ORIGINAL ARTICLE

Tc99m-Besilesomab With the Added Benefit of Single Photon Emission Computed Tomography/Computed Tomography (SPECT/CT): Current Role in Infection Detection and Localisation

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ABSTRACT

Introduction: Imaging modality has become increasingly important in hospital setting especially in cases of unknown site of infection/pyrexia of unknown origin (PUO) and osteomyelitis (OM). In recent years, nuclear imaging has been used and is known to deliver prompt and precise diagnoses of numerous infectious diseases. The purpose of the study is to detect and localise the site of infection using Tc99m-besilesomab and to assess the added contributions of single photon emission computed tomography/computed tomography (SPECT/CT) over planar scan in patients with PUO and OM. **Methods:** Tc99m-besilesomab with SPECT/CT were prospectively performed in 23 patients (eight males, 15 females) with suspected infection. True findings were diagnosed by both cold and hot spot in the scan with reference to positive blood or tissue cultures, or other additional imaging. **Results:** Tc99m-besilesomab managed to detect presence of infection with high sensitivity of 87.5% and specificity of 71.4%. Interobserver variability agreement that was obtained between the presence of infection and the ability of Tc99m-besilesomab imaging to detect it was significant ($p<0.05$), Kappa=0.7. SPECT/CT has increased the detection sensitivity by 6.3% and specificity by 28.6%. Out of 23 patients, 15 had true positive, seven had true negative and only one patient had false negative study. SPECT/CT has changed the management in one patient which was missed by planar imaging. **Conclusions:** Indeed, SPECT/CT has further increased the detection sensitivity and specificity, provides extra information of the anatomical location and the extent of involvement of the disease as compared to planar imaging alone.

Keywords: Tc99m-besilesomab, SPECT/CT, Pyrexia of Unknown Origin, Osteomyelitis, Infection

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INTRODUCTION

Nuclear imaging is very useful in detecting and localising site of infection and inflammation due to its overall good test characteristics, low toxicity and capability to image the whole body as compared to other current imaging examinations (1). The radiopharmaceuticals currently being used for imaging infections include labelled leukocytes (indium-111 oxine and Tc99m-HMPAO), antigranulocyte antibody (Tc99m-besilesomab) and fluorine-18 fluorodeoxyglucose (18F-FDG), with many other newer agents being investigated. Besilesomab is an antigranulocyte antibody kit that binds to murine immunoglobulin (MoAbs) of IgG1 to perform the scan. The use of Tc99m-besilesomab as a functional imaging study is to identify infection site early so that treatment can be started with the appropriate antibiotics and reduce hospital stay. The most common indication for this scan is to detect infection in cases of suspected osteomyelitis (OM), prosthesis infection and pyrexia of unknown origin (PUO).

In Nuclear Medicine, infection imaging with single photon emission computed tomography (SPECT) in addition to planar scan has dated years back. Planar imaging is similar to X-ray, except that it uses the random photons generated by gamma rays produced by radiotracers from the patient. Planar scan has

its own limitation due to its poor resolution and its inability to localise the exact and precise anatomical site of infection (2). SPECT shows three-dimensional radiotracer distributions which were formed by photons detection from acquired multiple-planar images (3) and improves lesion to background signal and anatomic localisation however still lacks information on the nature, composition and characterisation of the lesion, making it insufficiently specific for diagnostic purposes. Anatomical localisation with additional imaging such as radiography, computed tomography (CT) or magnetic resonance imaging (MRI) is still needed in some cases to characterise lesions on planar scan and SPECT alone. By combining anatomical imaging such as CT with SPECT, the Nuclear Medicine fraternity is able to overcome this limitation.

Hence, the overall objective of this study is to assess the usefulness of Tc99m-besilesomab with added benefit of SPECT/CT for detecting and localising infection in symptomatic patients with unknown site of origin, and to determine agreement between both scans.

MATERIALS AND METHODS

Study Population

This prospective study was conducted in 23 patients (above 18 years of age) between May and October 2016 in Nuclear Medicine Department, Hospital Kuala Lumpur with the clinical suspicion of infection with at least one of the followings: fever; positive blood culture with unknown site of infection; increased white blood cells (WBC) or erythrocyte sedimentation rate (ESR) above the normal level. The patients had never been administered with besilesomab before. Patients who were pregnant, breast feeding, and had history of taking immunosuppressive medication or underwent chemotherapy within one month of study were excluded.

