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FULL PAPER

Dosimetric analysis of patients with gastro entero pancreatic neuroendocrine tumors (NETs) treated with PRCRT (peptide receptor chemo radionuclide therapy) using Lu-177 DOTATATE and capecitabine/temozolomide (CAP/TEM)

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Objective: Two radiosensitizing chemotherapeutic drugs, capecitabine (CAP) and temozolomide (TEM), are administered concurrently to enhance the therapeutic efficacy of peptide receptor radionuclide therapy (PRRT). This study aims to assess the biodistribution and normal-organ and tumor radiation dosimetry for Lu-177 DOTATATE administered concurrently with CAP/TEM.

Methods: 20 patients with non-resectable histologically confirmed gastroenteropancreatic neuroendocrine tumors with normal kidney function, a normal haematological profile and somatostatin receptor expression of the tumor lesions, as scintigraphically assessed by a Ga-68 DOTANOC scan, were included in two groups—case group (n = 10) and control group (n = 10). Patients included in case group were those who were advised concomitant CAPTEM therapy by the treating medical oncologist. Patients were administered CAP orally at a dose of 600mg m^{-2} bovine serum albumin twice a day for 14 days starting 9 days prior to PRRT and oral TEM as a single dose at a dose of 75 mg m^{-2} was given concurrently for the last 5 days commencing on the day of PRRT (days 9–14). In the control group, patients were treated with Lu-177 DOTATATE only. For PRRT, 6.4 GBq–7.6 GBq (173–207 mCi) of Lu-177 DOTATATE was administered as infusion into each patient over 10–15 min in a solution with positively charged amino acids for renal protection. Dosimetric calculations were done using the HERMES software.

Results: Physiological uptake of Lu-177 DOTATATE was seen in all patients in liver, spleen kidneys, and bone marrow. Radiation absorbed doses (mean ± standard deviation) were obtained as 0.29 ± 0.12 mGy/MBq for kidneys, 0.30 ± 0.18 mGy/MBq for liver, 0.63 ± 0.37 mGy/MBq for spleen, 0.019 ± 0.001 mGy/MBq for bone marrow and 3.85 ± 1.74 mGy/MBq for tumours in the case group and they were 0.31± 0.26, 0.24 ± 0.14, 0.64 ± 0.42, 0.017 ± 0.016, 5.6 ± 11.27 mGy/MBq in kidneys, liver, spleen, bone marrow and neuroendocrine tumour, respectively, in the control group. Mann–Whitney U test between the variables of two groups showed an insignificant difference ($p > 0.05$).

Conclusions: The authors demonstrated no significant difference between the tumor and organ doses with Lu-177 DOTATATE in the patients treated with and without concomitant chemotherapy.

Advances in knowledge: To our knowledge, this is the first dedicated study exhibiting dosimetric analysis in patients undergoing PRRT in combination with chemotherapy.

INTRODUCTION

Peptide receptor radionuclide therapy (PRRT) using lutetium-177 labelled compounds has been effectively used for treating metastatic and inoperable well- differentiated gastroenteropancreatic neuroendocrine tumours (NETs) for almost three decades.[1] While the results obtained with PRRT have been encouraging in terms of prolonging life and symptom control, the objective response rates with

PRRT have been rather dismal, with most studies quoting an objective response rate of around 30%.[2]

Preliminary results have shown that a relationship exists between the dose delivered to the tumour lesions and the molecular response following PRRT. Higher doses delivered have been associated with better response rates.[3] However, the maximum acceptable absorbed doses to the dose-limiting organs, *i.e.* kidneys and bone marrow restricts the number of administered treatment cycles.[4–6] Maximum accepted doses of 23 Gy to the kidneys and 2 Gy to the bone marrow are widely used.[3]

Attempts have been made to improve the therapeutic efficacy of PRRT by administering the PRRT in combination with chemotherapeutic agents. Two chemotherapeutic drugs, capecitabine (CAP), the prodrug of 5-fluorouracil, and temozolomide (TEM), have been used in combination with PRRT in patients with both enteric and pancreatic NETs and have shown therapeutic benefit in patients when used with Lu-177 DOTATATE.[7] The rationale for using chemotherapy in combination with PRRT has been that the chemotherapeutic drugs exert a selective radiosensitization effect on the tumor cells. Little information, however, exists in the literature about the dosimetric pattern of target lesions and the normal tissues in this combination therapy. In this study, we report the comparative results of both critical organ and tumor dosimetry in the two groups of metastatic NET patients, one group treated with Lu-177 DOTATATE and CAP/TEM and other with Lu-177 DOTATATE only.

