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Targeted cancer chemotherapy with arterial microcapsule chemoembolization: review of 1013 patients

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Abstract To evaluate the feasibility of intraarterial infusion of microencapsulated anticancer drugs (chemoembolization), collective data on 1013 cancer patients were reviewed. Ethylcellulose microcapsules containing mitomycin C (median total dose 20 mg), cisplatin (60 mg) or peplomycin (40 mg) were given to tumor-feeding arteries by bolus infusion in 79% of the patients and by fractionated infusion in the others, as a palliative (71%) or preoperative measure (29%). The target sites were the liver (42%), kidney (24%), intrapelvic organs (18%), lung (4%), head and neck (3%), bone (1%) and others (9%), excluding the central nervous system and gastrointestinal tract. The incidence of overall adverse effects ranged from 0.2 to 54.9%, but grade 2–3 hematological, renal and hepatic toxicities, local pain, abdominal discomfort, cutaneous reaction, remote embolization and infection were $<10\%$. Nine patients (0.9%) in the early stages of trials suffered serious complications including treatment-related death in two with critical underlying diseases of the target organs. The remaining patients recovered from the adverse effects, except for grade 2 cutaneous reactions, within 2 months by routine palliative measures. A $\geq 50\%$ tumor reduction was seen in 28% of 427 evaluable tumors (42% for <25-cm^2 tumors and 20% for ≥ 25-cm^2 tumors) with a median treatment number of one. The response rate depended on both the tumor size and the treatment number ($P<0.05$), but it was not affected by prior therapies. Mitomycin C microcapsules produced a higher response rate. Complete or partial remission of intractable pain and genitourinary gross hemorrhage was found in two-thirds of eligible patients. The results indicate that this treatment modality, though restricted by catheter technique, can be applied to various tumor lesions with an acceptable morbidity and prospective trials are justified to evaluate the potential role of such a targeted chemotherapy.

Key words Microcapsules · Arterial infusion · Chemoembolization · Cancer chemotherapy · Targeting

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Introduction

Over the last two decades, targeting of drugs to tumor cells or tumor lesions by means of a drug carrier has been considered a promising approach to overcome the low therapeutic index of available anticancer drugs [8]. Investigations so far, however, have failed to detect any versatile carrier system which is capable of transporting the drugs from the site of application directly to the prescribed site of action [37]. Widder et al. [36] defined three sequential processes of intravascular drug targeting and emphasized that the drugs or drug-carrier complexes must be restrictively distributed into the tumor vascular beds and migrate into the parenchyma through the vascular wall (first-order targeting).

We have developed selective infusion of microencapsulated anticancer drugs into tumor-feeding arteries. The microcapsules (MC) entrapped by the target arterioles release the encased drug at a prescribed ratio into the surrounding tissues [11, 12]. Since the therapeutic function comes from both arteriolar embolization and prolonged drug action, this mode of treatment has been described as "chemoembolization" [13–15] and has been characterized as prototype first-order drug targeting [3, 37, 38]. Animal studies have demonstrated that chemoembolization with microencapsulated drugs significantly enhances the local drug availability while decreasing systemic drug availability, as compared with conventional intraarterial

infusion of nonencapsulated drugs either alone or in combination with vascular occlusion [3, 9, 12, 24]. This superiority of MC therapy has been supported by the pharmacokinetic profiles, tumor responses and systemic drug toxicities in patients with carcinoma of the kidney [14], liver [7, 27, 33], intrapelvic organs [22] and head and neck [29]. In addition, it has been suggested that this therapy prolongs the survival of responders with inoperable hepatic tumors [2, 28], controls intractable symptoms [5, 10, 30], facilitates radical surgery for locally advanced tumors and improves the postoperative survival of patients with these tumors [17, 18].

Arterial chemoembolization utilizing various drug carrier systems has become a treatment of choice for localized tumors resistant to conventional chemotherapy [2, 5, 6, 7, 20]. The results appear encouraging, but the trials are still sporadic and empirical. Data on a large number of patients will be required to verify the feasibility of such a targeted chemotherapy. We reviewed 1013 patients subjected to MC chemoembolization in our country.

