Effect of Nasally Administered Surfactant on Eustachian Tube Dysfunction

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INTRODUCTION

Eustachian tube dysfunction (ETD) in the presence of environmental pressure fluctuation can result in middle-ear barotrauma (MEB). Among the diving, aviation, and hyperbaric medicine communities MEB represents one of the most prevalent occupational medical or operational complications that often limits performance. There is currently no simple method for equalizing middle ear pressure once it occurs (short of myringotomy). This study used easily administered drugs in an attempt to prevent or delay the onset of ETD. Conclusive findings for the efficacy of pharmacological interventions in preventing ETD would provide valuable guidance to the operational communities for enhancing mission success during routine or special operations that involve hypo-/hyperbaric exposures.

OBJECTIVES

The aim of this study was to measure the efficacy of easily administered pharmacologics in preventing ETD. The tested medications were given via nasal mist into the nasopharynx or ingested in pill form (only pseudoephedrine). The intra-nasal medications included oxymetazoline, Mucomyst® (a mucolytic agent), surfactant (supplied by Survanta®), and saline. Subjects underwent pressure changes in the water while breathing compressed air or oxygen in two separate arms of the study to evaluate the impact of the drugs in both compressed air and hyperoxic environments.

METHODS

Eight male US Navy trained divers volunteered for the study. The endpoints for measurement included Eustachian tube opening pressure (ETOP), nine step inflation/deflation tympanogram (NSI/DT), and number of holds during the repetitive dives. All subjects took one of the medications prior to a dive "series" which consisted of several bounce dives conducted over 3 consecutive days. Each day, ETOP and NSI/DT was measured before and after the dives. Holds and aborts during the diving were noted as they occurred.

ETOP

This was measured by using sonotubometry. In this technique, the subject placed a pressure transducer over one nostril and a speaker over the contralateral nostril. Both of these devices completely occlude the nasal orifices, mimicking the action of pinching the nostrils shut. A microphone is placed in the ear canal ipsilateral to the speaker. When prompted, the subject attempts a smooth increase in effort to equalize pressure in the middle ears. When the sound levels at the microphone increase due to conduction of the sound through a patent Eustachian tube, successful equalization has occurred (see Figure 1).

The instrument superimposed the pressure tracing vs time over a graph of the sound levels at the microphone vs time. By determining the relative pressure at the time of increased sound levels, the ETOP could be determined. The higher the ETOP, the more difficult it was for a subject to clear, and thus, the more significant the degree of ETD.

Procedures

After baseline ETOP and NSI/DT were taken, each subject took a pill and an intranasal fluid 15-30 minutes prior to the first dive. Subjects were blinded to the nature of individual medications. When one of the four intranasal test medications was administered, a lactose placebo pill was used. When the oral pseudoephedrine was tested, intranasal saline was administered as a "placebo" for blinding purposes.

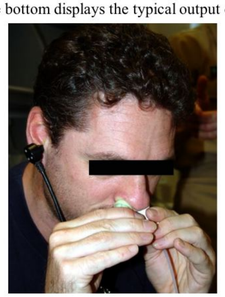
A hyperbaric chamber with immersion tanks inside was utilized for the dives. Divers wore wet suits without hoods and were completely submerged in 60ºF water to simulate operational conditions. An air dive consisted of descent to 60 fsw, staying for 2 minutes, followed by an ascent to surface, a one-minute interval, and then repeating this procedure until 4 excursions had been completed. When the oxygen arm of this study was executed, the protocol was identical except descents were limited to 15 fsw instead of 60 fsw.

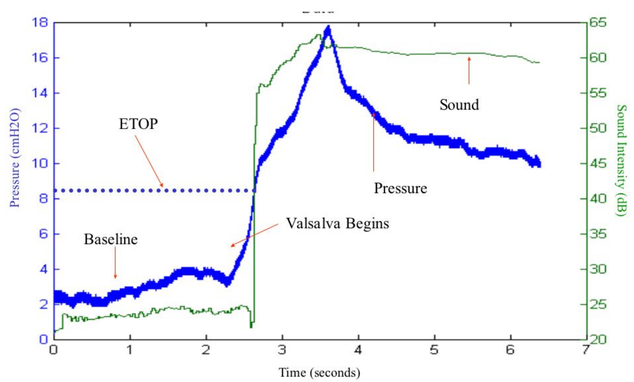
After the dive, repeat ETOPs and NSI/DTs were obtained on all divers. This routine was repeated for 3 consecutive days with a subject taking the same medication prior to the dive each day for a 3-day series.

RESULTS

Only 4 of the 8 divers completed the air dives on all 5 of the drugs while all eight subjects achieved this under oxygen conditions. After normal distributions were confirmed, a linear mixed model ANOVA analysis revealed several significant differences when considering the changes in gases (oxygen vs air diving), the 5 drug conditions, and the consecutive days of diving. In all cases, a lower ETOP indicated that the subject was able to equalize the middle ear pressures with less effort in that circumstance.