The patients were then divided into those with unknown site of infection/PUO and orthopaedic infection (OM/infected implants). The patients were categorised as having PUO after having high temperature of more than 38.3°C that lasted for more than three weeks with no obvious source despite appropriate investigation. All culture tests performed were negative at the time of referrals. The final diagnosis was obtained from one of the reference standard used for diagnosis of infection such as confirmation by other imaging modality (radiography, ultrasound, CT or MRI), biopsy findings or culture confirmation, supported by clinical findings or response by the treating clinicians.

All patients enrolled in the study were explained in details about the procedure and the possible risks involved in using besilesomab during the procedure. The possible side effect of the body producing the human anti-mouse antibodies (HAMA) that may cause allergy reaction in those receiving besilesomab for the second time was also explained.

Consent was then taken from the patients prior to the study. This study had received ethical approvals from Medical Research Ethics Committee, Kementerian Kesihatan Malaysia and Human Research Ethics Committee, Universiti Sains Malaysia.

Tc99m-besilesomab and SPECT/CT imaging

Positive whole body scan was defined as foci with greater uptake than the background (bone marrow); this uptake was localised anywhere in the body according to reader observation. The images were acquired at 1, 3 and 5 hours post radiopharmaceutical administration. A dual-head gamma camera with parallel-hole low-energy high resolution collimators and a 20% energy window set at 140 keV ± 15% was used to perform the planar imaging. Table speed of 10 cm/s was set for whole-body images. SPECT/CT was then performed with dual-head hybrid gamma camera with aligned 6-slice CT capability (Siemens Symbia T6, Siemens Healthcare, Germany). A 128 x 128 matrix was used to acquire the SPECT images.

Data Interpretation and Analysis

All acquired images were interpreted independently by two blinded experts (Nuclear Medicine Physicians) that were unaware of patients' medical condition and other related investigation findings. Consensus was obtained by joint reading in cases of discrepancy between both experts who have more than two years of experience in reporting Nuclear Medicine scans. The images were interpreted separately: first the planar Tc99m-besilesomab images, followed by the fused SPECT/CT images.

A Tc99m-besilesomab was considered positive for infection when there was presence of abnormal uptake focus. Based on clinical correlation and diagnostic images, presence of photopenic area (cold spot) or increased uptake (hot spot) at suspected area, without any relation to normal radiopharmaceutical physiologic biodistribution was considered as infective in nature. For PUO cases without suspected site of origin, increased uptake at a site with abnormal non-physiologic biodistribution would also be considered as infective. A study was considered negative when there was no abnormal tracer uptake noted. An equivocal case was defined as increased uptake that could not be classified as either physiologic or infective. For site-based and patient-based analysis, SPECT/CT examination was considered contributory when it was capable to provide data that could not be obtained from planar images in detecting infection or its exact anatomical sites, and provide incremental data for at least one suggestive site respectively.

A final diagnosis for the true status of lesions was made after reviewing the diagnosis within one to three months

(data was obtained from patients' medical record).

Statistical Analysis

The first part of data analysis consists of descriptive analysis describing the characteristics of the study samples. The second part of the analysis was to assess the agreement in infection localisation between the Tc99m-besilesomab and SPECT/CT images. Statistical software SPSS version 20 (IBM corp, 2011) and STATA version 11 (StataCorp, 2009) was used to carry out the statistical analysis. For categorical outcome assessment, McNemar's test was used to assess the significant difference between the diagnostic value of Tc99m-besilesomab and SPECT/CT in diagnosing the infection site and Kappa statistic was used to measure the agreement between the two diagnostic methods. The results of McNemar's test yielded the proportion with positive diagnosis between the two tests, while the confidence intervals suggested the precision of the difference. To determine the significance difference, a P-value of 0.05 was taken as the critical limit.

RESULTS

Patients' Demography

Out of the 23 patients, 15 (65.2%) were females and eight (34.8%) were males. The patients were predominantly Malays (52.2%), followed by Indians (30.4%) and Chinese (17.4%). A higher percentage was seen in the older age groups (more than 40 years old). Patients within age of 41 to 60 years comprised of 34.8% which was similar to the group of those more than 61 years of age.