PATIENTS AND METHODS

Patients

20 patients with inoperable metastatic NET's were included in this prospective double arm study. The case group received 177-Lu DOTATATE therapy along with CAP/TEM therapy ($n = 10$) and the control group received only 177- Lu DOTATATE therapy ($n = 10$). The patient had to have a histologically proven NET, standard normal kidney function, a normal haematological profile and overexpression of somatostatin receptor in the tumour lesions, as scintigraphically assessed by a 68-Ga DOTANOC scan, to be included in the therapeutic cycles. All patients had a Karnofsky performance score ≥50 and patients with an anticipated life expectancy of less than 3 months were excluded from the study. All patients were advised of the possible benefits and adverse effects of the treatment and informed and written consent was obtained from all participants before enrolment. An Institutional Ethics Committee clearance was taken for the study.

Radiopharmaceuticals

Non-carrier added Lutetium-177 was obtained from ITG GmbH,Bavaria, Germany. It was supplied as a sterile solution of Lu-177 chloride in a 0.01 M HCl solution with a specific activity ~90 mCi/mg and radionuclidic purity of more than 99%. Good Manufacturing Practices—grade [DOTA0,Tyr3] octreotate was obtained from ABX,GmbH,Radeberg,Germany. Lu-177 DOTATATE was prepared in-house as previously described by Das et al.[8] radiolabelled efficiency of more than 95% of Lu-177 DOTATATE was used for therapy.

Radiolabelling procedure

Lu-177 DOTATATE was prepared in-house by chelating 100 μg octreotate [DOTA,Tyr3] to 7.4 GBq (200mCi) Lu-177 chloride in a semi-automated module (Synthera IBA, Louvain-la-Neuve, Belgium) by heating Lu-177 in HCl with DOTATATE and sodium acetate buffer (pH, 5.5) at 95°C for 15–20 mins. Radiochemical purity was estimated by using thin-layer chromatography.

PRRT protocol

The PRRT was administered as an fixed dose of 7.4 GBq of Lu-177 DOTATATE. All patients underwent appropriate prophylactic anti emetic therapy with intravenous ondensetron and low dose corticosteroid prior to PRRT. They also underwent a renal protection protocol with an infusion of cocktail of lysine and arginine. Following radiopeptide administration, the patients were admitted to the isolation ward. There, they underwent intravenous hydration with a combination of ringer lactate and normal saline over a period of 24 h following infusion of Lu-177 DOTATATE. The patients were monitored for any acute adverse effects for 24 h after therapy and were discharged when the radiation levels declined below the permissible environmental level of radiation limits (50 μSv/h) as pursuant to the National Regulatory Guideline.

PRCRT (peptide receptor chemoradionuclide therapy)

Patients in the case group were administered CAP orally at a dose of 600 mg m^{-2} bovine serum albumin twice a day for 14 days starting 9 days prior to PRRT. Oral TEM was given concurrently for the last 5 days commencing on the day of PRRT at a dose of 75 mg m^{-2} (Days 9–14).

Post therapy 177Lu-DOTATATE whole-body scans

Serial whole body anterior and posterior planar images were acquired at different times post administration, on a dual head gamma camera (Philips Brightview). The camera was equipped with a low-energy all-purpose parallel-hole collimator and the energy peaks were centered at 113 keV and 208 keV, respectively, with a 20% energy windows and scan speed of 15 cm/min. A series of whole-body images at 2, 24 and 96 h with a standard marker of 37MBq (1 mCi) at the level of lateral malleolus were acquired for each patient.