Materials and methods

Patients

Between March 1978 and December 1992, 1013 cancer patients were subjected to MC therapy in 83 hospitals in Japan, including our institution. MC were supplied from our laboratory to these institutions in response to a request by the responsible doctors, who obtained informed consent from their patients and/or families and cleared any relevant ethical regulations.

Microcapsules and infusion technique

Ethylcellulose MC with a maximal diameter of 225 ± 55 μM (mean ± SD), encasing mitomycin C (MMC), cisplatin (CDDP) or peplomycin (PEP), were prepared as described previously [9, 16]. The dose was expressed as the biologically active drug content of the MC. The mean drug content was 55% (w/w) for MMC-MC (mean drug release in 25° C physiological saline stirred at 25 rpm, 2.1 μg/mg per min), 60% for CDDP-MC (mean drug release, 4.2 μg/mg per min) and 56% for PEP-MC (mean drug release, 29.4 μg/mg per min). MMC-MC were supplied to most of the doctors because MMC is better suited to microencapsulation and has been commonly used in this country for more than 30 years with a low market price.

MC dispersed in physiological saline were selectively infused into the tumor-feeding arteries through percutaneous catheterization under X-ray monitoring. When selective catheterization was difficult, MC were administered after mechanical embolization of the adjacent nontarget arteries with gelfoam pieces or steel coils. For tumors such as renal and hepatic carcinoma having arterio-venous fistulae, MC were infused after mechanical embolization of the fistulae to avoid inadvertent migration of MC into the systemic circulation.

The maximum dose was settled at 40 mg/m^2 for MMC-MC, 80 mg/m^2 for CDDP-MC and 60 mg/m^2 for PEP-MC. The dose for individual tumors was determined by the volume of the tumor vascular bed under angiographic monitoring, that is, MC were infused until the tumor vascularity disappeared. Repeat treatment at a 4-week interval was recommended.

Evaluation

The present study was based on the treatment reports collected from the responsible doctors 3 to 6 months after the completion of MC therapy. The median follow-up period of the patients was 98 days (range 21–327 days) after treatment initiation. Evaluations were made for the patients who received no other therapies for at least 4 weeks before and after MC therapy, unless otherwise specified. The Chi-squared method was used for comparisons and a P-value of <0.05 was taken as significant. Performance status at treatment initiation was classified by a 5 grade system [23].

Side effects and complications

Hematological toxicity was defined by the maximal decrease in hemoglobin, leukocyte and/or platelet counts of the peripheral blood in relation to the pretreatment values: grade 0 (a decrease of $\leq$25%), grade 1 (26–50%), grade 2 (51–100%) and grade 3 ($\geq$100%). Renal toxicity was defined by the relative increase in serum creatinine values: grade 0 (an increase of $\leq$25%), grade 1 (26–100%), grade 2 (101–200%) and grade 3 ($>$200%). Hepatic toxicity was defined by the relative increase in serum glutamicoxaloacetic transaminase, glutamic-pyruvic transaminase and/or bilirubin values: grade 0 (an increase of $\leq$25%), grade 1 (26–100%), grade 2 (101–200%) and grade 3 ($>$200%). Renal toxicity was evaluated in the patients undergoing renal arterial infusion and hepatic toxicity in those undergoing hepatic arterial infusion, because each adverse effect was exceptionally encountered in the corresponding treatment.

Elevation of temperature over 38° C (fever) was defined by the duration: grade 0 (afebrile), grade 1 (fever for $\leq$7 days), grade 2 (8–14 days) and grade 3 ($>$14 days). Abdominal discomfort such as anorexia, nausea and vomiting was defined by the duration: grade 0 (asymptomatic), grade 1 (symptoms for $\leq$7 days), grade 2 (8–14 days) and grade 3 ($>$14 days). Pain in the target area (local pain) was defined by the duration requiring analgesic treatments: grade 0 (no pain nor analgesic treatment), grade 1 (analgesic treatment for $\leq$7 days), grade 2 (8–14 days) and grade 3 ($>$ 14 days). Cutaneous reactions in the target area were defined as: grade 0 (no reaction), grade 1 (erythema or vesiculation), grade 2 (ulceration) and grade 3 (ulceration requiring surgical intervention). Inadvertent migration of the embolic substances to distant sites (remote embolization) was defined as: grade 0 (no objective or subjective signs), grade 1 (slight symptoms requiring no treatment), grade 2 (symptoms requiring intensive palliative care) and grade 3 (surgical intervention required). Infection in the target organs was defined as: grade 0 (no infectious sign), grade 1 (improved by antibiotic agents), grade 2 (abscess formation) and grade 3 (sepsis). These and miscellaneous adverse effects were evaluated in all patients regardless of the follow-up periods and other therapies.