Clinical Characteristics

From the referrals, 18 out of the 23 patients had no fever at the time of first encounter at Nuclear Medicine clinic (Table I). On analysis of blood investigation results, only eight patients (34.8%) had raised WBC while 15 patients (65.2%) had normal WBC value. ESR value was not analysed in this study as most of the patients did not have ESR results available at the time of consultation (only 7 results available).

Factors affecting Tc99m-besilesomab

The factors that could affect the findings of Tc99m-besilesomab were the level of WBC (whether it was normal or raised) and the initiation of antibiotics prior to the scan. 11 patients with normal WBC had infections and in two patients with raised WBC had no sign of infection found in them. From the five patients that were not started on antibiotics, three of them had infection. Among 18 patients that were on antibiotics, 14 had infection detected in them. There was no significant agreement between antibiotics initiation and the presence of infection (p=0.423), Kappa 0.166.

Table I: Clinical characteristics of patients during referrals

Characteristics	Number (n)	Percent (%)
Fever		
Yes	18	78.3
No	5	21.7
ESR (normal range 0-22mm/ hour)		
Above normal range	7	30.4
Not available	16	69.6
WBC (normal range 4.0-11.0 x10^9/l)		
Less than 11	15	65.2
More than 11	8	34.8
Antibiotic started		
Yes	18	78.3
No	5	21.7
Provisional diagnosis / reason for referrals		
Osteomyelitis (OM)	10	43.5
Unknown infection/Pyrexia of unknown origin (PUO)	13	56.5

Imaging findings in patients with unknown site of infection/pyrexia of unknown origin (PUO)

In 13 patients with initial diagnosis of unknown site of infection/PUO that were referred, our planar imaging showed true positive findings in six patients, false positive findings in two patients, true negative findings in three patients and false negative findings in two patients, as compared to SPECT/CT findings of true positive for infection in seven out of 13 patients, true negative findings in five patients and false negative findings in a patient. As compared to planar imaging, SPECT/CT was able to provide accurate anatomical localisation and also the extent of infection in all patients with true positive lesions. Most of these patients that were categorised as having true positive lesions by SPECT/CT were thoroughly investigated by performing culture tests and plain radiographs with clinical findings to confirm and support the diagnosis. SPECT/CT was able to detect bowel wall infection in a patient which was not visualised on planar imaging. In another patient, the CT component managed to detect irregular soft tissue mass at the porta hepatis region which was not detected on planar imaging. This finding on CT helped to rule out infection and provide the clinician with other possibility for further investigation. There were four patients with true negative scan where SPECT/CT did not provide any extra information. Description of the planar and SPECT/CT findings in unknown site of infection/PUO is summarised in Table II.

Table II: Descriptive cases of unknown site of infection/pyrexia of unknown origin