Activity quantification from planar imaging

Activity quantification for planar images was performed by using pixel-based method described by Sjögreen et al.[9] Calculation of geometric mean of the measured anteroposterior images was done on a pixel-by-pixel basis. The sensitivity was calculated as 1.28 cycles per second/ MBq from the counts of a known amount of 177Lu- DOTATATE activity placed in a Petri dish 10 cm from the anterior camera head. Geometric mean of the anterior and posterior counts in the region of interest (ROI) was divided by an attenuation factor, which is equal to the square root of the transmission factor obtained from the transmission scan of flood source filled with 10mCi of 177LuCl3 to perform the attenuation correction of emission images.

Method of dosimetry

The quantitative dosimetric analysis was performed on the 2 h whole body images by drawing ROIs manually demarcating the contour of organs showing the uptake of radiopharmaceutical on the anterior and posterior images by using a dedicated HERMES system (Hermes Medical Solutions, Stockholm, Sweden). The ROIs drawn on the 2 h image were then replicated on the remaining whole body scans acquired at different times post-injection to minimize intra observer variations. All the ROIs were drawn by a single physicist to minimize inter observer variability and care was taken such that ROI of one organ did not overlap the ROI of another organ. A small background ROI was defined on nonvascular region on the thigh. Standard counts were obtained from the marker placed on the whole body scans. The standard marker was placed at a reasonable distance from the body so that it is not included while making the contour for whole body. For the quantitative analysis, the geometric mean of the counts were taken which corrected for the patient's physical characteristics and also for the counts from underlying organs or high background areas.

The time activity curves thus obtained were fitted using mono and/or bi-exponential functions. The integration of these curves provided the residence times or total number of disintegrations of the region. Finally, S-values for the radionuclide from the computer software OLINDA/EXM along with the residence times were used to calculate the absorbed organ and tumor doses. The unit density sphere module of OLINDA/EXM was specifically used to estimate the mean absorbed tumor doses. A dosimetric analysis was done for whole body, liver, spleen, kidneys, bone marrow and tumor lesions.

Uptakes as fractions of administered activity, mean absorbed organ doses, total body doses and kidney biological effective dose(BED) for all 20 patients were obtained. Figure 1 represents the whole-body images of the Lu-177-DOTATATE uptake at different time points after a therapeutic administration. The foregoing whole-body and normal tissue parameters were calculated for all the patients. The parts of organs showing tumor involvement or superimposition were excluded from the calculation of organ uptake and mean absorbed dose. For this reason, dose calculation was excluded in 2 patients showing abnormally increased uptake of Lu-177 DOTATATE in liver.

RESULTS

Demographics

The patients demographics and various quantitative parameters in the two groups are presented in Tables 1 and 2, respectively. Since the study was not a randomized study, both the patient groups were analysed for the pretreatment parameters such as age, sex, prior surgery, prior chemotherapy, prior radiotherapy, sites of metastasis, administered activity, no. of 177Lu-DOTATATE therapies etc. The analysis showed that the two groups matched and there was insignificant difference between the various parameters ($p > 0.05$). The mean age of patients in case group and control group was 59 ± 7 years and 53 ± 9 years, respectively. The mean administered activity to patients was 7.4 ± 0.026 GBq (range, 6.4–7.6 GBq, 237-281mCi). The patients well tolerated the treatment with Lu-177 DOTATATE, and no serious adverse events were observed.

Biodistribution and dosimetry

On the post treatment scans, the planar scans revealed normal expected physiological uptake of the radiopeptide

Figure 1. Whole-body anterior and posterior images after the therapeutic administration of Lu-177 DOTATATE at 2, 24 and 96 h with a standard marker of 1 mCi at the level of lateral malleolus.

