Lytic Effects Of Water On Bladder Cancer Cells – Implications For Continuous Bladder Irrigation After TURBT

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INTRODUCTION

- Recurrence of NMIBC after TURBT is observed in 40-80% of patients
- Intraoperative spillage of cells can lead to tumour cell re-implantation and local recurrence
- Intravesical chemotherapy is effective at reducing recurrence, but is underutilised due to high cost and toxicity
- Bladder irrigation with water as opposed to saline may be a comparable alternative to chemotherapy as it causes osmotic cytolysis in addition to mechanical dilution to remove remaining viable cells

AIMS

1. To determine the time course of osmotic effects of water on bladder cancer cells in vitro and in vivo
2. To determine whether water is able to lyse cancer cell lines other than bladder cancer in vitro
3. To determine what degree of contamination by urine or blood nullifies the effects of water’s osmolytic properties

METHOD

IN VITRO

- Two bladder cancer cell lines (HT1197, HT1376) were exposed to water, 0.9% saline or 1.5% glycine
- Cell counts were performed with trypan blue exclusion in triplicate at regular intervals for 5h
- These experiments were repeated for colorectal (UIM4205, KM23), ovarian (COV434), and renal (SKRC52) cancer cell lines
- HT1197 & HT1376 were also exposed to varying concentrations of NaCl to determine if increases in osmolarity would impede water’s efficacy

IN VIVO

- 23 patients received saline or water irrigation for 3h post-TURBT
- Hourly 200mL washout samples were collected for cell counting at 0, 1, 2, and 3 hours post-TURBT
- Selected patient samples were sent for immunohistochemistry (IHC)

RESULTS

IN VITRO (Figures 1 & 2)

- Water caused 100% cell lysis within 20 minutes
- Both saline- and glycine-irrigated samples had viable cells remaining at 5h
- Similar results were achieved on all 4 other cancer cell lines
- Gradation study showed that an increase to 0.045% NaCl would impact the osmotic functions of water

IN VIVO (Figure 3)

- 14 patients received water irrigation in vivo
  - Time 0 (median) = 14 x 10^3 cells
  - 1 hour onwards (median) = 0 cells
- 9 patients received saline irrigation in vivo
  - Time 0 (median) = 40 x 10^3 cells
  - 3 hours (median) = 20 x 10^3 cells
  - Median cell count never reached zero

RESULTS CONT.

- IHC (Figures 4 & 5) on ex vivo samples showed significant numbers of bladder epithelial cells in saline-irrigated patients and low numbers in water-irrigated patients
- Cytokeratin 7 (CK7) shows bladder epithelial cells in brown

CONCLUSIONS

Water is able to rapidly lyse bladder cancer cells in vitro and in vivo. A short 3-hour period of water irrigation post-TURBT may be an effective intervention to reduce bladder cancer recurrence

- Water is able to lyse viable cells in at least 4 other cancer cell lines
- An increase from 0% NaCl (pure water) to 0.045% NaCl is sufficient to alter the efficiency of cytolysis

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Figure 1. Visible cell numbers for bladder cancer cell line HT1197 when exposed to water, saline or glycine for up to 5h.

Figure 2. Viable cell numbers for bladder cancer cell line HT1197 when exposed to decreasing concentrations of NaCl. Data represents median values of n = 3 measures.

Figure 3. Water vs saline in vivo.

Figure 4. IHC for a saline-irrigated patient.

Figure 5. IHC for a water-irrigated patient.