Patient no.	Suspected infection	Planar findings	SPECT/CT findings	SPECT/CT contribution	Final diagnosis/ (Method to achieve final diagnosis)
1	Unknown site of infection	No infection	No infection	-	Positive Retro Viral Disease (by blood investigation)
2	PUO	Infection or degenerative changes at L2/L3 vertebra	1) Infection in L2 vertebra with lytic lesion 2) Soft tissue calcification at left gluteal with no uptake	Define OM with information on the extent of involvement	OM (Clinical diagnosis, radiograph)
3	PUO	Infection or degenerative changes at T12/L1 vertebra	Infection in L1 vertebra with lytic lesion	Define OM with information on the extent of involvement	OM (Clinical diagnosis, radiograph)
4	PUO	Infection at left mid calf region	Soft tissue infection at soleus muscle	Define extent of soft tissue infection and exclude OM	Soft tissue infection (Clinical diagnosis)
5	PUO	Infection/ Inflammation at bilateral knee region	1) Heterogenous uptake at bilateral knee joints and the surrounding bursa (left >right) with areas of calcification within the joints 2) Mild uptake seen at left ankle with no CT lesion	Define OM in ankle joint	Left ankle OM with bilateral knee inflammation (Clinical diagnosis, radiograph)
6	PUO	No infection	No infection. CT noted irregular soft tissue mass at the porta hepatis region at the level of T11 extending down to L4 vertebra	Exclude infection, detect malignancy	Abdominal malignancy (CT TAP)
7	PUO	1) Infection at left pelvic region 2) Infection at right pelvis	1) Uptake at left anterior aspect of the large pelvic mass adjacent to left stoma with no clear demarcation with the bowel 2) Another uptake at lateral aspect of smaller right pelvic mass Uptake at pelvic masses could be due to tumour itself or inflammatory processes in the tumour	Exclude infection, detect malignancy	Ovarian malignancy (CT TAP and clinical diagnosis)
8	PUO	Infection / Inflammation at T10 and T12 vertebra	Degenerative changes at T10 and T12 vertebra with reduced vertebral height	Exclude infection	Degenerative changes at T10-T12 (Clinical diagnosis, radiograph)
9	PUO	No infection	Infection and inflammation in bowel wall of transverse colon and in the descending colon with no CT lesion	Define infection and inflammation	Colitis (Clinical diagnosis)
10	PUO	No infection	No infection	Unable to detect infection	Urosepsis and pneumonia (Urine culture and chest radiograph)
11	PUO	Infection in abdomen likely transverse colon and descending colon	Infection in wall of distal half of transverse, descending and sigmoid colon	Define infection and inflammation	Colitis (Clinical diagnosis)
12	PUO	No infection. Multiple photon deficient area seen throughout the spine, skull and right hemipelvic region likely caused by malignancy	No infection. Multiple photon deficient area at the spine with compression fractures at T9 and T12 with multilevel extensive lytic sclerotic lesions at vertebral body with photon deficient area at right parietal skull	Exclude infection, detect malignancy	Advanced gastric carcinoma with metastases to bones and lymph nodes (CT TAP)
13	PUO	1) Infection or physiological uptake at bilateral lung fields 2) Multiple photon deficient area at the left abdominal region likely splenic infarct	1) Infection or physiological uptake at bilateral lung fields with no CT lesion 2) Multiple photon deficient area at spleen corresponding to hypodense lesion likely splenic infarct	Lung infection, exclude infection elsewhere	Pneumonia, splenic infarct (Blood culture and CT TAP)

SPECT/CT, single photon emission computed tomography/computed tomography; PUO, pyrexia of unknown origin; OM, osteomyelitis; CT, computed tomography; TAP, thorax, abdomen and pelvis

Imaging findings in patients with osteomyelitis (OM)/ infected implants

In this group of 10 patients, true positive findings were seen in eight patients and true negative findings in two patients on planar imaging. Neither false positive nor false negative findings were seen in this group. From the findings in this study, SPECT/CT demonstrated the capability to differentiate between infected implants and infection involving soft tissues. The final diagnosis was mostly confirmed and supported by culture tests, plain radiograph and clinical findings. Description of the planar and SPECT/CT findings of these orthopaedic infection cases is summarised in Table III.

Table III: Descriptive cases of osteomyelitis

Patient no.	Suspected infection	Planar findings	SPECT/CT findings	SPECT/CT contribution	Final diagnosis/ (Method to achieve final diagnosis)
1	OM	No infection	No infection	Exclude infection	Gouty arthritis (Clinical diagnosis, radiograph)
2	OM	Infection at left ankle region	Infection at left medial malleolus with lytic sclerotic lesion on CT	Defining OM	OM of left ankle joint (Clinical diagnosis, radiograph)
3	OM	Infection at right proximal femur	Infection along trochanteric region of right femur with photon deficient area seen in the head and neck of right femur corresponding to lytic lesion at the right femoral head.	Defining OM	OM of the right proximal femur (Clinical diagnosis, radiograph)
4	OM	Infection at distal right femur	Infection at distal right femur and periprosthetic area (Infected implant)	Defining OM	Infected implant (Tissue culture, radiograph)
5	OM	Infection at region of right end of femur and proximal right tibia	Infected right total knee replacement prosthesis (right distal femur, proximal right tibia and at tip of the prosthesis)	Defining OM	Infected right total knee replacement (Tissue culture, radiograph)
6	OM	Infection at left knee region with prominent uptake at the distal end of left femur	Infection at the periarticular region of left knee with prominent uptake at the distal end of left femur (above the lateral epicondyle) with no corresponding CT lesion	Defining OM	Infected implant (Tissue culture, radiograph)
7	OM	Infection at right knee region	Infected right knee prosthesis	Defining OM	Infected implant (Clinical diagnosis, radiograph)
8	OM	No infection	No infection	Exclude infected prosthesis	Loosening of implant (Triple phase bone scan, radiograph)
9	OM	Infection at shaft of left femur	Infection at marrow of shaft of left femur	Defining OM	OM of left shaft of femur (Tissue culture, radiograph)
10	OM	Infection at right ankle region	Infection at right talocrural and subtalar joints with periarticular sclerotic changes of right talocrural and subtalar joints	Defining OM	OM of right ankle joint (Clinical diagnosis, radiograph)