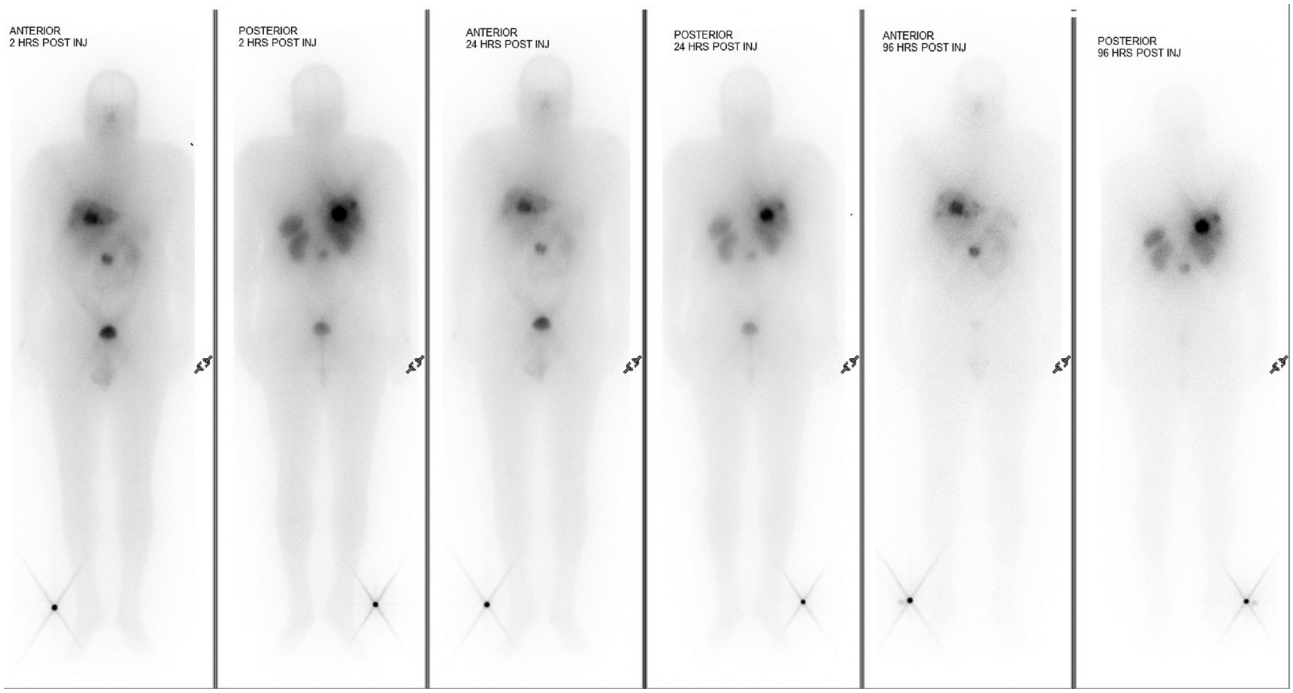

Table 1. Demographic details of the patients incase group with the amount of activity administered and total body dose

Pt. No	Age (years)	Sex	Diagnosis, Primary site	Ki 67	177Lu-DOTATATE injected dose (MBq)	Total Body Dose mGy/MBq
1	57	M	Gr- I NET, 2nd part of duodenum	2–3%	7474	0.008
2	61	M	Gr- II NET , Rectum	2–10%	6401	0.042
3	58	F	Gr-II NET, Rectum	<2 %	6845	0.023
4	63	M	Gr-II NET, 2nd part of duodenum	1-2%	7326	0.040
5	67	M	Gr- II NET, Small bowel	20%	6697	0.022
6	45	M	Gr-1 NET, Pancreas	15%	6919	0.230
7	67	M	Gr-I NET - Small bowel	10–15%	7659	0.019
8	65	M	Gr-I NET , Pancreas	3–4%	7030	0.025
9	53	M	Gr-II NET , 4th part of duodenum	2–4%	7178	0.039
10	54	M	Gr-II , Pancreas	10–15%	7363	0.056