Tumor response

The sum of the products of the two longest perpendicular diameters of all tumors in the target sites was assessed by computed tomography (CT scan), echography or endoscopy. Tumor response for a minimum of 4 weeks was defined as complete response (CR; disappearance of all measurable tumors), partial response (PR; $\geq$50% tumor reduction), minor response (MR; 25–49% tumor reduction), no change (NC; $<$ 25% tumor reduction or increase) or progressive disease (PD; $\geq$25% tumor increase). Bone lesions were excluded from the evaluation.

Palliative effects

Pain relief in the target sites was defined as complete remission (CR; complete disappearance of pain for $\geq$4 weeks) or partial remission (PR; improvement in pain with a substantial decrease in other analgesic regimens for $\geq$4 weeks). The hemostatic effect on urogenital hemorrhage was defined as complete remission (CR; complete disappearance of gross hemorrhage for $\geq$4 weeks) or partial remission (PR; substantial decrease in gross hemorrhage requiring no hemostatic regimens for $\geq$4 weeks).

Results

Profiles of the patients

Of the 1013 patients treated with MC therapy, 71% had inoperable tumors, 59% had metastatic tumors, 58% had failed in previous therapies including conventional chemotherapy, hormone therapy and/or radiotherapy, and 43% were grade 2–4 performance status (Table 1). MC therapy was employed as a palliative measure for 718 patients with inoperable tumors and as a preoperative adjuvant for 295 patients with locally advanced tumors in the kidney (146 patients), urinary bladder (117), head and neck (25), prostate (4) and liver (3). Surgery in the latter group was done at a median interval of 29 days (range 4 to 157 days) from treatment initiation.

Tumor sites and dosing schedules

A total of 1043 primary or metastatic tumor lesions were treated. The target sites included the liver, kidney, urinary bladder, prostate, lung, head and neck, bone and others such as the retroperitoneal lymph nodes, uterus and Douglas pouch. The liver and kidney comprised 65.5% of the targets (Table 2).

The number of treatments ranged from 1 to 5, but 801 patients (79%) were given only one treatment. The physicians' reports indicated that 445 (56%) of the 801 patients were in far advanced stages of disease, thus making subsequent treatment difficult, 273 (34%) received MC therapy as a bolus preoperative adjuvant, 48 obtained a sufficient therapeutic effect by the first treatment and 35 rejected subsequent treatment. The median interval of treatment in the 212 patients with repeat infusions was 23 days (range 5 to 67 days). MMC-MC, either alone or in combination with other MC, were given to 917 patients (Table 3). Mechanical embolization for the arteriovenous fistulae or adjacent nontarget arteries was performed in 388 patients (Table 4).

Table 1 Patients subjected to microcapsule chemoembolization

Patients	
Number	1013
Median age (years)	62 (range 13–88)
Male : female	701 : 312
Status of tumors	
Localized : metastasized	415 : 598
Operable : inoperable	295 : 718
Previous treatments[a]	
Yes : no	588 : 425
Performanmce status	
Grade 0 : 1 : 2 : 3 : 4	235 : 342 : 283 : 148 : 5

[a] Chemotherapy, hormone therapy and/or radiotheraphy

Table 2 Tumor sites treated by microcapsule chemoembolization

Tumor sites	No. of tumors
Liver	437
Primary	295
Secondary	142
Kidney	246
Urinary bladder	125
Prostate	58
Lung	43
Head and neck	28
Bone	15
Primary	4
Secondary	11
Miscellaneous	91
Primary	67
Secondary	24
Total	1043