SPECT/CT, single photon emission computed tomography/computed tomography; OM, osteomyelitis; CT, computed tomography

SPECT/CT contribution to the final diagnosis

Planar imaging was able to detect most of the foci of uptake in all patients with infection which was also detected by SPECT/CT (Table IV). SPECT/CT managed to detect infection in a patient which was missed in the planar imaging, hence changed the management of this patient. The agreement between the two modalities was significant with a Kappa value of 0.8 ($p<0.05$). Besides the uptake similarity, SPECT/CT demonstrated its capability to change the diagnosis in two patients from unknown site of infection/PUO group. The CT component was able to pick up a mass at porta hepatis region in a patient, which was diagnosed to be an abdominal malignancy on further investigation (Table II, patient no 6). In another patient, SPECT/CT managed to detect degenerative changes involving the vertebrae which was misinterpreted as infection on planar imaging alone (Table II, patient no 8).

Agreement between presence of infection and planar uptake

Planar imaging is able to detect infection with high sensitivity of 87.5% and with a specificity of 71.4%. The agreement that was obtained in this study between the presence of infection and the ability of planar imaging to detect infection was significant ($p<0.05$) with Kappa agreement of 0.7. Planar imaging was able to correctly localise infection in 14 out of 23 patients (Table V).

Table IV: Correlation between planar and SPECT/CT in localising infection

Planar	SPECT/CT		Total
	No infection (No. of patients, Percentage)	Infection (No. of patients, Percentage)	
No infection (No. of patients, Percentage)	6 (75.0%)	1 (6.7%)	7 (30.4%)
Infection (No. of patients, Percentage)	2 (25.0%)	14 (93.3%)	16 (69.6%)
Total	8 (100%)	15 (100%)	23 (100%)

SPECT/CT, single photon emission computed tomography/computed tomography

Agreement between presence of infection and SPECT/CT imaging

SPECT/CT imaging has the capability to detect infection

Table V: Correlation between planar imaging findings with final diagnosis

		Final diagnosis of infection		Total
		No	Yes	
Planar	No infection (No. of patients, Percentage)	5 (71.4%)	2 (12.5%)	7 (30.4%)
	Infection (No. of patients, Percentage)	2 (28.6%)	14 (87.5%)	16 (69.6%)
Total		7 (100%)	16 (100%)	23 (100%)

with high sensitivityof 93.8% and specificity of 100%. The agreement that was obtained in this study between the presence of infection and the ability of SPECT/CT imaging to detect infection was significant ($p<0.05$) and superior to planar imaging with Kappa agreement of 0.9. SPECT/CT managed to detect infection in 15 out of 23 patients (Table VI).

Table VI: Correlation between SPECT/CT imaging findings with final diagnosis

		Final diagnosis of infection		Total
		No	Yes	
SPECT/CT	No infection (No. of patients, Percentage)	7 (100%)	1 (6.3%)	8 (34.8%)
	Infection (No. of patients, Percentage)	0 (0%)	15 (93.7%)	15 (65.2%)
Total		7 (100%)	16 (100%)	23 (100%)

SPECT/CT, single photon emission computed tomography/computed tomography

Sensitivity and Specificity

Sensitivity and specificity were separately calculated for planar imaging and SPECT/CT. From the data obtained, SPECT/CT had higher sensitivity and specificity in detecting infection as compared to planar imaging alone (Table VII).

Table VII: Sensitivity and specificity of planar and SPECT/CT Tc99m-besilesomab in detecting infection

Parameters	Planar	SPECT/CT
Sensitivity (%)	87.5	93.8
Specificity (%)	71.4	100.0

SPECT/CT, single photon emission computed tomography/computed tomography

DISCUSSION

In the sociodemographic aspect of the study, a total of 23 patients underwent Tc99m-besilesomab study for duration of five months in 2016. Both planar imaging and SPECT/CT were performed in these patients. The patients were predominantly Malays, followed by Indians and Chinese, reflecting the majority of Malay race in our general population. Looking at the age groups, it was found that older people were referred more for this study. The higher number of patients referred from the older age group is likely related to the fact that older people are prone to have weaker immunity, and some other diseases and co-morbids that easily predispose them to bacterial and viral infection.