in the liver, spleen, kidneys, and bone marrow, and specific uptake in all known NETs. The serial images of all the patients were analyzed for the estimation of radiation absorbed dose of the liver, spleen kidneys, bone marrow and tumors using HERMES software. The radiopharmaceutical (RP) showed a rapid uptake over 2 h followed by a protracted washout from all the organs. For this reason, the uptake curves for the different organs were fitted to biexponential functions. The highest uptake of radiopharmaceutical was noted in the tumors, followed by liver and spleen. Owing to their close proximity to the kidneys, the uptake in these organs has a bearing on the overall kidney dose. The absorbed dose (mean ± standard deviation) to liver, spleen, kidneys, bone marrow and NETs in the case group was calculated as 0.30 ± 0.18, 0.63 ± 0.37, 0.29 ± 0.12, 0.019 ± 0.0018 and 3.86 ± 1.74 mGy/MBq, respectively. The mean doses in the control group were 0.24 ± 0.14, 0.64 ± 0.42, 0.31 ± 0.26 mGy/MBq, 0.017 ± 0.016 mGy/MBq , 5.6 ± 11.27 mGy/MBq in liver, spleen, kidneys, bone marrow and NETs, respectively. A Mann-Whitney U test between the variables showed an insignificant difference ($p > 0.05$) in the absorbed doses of the two groups. The total absorbed doses as calculated in kidneys, liver , spleen, bone marrow and tumors per fractionated cycle of PRRT cycle in the case group and control group are presented in Table 3. The critical organ in both groups was observed to be the kidneys, which received a mean absorbed dose of 0.29 ± 0.12 mGy/MBq (0.12–0.46 mGy/MBq)) in the case group and 0.31 ± 0.26 mGy/MBq (0.02–0.89 mGy/MBq) in the control group. Accordingly, the calculated maximum activity that could be administered within the permissible renal threshold of 23 Gy was found to be 79GBq (2135 mCi) in case group and 74GBq (1998 mCi) in the control group. The average total body dose as calculated in case group and control group was 0.04 ± 0.02 mSv/MBq and 0.03 ± 0.01 mSv/MBq, respectively, in a single cycle of 177Lu-DOTATATE. The kidney biological effective dose (BED) was 3.42 ± 1.3 Gy (range, 0.99–7.1 Gy) and 4.23 ± 1.8 Gy (range, 0.87–6.6 Gy) in case and control group ($p > 0.05$), respectively.

DISCUSSION

Response and toxicity prediction is an important component of implementing PRRT in NET and individual dosimetry is a

Table 2. Demographic details of the patients in control group with the amount of activity administered

Pt.No	Age (years)	Sex	Diagnosis, Primary site	Ki 67	177Lu-DOTATATE injected dose (MBq)	Total Body Dose mGy/MBq
1	58	M	Gr -II NET, 2nd part of duodenum	20%	7400	0.009
2	66	F	Gr-II NET, Small bowel	10–15%	6475	0.043
3	41	M	Gr-I NET, 2nd part of duodenum	3–4%	6586	0.016
4	42	M	Gr-II NET , Rectum	3–4%	7585	0.032
5	56	M	Gr-II NET, Rectum carcinoid	10–15%	6845	0.031
6	67	M	Gr-II NET , 4th part of duodenum	2–4%	6771	0.019
7	42	M	Gr-II NET , Pancreas	3–10%	7400	0.023
8	49	M	Gr-1 NET, Pancreas	<2 %	7289	0.035
9	57	M	Gr-I NET , Small bowel	1–2%	7141	0.023
10	52	M	Gr-II NET, Pancreas	20%	7400	0.037

Table 3. Total absorbed dose (Gy) of the organs and tumors corresponding to 7.4 ± 0.026 GBq (6.4–7.6 GBq) of injected activity in the case group and control group

Organ	Case group mean ± SD(Gy)	Control group mean ± SD(Gy)
Liver	2.7 ± 1.7	1.8 ± 1.8
Spleen	4.4 ± 2.9	4.8 ± 2.8
Kidneys	2.0 ± 0.8	2.3 ± 0.9
Bone marrow	0.14 ± 0.23	0.17 ± 0.34
Tumors	27.7± 10.1	41.4 ± 12.02

crucial factor in treatment planning. In this study, we present individual dosimetry data of a cohort of NET patients undergoing a concomitant 177Lu-DOTATATE and CAP/TEM therapy in one group and only Lu-177 DOTATATE therapy in the other group. To our knowledge, this is the first dedicated study of its kind evaluating doses in patients undergoing PRRT in combination with chemotherapy.

