Hyperbaric oxygen (HBO) therapy involves the inhalation of 100% oxygen under a pressure greater than 1 atm. Both therapeutic and toxic effects result from two features of treatment: mechanical effects of increased pressure and physiologic effects of hyperoxia. HBO therapy has long been accepted as the primary treatment for decompression sickness. Other common clinical indications include...
suggested by the Undersea and Hyperbaric Medical Society included air embolism, carbon monoxide and/or cyanide poisoning, acute traumatic ischemia, necrotizing soft-tissue infection, probable skin grafts and flaps, thermal burns, and exceptional blood loss anemia when transfusions are not possible. The urological indications of HBO included hem or rhagic cystitis, Fournier’s gangrene and necrotizing fasciitis. Although oxygen has no significant direct antimicrobial effects on aerobic or facultative anaerobes, neutrophils require oxygen to aid in phagocytosis of all microbials. Also, HBO can facilitate the transport of some antibiotic agents across the bacterial cell wall and improve their overall effect. In the treatment of infections and open wounds, an increase in oxygen concentrations may lead to a direct toxic effect on some aerobic bacteria by inducing free radical formation. Thus, HBO is clearly of value for carefully defined indications. Successful extension of its use in other situations will be predicated on in vitro and in vivo experimental evidence and appropriate, well-controlled clinical trials.

Up to now, there is a small amount of data available concerning the effect of HBO on an i mal pyelonephritis, but no clinical study on the therapeutic efficacy of HBO in acute bacterial pyelonephritis or pyonephrosis. As kidney function is deteriorated by stone obstruction, local anti-biotic concentrations can hardly reach the therapeutic levels. It seems reasonable to consider that HBO might be beneficial for in vitro stone pa tients with pyelonephritis and/or pyonephrosis. Furthermore, an interesting question accompanying the potential application of HBO in urology is whether HBO can improve the dissolution of in vitro stone stones. The present study was thus aimed at in vitro testing the dissolution activity of human in vitro stone stones under hyperbaric oxygen conditions.

**Methods**

All the in vitro stone stones used for this experiment were obtained from 8 different patients either through percutaneous nephrolithotomy or open surgery. Group 1 stones were dissolved in UROCITRA solution (Gen tle Corp., Taiwan) under room temperature and normal atmospheric condition. Group 1 consisted of 7 pure struvite stones and 10 mixed struvite and carbonate apatite stones. Group 2 stones were dissolved in UROCITRA solution under room temperature and 2.5 atmospheres (2.5 atm) hyperbaric oxygen. Group 2 consisted of 7 pure struvite stones and 11 mixed struvite and carbonate apatite stones. The compositions of 1 liter UROCITRA were citric acid: 32.3 gm, MgO: 3.8 gm, sodium carbonate: 7 gm. The compositions of obtained stones were examined by infrared spectrometer (Jasco FT/IR-5300, Tokyo, Japan). The dissolution apparatus is shown in Fig. 1. The UROCITRA solution was dripped by gravity and controlled by an IV set at a continuous flow rate of 150 ml/hour. Hyperbaric oxygen treatment of group 2 stones consisted of 2 experiments (2 hours for each experiment) in the monoplace chamber (Sigma IN-124, Florida, USA) at 2.5 atm. At a fixed time interval in each experiment (2 and 4 hours, respectively), the stones were dried in an oven (50 °C, 30 minutes) and then weighed. The gross appearance and the maximum diameter of each stone were recorded. Decrease in the dried stone weight after dissolution was calculated as the percentage of stone weight left after UROCITRA dissolution, i.e., % stone weight decrease = (ISW-ESW)/ISW × 100, where ISW is the initial stone weight and ESW is the stone weight after a fixed time in ter val of dissolution treatment. By using the initial stone weight as the denominator of the formula, we could avoid the errors caused by the different dis-
solution rates and different surface area between stones as suggested by Burns et al.\textsuperscript{14} The measurements of the partial pressure of oxygen (PO\textsubscript{2}) in tap water and UROCITRA solution were performed with an oxygen analyzer (Ciba Corning, Model-288, USA). In order to verify the renal action of HBO in humans, the oxygen concentrations of urine samples collected immediately before and after 2.5 atm HBO treatment from 5 osteomyelitis patients were also measured for comparison.

Statistics

Statistical analysis was carried out using Student’s \( t \) test. A probability less than 0.05 was considered significant. Results are expressed as mean ± SD.

Results

Of the group 1, 7 were struvite stones with an average weight of 166.8 ± 43 mg (range 107.6 to 219.9 mg), which was not significantly different from that of group 2 (170.3 ± 39.3 mg, range 121.2 to 220.8 mg). Similarly, there was no significant difference in the weight of mixed struvite and carbonate apatite stones between groups (185.8 ± 58 mg, range 120.9 to 327.8 mg vs. 185.5 ± 55.9 mg, range 124.3 to 320.1 mg).

