Effect of Local Hyperthermia of the Bladder on Mitomycin C Pharmacokinetics during Intravesical Chemotherapy for the Treatment of Superficial Transitional Cell Carcinoma.


Abstract:

AIMS: To assess the effect of local hyperthermia on the systemic absorption of mitomycin C (MMC) during intravesical chemotherapy for the treatment of superficial transitional cell carcinoma of the bladder, and to establish the likely safety of this procedure.

METHODS: Group 1 (n = 12) received 20 mg intravesical MMC plus local hyperthermia, group 2 (n = 13) 20 mg MMC alone, group 3 (n = 16) 40 mg MMC plus local hyperthermia and group 4 (n = 10) 40 mg MMC alone. Patients in groups 1, 2, and 4 underwent post-tumour resection adjuvant treatment, whereas those in group 3 still had tumour present and were treated to eradicate it. Intravesical instillation lasted 60 min, with the solution (50 ml) being replaced after the first 30 min. Blood samples were taken before, and every 15 min during instillation. MMC concentrations in plasma and in urine were determined by h.p.l.c.

RESULTS: The highest MMC plasma concentration (67.9 ng ml(-1)) occurred in a patient in group 3. This value was well below the threshold concentration (400 ng ml-1) for myelosuppression. Local hyperthermia associated with the intravesical chemotherapy enhanced plasma MMC concentrations at 30, 45 and 60 min compared with chemotherapy alone (Group 1 vs 2, P < or = 0.008). Systemic exposure to MMC was not significantly increased by doubling the intravesical dose when intravesical chemotherapy alone was administered. Patients in group 3 displayed the highest degree of MMC absorption and the greatest variability in pharmacokinetics between patients.

CONCLUSIONS: Local hyperthermia enhances the systemic absorption of MMC during intravesical chemotherapy for bladder cancer. In the doses used, plasma MMC concentrations were always more than six times lower than those shown to cause toxicity.