PRRT with Lu-177 octreotate as a single agent has been established as a treatment of choice in patients with somatostatin receptor expressing gastroenteropancreatic neuroendocrine tumurs. However, strategies to increment the efficacy of such treatment are continuously being investigated. One possible way to boost the therapeutic efficacy is combining Lu-177-octreotate with chemotherapeutic drugs as radiosensitizer. CAP, a prodrug of 5-fluorouracil, is often used as radiosensitizers and has attractive features when used with external beam radiation therapy.[10] The other drug, TEM, is an imidazotetrazine derivative of the alkylating agent dacarbazine. It causes methylation of DNA, which leads to tumor cell death. The rationale for using CAP/TEM is based on the hypothesis that slow-growing NETs might be more responsive to cytotoxic drugs. Consequently, continuous exposure to an antimetabolite such as CAP and a lipophilic methylator such as TEM could be beneficial.[11] Several reports have exploited this synergy and demonstrated good response rates in patients with pancreatic neuroendocrine tumours (PNETs) with the combination chemotherapy of CAP and TEM.[12,13] Strosberg et al[14] in 30 patients with advanced pancreatic neuroendocrine tumours have confirmed these preliminary results by achieving a wonderful response of more than 70% with the combination of CAP, TEM and Lu-177.

While response evaluation studies have shown a good clinical and radiological response in patients undergoing PRRT in combination with chemotherapy, scant data exist on the dosimetric impact of introducing these radiosensitizers to the PRRT treatment regimens. It is intuitively believed that the addition of radiosensitizers would selectively increase the radiation absorbed by the tumour cells while sparing the normal organs.[15,16]

Garkavij et al[17] in a study demonstrated a huge difference in calculated absorbed doses to the kidneys depending on the dosimetry method used. The planar and SPECT based methods show different results with planar method consistent with higher doses due to activity estimation from the overlapping organs. They also demonstrated substantially different dose estimates with the planar method depending on the placement of background ROI with the ROI close to kidneys more consistent with dosimetry with SPECT than the ROI in the thigh region. The dosimetric calculations in the current study were done using the planar sequential images at 2, 24 and 96 h, background ROI in the thigh region and the HERMES software. While it is recommended to use a medium energy collimator for imaging Lu-177 to reduce contribution from events that undergo septal penetration,[18] such a collimator was not available at the institution and a low energy collimator was used by both the case and the control cohorts. However, we assume, since the low energy collimator was used both, in the case and the control group, the error in calculating the relative differences in uptake between the two groups would be mitigated. Also, the absorbed tumor and organ doses in both the groups were consistent with the published literature, it can be assumed that the imaging with low energy collimator does not result in major difference in the calculation of absorbed doses.

Regarding the time points of image acquisition, different studies have chosen different time points to generate the time activity curves even less than 96 hrs.[19] Although, it has been postulated that a last time point near the physical half-life of the radionuclide allows more reliable estimation of the time-integrated activities, it was not possible in the current setting due to logistic issues and 96 h image was taken as the last time point. Apart from the dosimetry softwares, Cremonisi et al[20] has pointed out that various pathological and biological factors such as binding affinity heterogeneity, difference in tumor volume, hypoxia, necrosis, receptor density etc. may result in differences in intralesional and intrapatient tumor uptake in PRRT studies. Therefore, it is not advisable to generalize the results when the comparison is done from the results of different studies.

Kidneys have been established as the critical organs in many previous studies on PRRT and the cumulative Lu-177 DOTATATE activity administered is often limited by the development of nephrotoxicity.[21] Based on experiences obtained from conventional external beam radiotherapy, a maximum radiation exposure of 23 Gy to the kidney is generally accepted.[22] In the current study, the kidney dose per unit activity was found to be 0.29 ± 0.12 mGy/MBq in the case group and 0.31 ± 0.26 mGy/MBq in the control group allowing administration of a higher activity without exceeding the kidney tolerance dose. Our renal dosimetry results in both the groups matched the results of study by Turner et al who also used the same combination peptide receptor chemo radionuclide therapy (PRCRT) [0.30 (0.13–0.45) mGy/MBq].[23] The reported absorbed doses to the kidneys range from 0.62 to 1.96 mGy/MBq in the published literature.[21]

BED is a parameter which quantitatively incorporates the dose rate related factors into the absorbed-dose estimates. It takes into account the biological parameters such as α/β ratio and sublethal damage recovery time. Renal toxicity can be better predicted by BED estimates than absorbed dose alone. An annual decrease

of creatinine clearance (CRL) of 10% is noted with a renal BED of 27–42 Gy which rises to yearly loss of 26–56% with a BED greater than 45 Gy.[6] Various authors have proposed safe kidney BED values to be around 37–40 Gy.[24,25] However, risk factors such as diabetes mellitus, hypertension as well as chemotherapy may further aggravate the renal toxicity limiting the cumulative activity that can be administered. In our experience, the kidney BED was 0.87–7.1 Gy per cycle for the administered activity of 6.4–7.6 GBq (173–207 mCi) in both the groups.