Under 2.5 atm hyperbaric oxygen status, the PO\textsubscript{2} of tap water and UROCITRA solution were 358 ± 56 mmHg and 365 ± 44 mmHg, respectively (Fig. 2), which was significantly higher than those of tap water (113 ± 62 mmHg) and UROCITRA solution (125 ± 12 mmHg) in normobaric condition (\( p < 0.001 \)). The oxygen concentrations of urine samples from 5 osteomyelitis patients after 2.5 atm HBO treatment (228 ± 66 mmHg) in increased significantly when compared to that of the control urine collected immediately before HBO (126 ± 32 mmHg, \( p = 0.014 \)).

The dissolution response of pure struvite and mixed struvite and carbonate apatite stones appeared to be linear with time. The dissolution curves of struvite stone after UROCITRA solution chemolysis under normol and HBO condition are shown in Figs. 3 and 4. The percentage decreases in the dried weight of struvite under normal condition were 31 ± 8.8% and 48 ± 15% at the 2\textsuperscript{nd} and 4\textsuperscript{th} post-treatment hours, respectively. UROCITRA solution enriched with HBO did not significantly increase the dissolution of struvite as in indicated in the comparable weight loss at the corresponding time intervals (31.2 ± 14.6% and 54 ± 19%, respectively, \( p > 0.05 \)). As shown in Figs 3 and 4, struvite stones from different patients and different stone sizes from the same patient exhibited distinctly different dissolution curves, suggesting that the density and the size of stones may influence the dissolution activity.

Fig. 2. The oxygen concentration of 2.5 atm HBO-treated tap water and UROCITRA solution were significantly higher than those of tap water and normal UROCITRA solution (\( * p < 0.001 \)). After 2.5 atm HBO treatment, the PO\textsubscript{2} of patient’s urine were significantly increased (\( **p = 0.014 \)).

Fig. 3. Dissolution curve of struvite stone under normal condition.
The dissolution curves of mixed struvite and carbonate apatite stone after UROCITRA chemolysis under normal and HBO conditions are respectively shown in Figs. 5 and 6. No significant differences in the % decreases of the dried stone weight after 2 or 4 h of chemolysis were found between normal and HBO conditions (17.1 ± 3.8% and 26.7 ± 4% after 2 h of treatment, p = 0.0005; and 48 ± 15% vs. 26.7 ± 4% after 4 h of treatment, p = 0.0007) or HBO condition (31.2 ± 14.6 vs. 15.3 ± 4.6% at the corresponding time, p = 0.004 and 54 ± 19% vs. 28.2 ± 9.3% at the corresponding time, p = 0.001).

Discussion

Fundamental knowledge regarding HBO therapy is continuously increasing, and HBO is clearly of value for carefully defined indications. Recently, Kolski et al. demonstrated HBO treatments significantly reduce ischemia-reperfusion-induced injury to the testis in animal. Klotz studied the effect of HBO on chronic pyelonephritis in rats and reported that HBO at 2 atm was of no value in the prevention or amelioration of chronic pyelonephritis in this animal. However, the resurgence of interest and comprehensive study of HBO therapy for acute pyelonephritis and pyonephrosis may be worthwhile. Successful extension of its use in other situations will be predicted on in vitro and in vivo evidence and appropriate, well-controlled clinical trials. We assumed that HBO might be beneficial for infective stone patients with pyelonephritis and/or pyonephrosis. As deterioration in renal function due to stone obstruction may result in impaired oxygen delivery and oxygen metabolism, local antibiotic concentration...
tions can hardly reach therapeutic levels. HBO may increase local kidney tissue oxygen concentration and thereby facilitate the resolubilization of the infected stones. To our knowledge, the effect of HBO on the dissolution activity of human infected stones has not been explored. By using UROCITRA solution as a chemolytic agent, the present study aimed to examine the dissolution activity of human infected stones and determine if HBO treatment would facilitate the resolution of infected stones.

Obviously, the variability of size, porosity, density, and permeability of stones may influence their dissolution activity. Artificial stones may be a good alternative for further dissolution study.

In conclusion, this study demonstrated that UROCITRA solution enriched with 2.5 atm HBO did not augment the dissolution of infected stones. The percentage decreases in the dried weight of pure struvite and mixed struvite and car bonate apatite after treatment with UROCITRA solution were not significantly different from those obtained under normobaric HBO conditions. However, the dissolution of pure struvite was significantly greater than that of the mixed stone. The results of the present study provide some useful information on the treatment of acute pyelonephritis and pyonephrosis.

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References


22. Suby HI, Alb right F. Dis so lu tion of phos phatic uri nary cal culi by the re tro grade in tro duc tion of a ci trate so lu tion con tain ing mag ne sium. *N Engl J Med* 1943;228:81-91.