Side effects and complications

The adverse effects are listed in Table 4. The incidence of grade 1–3 toxicities ranged from 0.2 to 54.9% in eligible patients, but the incidence was $<$10% for grade 2–3 toxicities except for fever (17.5%) and was $<$1% for grade 3 toxicities except for hepatic toxicity (1.4%). The incidence of hepatic and renal toxicities, fever, abdominal discomfort, local pain and remote embolization was significantly increased by combination with gelfoam or steel coil embolization ($P < 0.01$). Grade 2–3 cutaneous reactions, which usually lasted for more than 3 months, was conspicuous in patients undergoing hypogastric arterial infusion (15.3%). The site of remote embolization in 11 patients was the descending colon, gall bladder, spleen, pancreas, lung and lower extremities. Miscellaneous adverse effects included subcutaneous hematoma at the site of catheter puncture and local skin flush.

Nine patients overall (0.9%) suffered serious complications requiring intensive palliative treatments or surgical interventions and two of these died of treatment-related complications. Of the patients with remote embolization, two needed intensive care for acute cholecystitis or pancreatitis and one underwent colostomy because of perforation of the sigmoid colon. Two patients with gluteal necrosis underwent surgical

Table 3 Dosing schedules in 1013 patients

Microcapsules	No. of patients	No. of treatments			Total dose[b] (mg)
		1	2[a]	3–5[a]	
MMC	864	712	87	65	20 (5 ~ 80)
CDDP	58	31	25	2	60 (40 ~ 100)
PEP	33	20	12	1	40 (20 ~ 80)
MMC + CDDP	35	26	9	0	20 + 60
MMC + PEP	18	11	7	0	20 + 20
PEP + CDDP	5	1	3	1	60 + 40
Total	1013	801(79%)	143(14%)	69(%)	

[a] Median interval between treatments, 23 (range 5–67) days
[b] Median (range)

Table 4 Side effects and complications

Toxic effects (Eligible patients)	Incidence of grade 1–3 toxicity (%)[a]			
	Grade 1	Grade 2	Grade 3	Total
Hematological (849)	16.3	3.7	0.7	21.1
Renal (221)[b]	11.8	2.3	0	14.0
Microcapsules (20)	10.0	0	0	10.0
+ Embolization (201)	4.4	2.4	0	16.8
Hepatic (341)[c]	20.5	7.9	1.4	29.9
Microcapsules (239)	17.1	5.4	1.2	23.7
+ Embolization (102)	28.4	13.7	2.0	44.1
Fever (1013)	37.3	17.2	0.3	54.9
Microcapsules (625)	29.9	11.5	0	41.1
+ Embolization (388)	49.2	26.5	0.8	76.6
Abdominal (1013)	26.4	4.3	0.2	30.9
Microcapsules (625)	20.3	1.8	0.2	22.3
+ Embolization (388)	36.1	8.5	0.3	44.9
Local Pain (1013)	39.2	5.2	0.3	44.7
Microcapsules (625)	19.8	1.0	0	20.8
+ Embolization (388)	70.4	12.1	0.8	83.3
Cutaneous (1013)	3.1	4.3	0.2	7.6
Hypogastric (216)[d]	12.0	14.4	0.9	27.3
Remote Emboliz. (1013)	0.8	0.2	0.1	1.1
Microcapsules (625)	0.3	0.2	0.2	0.7
+ Embolization (388)	1.5	0.3	0	1.8
Infection (1013)	0.7	0.2	0.1	1.0
Miscellaneous (1013)	5.8	0.8	0	6.6
Death (1013)				0.2

[a] See text for the grading system
[b] Patients with renal arterial infusion
[c] Patients with hepatic arterial infusion
[d] Patients with hypogastric arterial infusion

intervention. Two patients with renal abscess required immediate nephrectomy. A patient with Child class C hepatic cirrhosis died of progressive hepatic dysfunction after hepatic MC infusion, and one having hemodialysis for chronic renal failure died of sepsis secondary to renal abscess after renal MC infusion. All of these complications were experienced before 1986.

The toxic effects in the remaining patients were improved by routine palliative measures within 2 months, except for the long-lasting cutaneous reactions.