The bone marrow received an average of 0.019 ± 0.001 mGy/MBq with a total absorbed dose in a range of 67.1–160 mGy per fractionated cycle of 177-Lu DOTATATE. The results are consistent with those of an earlier study.[26] Among the other critical organs, the liver and spleen receive the highest doses. The average absorbed dose per unit activity to liver in the case group was 0.30 ± 0.18 and 0.24 ± 0.14 mGy/MBq in the control group, which are well within the published range of 0.18–0.59 mGy/MBq in literature.[5,26,27] The high doses to the liver are due to the normal tissue uptake as well the uptake by the hepatic metastases. The radiation absorbed dose to the spleen was 0.63 ± 0.37 mGy/MBq in the case group and 0.64 ± 0.42 mGy/MBq in the control group, which also matches the results of the published studies.[5,26,27] The high radiation dose to the spleen occurs due to the usual presence of somatostatin receptors in the splenic tissue.[28,29] Spleen shows a predominance of somatostatin receptor subtype 2A in the immunohistochemical studies when measured along with mRNA.[30] This receptor subtype is preferred by both the somatostatin analogues, octreotide and octreotate used for the diagnosis and treatment of NETs.[31] The absorbed doses to the tumours in the study was 3.84 ± 1.74 mGy/MBq in the case group and 5.6 ± 11.27 mGy/MBq in control group ($p > 0.05$) with a range of 1.08–8.73 mGy/MBq. The published literature with Lu-177 DOTATATE demonstrates a wide range of tumour absorbed doses ranging from 0.1 to 56 mGy/MBq.[21] The wide range of these results are attributed to several parameters such as tumour size, heterogeneity in somatostatin receptor expression, radiosensitivity, differences in vascularization and other tumoral characteristics. The difference in tumour absorbed doses between the case and the control group is not statistically significant, indicating the co-administration of the radiosensitizing drugs does not affect the tumour uptake of the absorbed dose from 177-Lu DOTATATE. Rather, the improved response to CAPTEM, as documented in many studies, may possibly be due to the synergistic effect of radiation and the changes in the biological molecular microenvironment caused by the addition of the radiosensitizing drugs.

The predicted maximum tolerated activity of Lu-177 DOTATATE in our study was found to be 79 GBq (2133 mCi) () for the combined PRCRT protocol and 74 GBq (1998 mCi) when Lu-177 DOTATATE is used as a single agent. However, the prior estimate was 40 GBq (1080 mCi), when Lu-177 DOTATATE was used as a single agent.[21] With this, we can conclude that a maximum of 10 therapeutic cycles of 7.4 GBq (200 mCi) per cycle can be administered to the patient with a limit of 2 and 23 Gy for bone marrow and kidneys, respectively. Authors could also demonstrate a higher tumour to kidney ratio as compared to reported results.[17,32] The reduced renal dose as compared to the historical controls is possibly due to non-carrier added Lu-177 used in this study. Whether this would result in a significant difference in overall response rate and patient outcomes, however, remains to be proven in further studies.

CONCLUSION

Strategies to improve PRRT include combining PRRT with radiosensitizing chemotherapy. While many studies have addressed the improved clinical outcomes of using combination PRCRT, scant data exist in literature regarding the dosimetric impact of combining radiosensitizing chemotherapy to PRRT. In the current study, there was an insignificant difference in the tumour and organ absorbed doses in PRRT between patients treated with Lu-177 DOTATATE only and patients receiving 177-Lu DOTATATE and radiosensitizing drugs.

CONSENT

All patients were explained the potential benefits and adverse effects of the treatment and written and informed consent was obtained from all participants before enrolment. An Institutional ethics committee clearance was taken for the conduct of study.

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