Figure.1: The left picture displays the sonotubometry setup used to elicit the Eustachian tube opening pressure (ETOP). The right picture displays a subject utilizing this system while performing a middle ear equalization maneuver to measure the ETOP. The graph at the bottom displays the typical output of the instrument.





RESULTS (continued)

The overall mean pre-dive and post-dive ETOP for the air dives was higher when compared to the same two measures in the oxygen group (both p <0.001). Otherwise, no differences between these two groups were observed.

When comparing mean pre-dive and post-dive ETOPs, the pre-dive ETOP was higher than the post-dive measurement for oxymetazoline (p =0.04). Also, the mean pre-dive ETOP for the Mucomyst® condition was lower than all other pre dive drug conditions (p-values from .007 to < .001). (Figure 2)

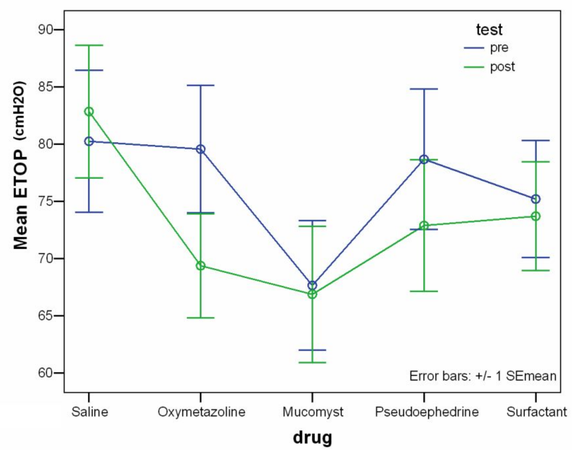
For dive effects, under the pre-dive measurements for oxymetazoline, dive 1 was shown to have significantly higher ETOP than both dive 2 and 3 (p < .001 and p = .04, respectively). The dive effect found for the Mucomyst® condition was that the mean for pre-dive 1 ETOP was lower than pre-dives 2 and 3 (p =.02 and p = .001, respectively). (Figure 3).

There were too few holds to draw conclusions and the NSI/DT data produced inconsistent and conflicting results.

CONCLUSION

Some of the findings in this study were counter-intuitive. For example, oxygen would be expected to be associated with higher ETOPs since most anecdotal reports indicate increased clearing difficulty with oxygen diving. The same would be expected post-dive and after consecutive diving days, but this was not observed. Perhaps the absence of these findings is because equalizing the middle ear can become easier after multiple successful attempts in a short period of time.

Figure 2: Drug by test interaction ($F_{8, 668} = 4.05$; $P < .001$). Oxymetazoline pre-dive ETOP was significantly higher than post-dive. Mucomyst was significantly lower than all other pre-dive drug conditions. Post-dive Mucomyst was significantly lower than saline.



ACKNOWLEDGMENTS

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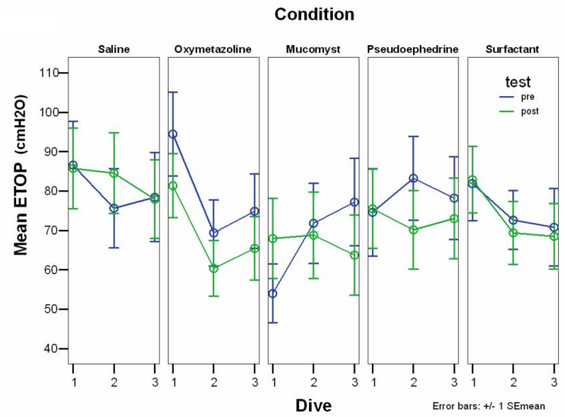
Figure 3: Test by drug by dive interaction, data from the air and oxygen dives is combined ($F_{16, 668} = 2.47$; $P = .001$). Pre-dive 1 ETOP of oxymetazoline is significantly higher than pre-dives 2 and 3. Mucomyst pre-dive 1 is significantly lower than pre-dive 2 and 3 ETOP.



CONCLUSION (continued)

Another disconcerting trend was the wide variance in mean pre-dive 1 ETOP. As these are "baseline" ETOPs, taken before any exposures to diving or drugs, the means should be fairly similar. The wide variability observed for those measurements is indicative of the extreme variability in ETOP measurements both within and between subjects.

The results suggest that oxymetazoline may offer the most improvement in function, as ETOPs consistently declined in both pre- and post-dive measurements from dive 1. They also suggest that Mucomyst® offers the least advantage in consecutive days of diving.

Although this study did find some observable differences, the large inter-/intrasubject variability in ET function, as measured by sonotubometry and NSI/DT in our sample divers with normal ET function, limited our ability to observe unequivocal benefits for the pharmacological interventions tested. Further refinement in sonotubometry as a tool for measuring ETD, and enrolling subjects with poor ET function may provide the best chance of observing a significant benefit for administering pharmacologics on ETD.

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