Tumor response to the treatment

An objective tumor response (CR + PR) was observed in 119 (27.9%) of 427 evaluable tumors with a median treatment number of one, including a CR in 11 tumors (Fig. 1). The <25-cm^2 tumors showed a higher objective response rate than the ≥ 25-cm^2 tumors (41.7% vs 19.9%, $P < 0.01$). Repeat infusion provided a higher tumor response rate than bolus infusion (36.7% vs 25.2%, $P < 0.05$), but the difference was not significant for the <25-cm^2 tumors (Table 5). In the ≥ 25-cm^2 tumors, the response rate of 165 tumors resistant to

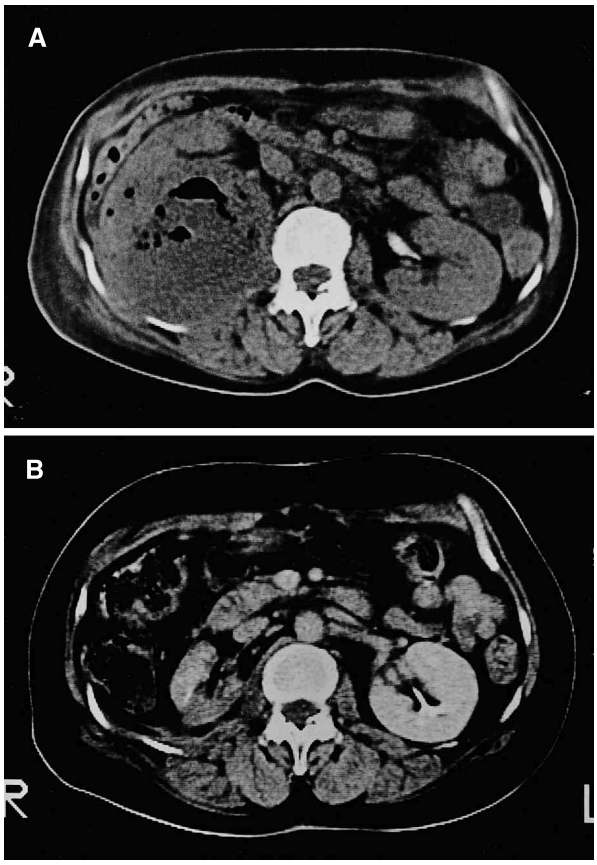

Fig. 1A, B CT scans of right renal cell carcinoma before (**A**) and 4 months after one-shot chemoembolization with 30 mg MMC microcapsules (**B**). A complete response of the large tumor is apparent

Table 5 Tumor responses to microcapsule chemoembolization (*CR* complete response, *PR* partial response, *MR* minor response, *NC* no change, *PD* progressive disease)

	Tumor response rates (%)			
	CR+PR	MR	NC	PD
Tumors $< 25\,cm^2$ ($n = 156$)	41.7	26.3	23.7	8.3
Single treatment ($n = 127$)	38.6	25.2	26.8	9.4
Repeat treatment ($n = 29$)	55.2	31.0	10.3	3.4
Tumors $\geq 25\,cm^2$ ($n = 271$)	19.9*	27.7	33.2	19.2
Single treatment ($n = 202$)	16.8	25.7	36.1	21.3
Repeat treatment (69)	29.0**	33.3	24.6	13.0
Totals ($n = 427$)	27.9	27.2	29.7	15.2
Single treatment ($n = 329$)	25.2	25.5	32.5	16.7
Repeat treatment ($n = 98$)	36.7**	32.6	20.4	10.2

*$P < 0.01$ vs tumors $< 25\,cm^2$, **$P < 0.05$ vs single treatment

prior chemotherapy or radiotherapy was not significantly different from that of 106 tumors without prior therapies (18.2% vs 22.6%, data are not listed in the table).

MMC-MC either alone or in combination with CDDP-MC and/or PEP-MC provided a higher response rate against bladder and prostate carcinomas, as compared with CDDP-MC and PEP-MC (59.0% vs 33.3%, $P < 0.05$). The combination of MMC-MC and either CDDP-MC or PEP-MC did not enhance the effect of MMC-MC alone. There were no significant differences in the tumor size and the number of treatments among the evaluated groups (Table 6).

