters (132 fsw) saturation. We postulated intravenous NTG might reduce Decompression Sickness (DCS) incidence in unsedated animals following saturation dropout from 60 feet of seawater (fsw) thus mitigating DCS in a mass casualty situation.

**MATERIALS AND METHODS**: Mature swine (n = 21, 71.0-75.8 kg, median wt 73.8 kg) underwent surgical central venous catheter placement then were placed in a Plexiglas box inside a hyperbaric chamber. The chamber was pressurized to 60fsw for 15.5 h; during the last 30 min at depth of the dive, pigs received either IV 5% Dextrose (D5W, n = 8) or NTG (n = 10, 0.4-1.05 μg • kg-1 • min -1). Animals were then decompressed at 30 fsw • min -1 directly to the surface. Signs of cutaneous (Type I), cardiopulmonary (CP) or neurologic (N) DCS (Type II) were recorded for a 2 observation period after surfacing. Data was analyzed by logistic regression methods.

**RESULTS:** There were no differences in body mass between groups (P > 0.5). Incidence of Type I (D5W=88%, NTG=100%, P > 0.5), Type II DCS (D5W=62%, NTG=90%, P > 0.2) or death (D5W=50%, NTG=30%, P > 0.3) did not differ between groups. There were no differences in time of onset for any DCS between groups (P > 0.3).

**CONCLUSIONS**: NTG does not appear to provide a benefit in reducing DCS. However, our delivery system resulted in a significant loss (30-60%) of NTG before entering the animal's circulation. Further investigation needs to be performed with modifications to the delivery system.

## BACKGROUND

- There is a need for DCS treatment adjuncts for diving missions with remote access to a hyperbaric chamber or a Disabled Submarine scenario when chamber resources would be overwhelmed
- Nitroglycerin has shown to decrease bubble formation in sedated swine at 0.4ug/kg/min for 30 min before surfacing
- This suggests there might be a DCS prevention benefit in unsedated 70kg swine, a realistic model for humans

## METHODS

***Animals***

- 21 neutered male Yorkshire swine (*sus scrofa*)
- Median weight 73.8 kg IQR 71.0-75.8 kg

***Pre-dive Preparation***

- Customized catheter inserted into left external jugular vein
- Custom designed fabric vest fitted around thorax and back secured and protected the catheter line and port
- After 24 h recovery animals lead into Plexiglas boxes within the Multiple Large Animal Chamber (MLAC)

***Hyperbaric Exposure Protocol***

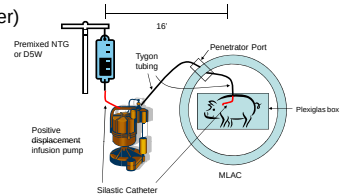
- 21 animals compressed to 60 fsw (1.8 ATA) with air
- Temperature maintained 26.7-29.4oC, humidity 50-75%, $CO_2$<0.3%
- After 15.5 h, dropout decompression to surface (30 fsw/min)

***2h Surface Observations***

- Cutis marmorata
- Cardiopulmonary
- Neurologic

***Study Groups***

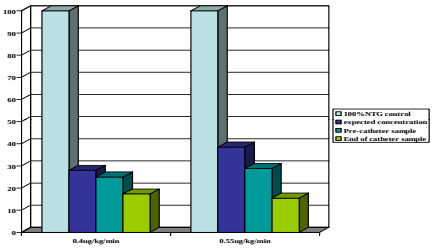
- 4 excluded from analysis (occluded/leaky catheter)
- Group I - 30 min D5W infusion (n=8)
- Group II - 30 min NTG infusion (n=9)
- No differences in weight (p > 0.5)




***Methodologic Problems***

- Initial results not promising
- Suspicions that catheter system (~16' long) was absorbing NTG
- Interim analysis used High Pressure Liquid Chromatography (HPLC)
- Dose adjusted to 0.55 ug/kg/min based on estimated loss; HPLC re-analyzed

**HPLC analysis of NTG degradation in catheter**




- HPLC analysis showed 38% loss of drug from desired dosage at 0.4ug/kg/min
- To compensate, increased dose to 0.55ug/kg/min

## RESULTS

- Repeat analysis showed 40% loss of drug
- Put pig in chamber on telemetry and increased dose until tachycardia and signs of agitation
- 0.8ug/kg/ml appeared effective
- Shortened tubing and re-piped with stainless steel

**Table 1. Deaths by study group 24 h post-dive**

| Group | Alive at 24 hours | Dead at 24 hours |
|---|---|---|
| Control (D5W) | 4 | 4 |
| NTG (low 0.4-0.55ug) | 3 | 2 |
| **NTG (high 0.8ug)** | **4** | **0** |
| Total | 11 | 6 |

**Table 2. Type I DCS by study group 24 h post-dive**

| Group | No Type I event | Type I event |
|---|---|---|
| Control (D5W) | 1 | 7 |
| NTG (low 0.4-0.55ug) | 0 | 5 |
| NTG (high 0.8ug) | 0 | 4 |
| Total | 1 | 16 |

**Table 3. Type II DCS by study group 24 h post-dive**

| Group | No Type II event | Type II event |
|---|---|---|
| Control (D5W) | 3 | 5 |
| NTG (low 0.4-0.55ug) | 3 | 2 |
| NTG (high 0.8ug) | 1 | 3 |
| Total | 7 | 10 |

## CONCLUSIONS

- **15h saturation at 60fsw achieved 35% death, 94% Type I and 59% Type II DCS**
- **NTG substantially degraded in long catheter system; shorter line and increased dose may be the solution**
- **NTG does not appear to impact Type I or Type II DCS**
- **It might be protective of death, but numbers are too small** If we assume that the lower dose of NTG is ineffective and thus pool the low dose pigs with the control arm, the approximate proportion of deaths is 0.50. Assuming 0.50 is the true proportion of deaths, a sample size of 15 to 20 pigs per group will provide 80% power to detect a reduction from 0.50 to 0.10
- We are in the process of diving another 23 animals

***ACKNOWLEDGEMENTS***

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