The objective response rate to MMC-MC was about 20% for hepatocellular and renal cell carcinomas, while it was about 60% for urinary bladder and prostate carcinomas ($P < 0.01$). The median total dose was 22 mg (range 10–50 mg) in the former two tumors and 17 mg (range 5–30 mg) in the latter two ($P > 0.05$; Table 7).

Table 6 Response of urinary bladder and prostate carcinoma to the encapsulated drugs (*CR* complete response, *PR* partial response, *MR* minor response)

Encapsulated drugs	CR + PR (%)	MR (%)
MMC (47 tumors)	59.6 (a)	21.3
MMC+CDDP, MMC+PEP (31 tumors)	58.1 (b)	29.0
CDDP, PEP (33 tumors)	33.3 (c)	39.4
Total (111 tumors)	51.3	28.8

$P < 0.05$ (a vs c, b vs c, a + b vs c)

Table 7 Response to MMC microcapsules according to tumor site (*CR* complete response, *PR* partial response, *MR* minor response)

Tumors	CR + PR (%)	MR (%)
Hepatocellular carcinoma ($n = 117$)	19.7*	23.9
Renal cell carcinoma ($n = 136$)	19.9*	21.3
Bladder carcinoma ($n = 58$)[a]	58.6	22.4
Prostate carcinoma ($n = 20$)[a]	60.0	30.0
Total (331)	29.0	22.9

*$P < 0.01$ vs bladder carcinoma and prostate carcinoma
[a]Includes the cases combined with PEP or CDDP microcapsules

Palliative effects

CR of pain in the liver, kidney, prostate, urinary bladder or bone was encountered in 23.6% of the eligible 89 patients and PR in 40.4% . Intractable bone pain due to metastases from kidney and prostate carcinomas was completely subsided in five of nine patients and partially in three (Fig. 2).

CR of genitourinary gross hemorrhage was experienced in 24.3% of the eligible 70 patients and PR in 44.3% (Table 8).

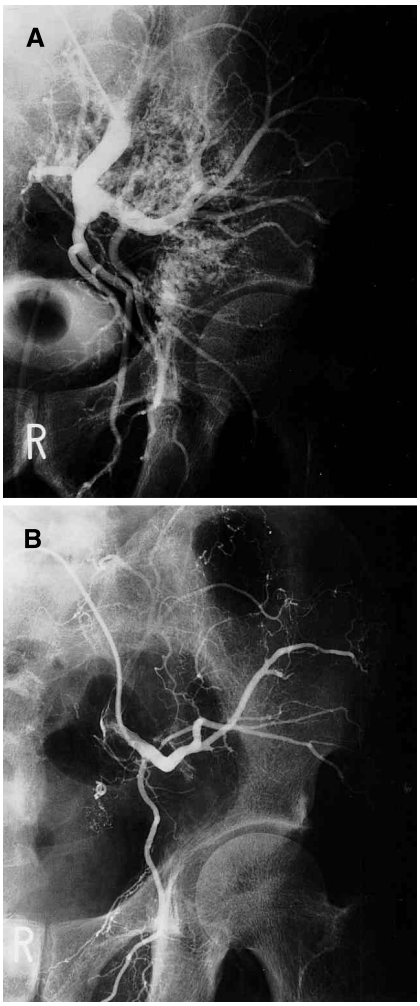

Fig. 2A, B Angiography of ileosacral bone metastasis from renal cell carcinoma before (**A**) and 4 months after fractionated chemoembolization with 50 mg MMC microcapsules (**B**). A complete remission of the intractable pain with disappearance of the tumor vasculature is apparent

Table 8 Effects on symptoms

Symptom	CR (%)	PR (%)	Total (%)
Pain (89 patients)	23.6	40.4	64.0
Bone metastases (9 patients)	55.6	33.3	88.9
Genitourinary hemorrhage (70 patients)	24.3	44.3	68.6

Discussion

Intraarterial infusion of anticancer drugs in usual dosage forms, which has been widely employed as a selective cancer chemotherapy, provides a higher drug availability in local tissues with a lower systemic drug availability as compared with intravenous infusion [21, 32, 35]. Theoretically, this advantage of intraarterial chemotherapy is achieved during the first pass through the infusing arteries and depends largely on the blood flow rate of target arteries (first pass effect); i.e. a low arterial blood flow rate in the target site will ensure the effect of intraarterial chemotherapy [4]. Vascular occlusion has been proved to increase the local drug concentration after intraarterial infusion [1] and to enhance the response of hepatic tumors to intraarterial chemotherapy [26]. Chemoembolization with MC, which act both as a vascular occlusive substance and a controlled drug-releasing device, meets the requirements to enhance the first pass effect [3, 9, 12, 37]. The same strategy has been practised in intraarterial infusion of drugs conjugated with albumin microspheres [6] or oily radiocontrast medium [20].

The present review reveals that MC chemoembolization was applied to various tumor lesions, two-thirds of which were renal and hepatic tumors. This must be because these two tumors are usually insensitive to conventional chemotherapy while accessible to arterial catheterization. The central nervous system and gastrointestinal tract were excluded from the target because of the high risk of neurological disorders and intestinal perforation, respectively. Although this therapy has proved to exert an enhanced and sustained effect [9, 12, 15], repeat MC infusions were recommended to the doctors in charge. Nevertheless, the number of treatments was only one in 80% of the patients in the present series. This was attributable to the fact that 44% of the patients were in far-advanced stages of disease and 27% were given this therapy as a one-shot preoperative adjuvant.

The systemic toxicity of this therapy was mild as shown by the extremely low incidence of grade 2–3 hematological toxicity. The rather high incidence of long-lasting gluteal necrosis after hypogastric infusion (15%) can be attributed to the complicated vascular diversion from the hypogastric artery. Fever, abdominal discomfort, local pain, remote embolization, cutaneous reaction and hepatic toxicity are considered characteristic of MC chemoembolization, but they also have been frequently encountered in mechanical arterial embolization utilizing gelfoam pieces or steel coils [18]. The present review shows that these adverse effects in MC therapy were significantly increased when combined with mechanical embolization. Whether mechanical embolization was combined or not, however, the incidence of grade 2–3 toxicities except for fever, was less than 10%. The serious complications in nine patients (0.9%), resulting in treatment-related death in two, were encountered only in the early stages of trials. This indicates that advances in infusion techniques and selection of patients have minimized the morbidity of this treatment. All of the adverse effects in the remaining patients, except for grade 2 cutaneous reactions, were improved by routine palliative measures within 2 months. MC chemoembolization

was well tolerated by 99% of the patients even though 43% of them had grade 2–4 performance status.

The overall objective tumor response rate of 27.8% is acceptable, considering that the number of treatment was only one in 80% of the patients, the majority of tumors were far advanced and there were considerable variations in both the target site and the dosing schedule. In fact, the tumor response depended significantly on the size and site of the tumor, the number of treatment and the drugs used. Apart from these problems, the low toxicity of this therapy allows a more intensive dosing schedule so that a higher tumor response rate can be obtained [7, 22]. It should be also noted that the antitumor effect of this therapy was scarcely affected by prior chemotherapy or radiotherapy.

The tumor response to MMC-MC was better than that to CDDP-MC and PEP-MC. This may be due , at least in part, to the difference in drug activity under the oxygen-deficient conditions produced by MC embolization. MMC is the bioreductive alkylating agent preferentially toxic to hypoxic cells, while CDDP and bleomycin (the parent drug of PEP) are less toxic to these cells [19, 25, 31, 34]. Besides such pharmacological considerations, pharmaceutical investigations on the shell material, size, drug-loading efficiency and drug-release rate of the carrier system are required for enhancing the therapeutic effect of chemoembolization [16, 37, 38].

CR or PR of intractable pain and genitourinary hemorrhage was achieved in approximately two-thirds of the eligible patients. In particular, the analgesic effect on bone lesions was promising. This is in line with the previous observation that MMC-MC definitely improved the pain, neurological symptoms or motor disturbances in all of a group of 12 patients with lumbar spinal metastases [5].

In conclusion, the present study shows that MC chemoembolization, though restricted by catheter technique, can be applied to a variety of tumor lesions with an acceptable morbidity. Further improvements in the dosing schedule and advances in pharmaceutical technology will maximize the benefits of this treatment modality. Prospective trials are justified to elucidate the potential role of such a targeted chemotherapy in the multidisciplinary treatment of solid tumors.

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