The provisional diagnosis or main reasons for the referrals in this study were unknown sites of infection/ PUO (56.5%) and suspected OM/infected implants (43.5%). Eversince the introduction of besilesomab about 21 years ago, numerous clinical studies had been conducted to evaluate the effectiveness of Tc99m-besilesomab in diagnosing OM. Tc99m-besilesomab were found to be helpful in diagnosing OM with high sensitivity and specificity, ranging between 70% and 90% (4). Besides OM and infected implants, Tc99m-besilesomab has been widely used for inflammation and infection detection in PUO (5) and inflammatory bowel disease cases. In PUO, the sensitivity and specificity of Tc99m-besilesomab was reported ranging between 40% and 73%, and between 92% and 97% respectively (6).

In analysing the WBC value, it was noted that from eight patients with raised WBC, six patients had infection in the final diagnosis. From the 15 patients with normal value WBC, 11 patients had infection. This could be attributed to early initiation of antibiotics or partially treated infections in these patients. In this study, 18 patients had been started on antibiotics. From this total number of patients, four patients were not having infection. This could be attributed by other causes such as inflammation in arthritis, loosening of implants and even malignancy. From this study, there was no significant agreement noted between antibiotics initiation and presence of infection on imaging. Our findings was similar to study by Datz and Thorne (7) whereby they did not find any significant differences in sensitivity between the groups that was started and not started on antibiotics prior to leukocyte scan. Antibiotics destroyed the bacteria and caused reduction of chemotactic inhibitors produced by bacteria that can inactivate chemotaxins (8). Therefore in their study, the leukocyte scan sensitivity was not reduced by the usage of antibiotic treatment as opposed to a study by Palestro et al. (9). Indeed, antibiotics has the capability to alter chemotaxis by binding to leucocytes and reducing the affinity of the chemotactic receptor on the cell membrane (10).

Prior to the availability of SPECT/CT, planar Tc99m-besilesomab was used to rule out infective cause of PUO, diagnose OM and infected implants. However, sensitivity of this scan may be decreased in certain areas due to the physiological uptake, lack of anatomical landmarks and poor resolution. The highest uptake was seen in the spine (11) due to bone marrow accumulation with up to 40% of the injected activity accumulating

there. Other variable sites include the spleen, bowel, liver and kidneys (12). We concluded that there was substantial agreement between the ability of planar Tc99m-besilesomab to detect infection with Kappa agreement of 0.7 (P<0.05). In this study, planar scan was able to detect infection in 14 out of 23 patients and rule out infection in five out of 23 patients. In two patients with false negative findings, infection was missed due to its near location to physiological uptake in the urinary system and in the other patient, the uptake in the bowel was missed however was later seen on SPECT/CT. In one patient, planar imaging showed false positive findings as it was unable to differentiate between inflammatory process due to degenerative changes and infection. Mourad et al in 2003 (13) studied 82 patients and found that in 35 patients (43%), the main limitation of the modality was inability to localise infective focus within a specific organ. The sensitivity and specificity of planar Tc99m-besilesomab to detect infective foci was 87.5% and 71.4% respectively. The specificity was lower as compared to the sensitivity due to the presence of false positive result in one patient. This sensitivity was higher as compared to study by Becker et al. (5) whereby in his study, the overall diagnostic sensitivity of Tc99m-besilesomab for infection was 40% with specificity of 92%. Due to poor gamma-camera imaging resolution, false-negative scans were seen in those with endocarditis, pneumonia and small brain abscesses. Only planar imaging were done for suspected cases of endocarditis, therefore many cases of endocarditis were missed, as planar imaging was unable to detect infective foci on the moving cardiac valves. However, when patients with diagnosis of endocarditis were excluded from their study, the sensitivity of their study increased to 57% from 40% and the specificity increased to 95% from 92%.

In recent years, the integration of anatomical imaging techniques and SPECT has undergone significant growth. Basically a SPECT/CT scan is made up of two separate components, a SPECT and a CT scan. The images from each scan are fused together to produce more accurate functional and anatomical information of the scanned area by giving more accurate localisation of lesion, defining the extent of disease and also adding up the specificity of disease localisation. On top of all the benefits, the addition of CT to SPECT also helps in correction of attenuation and partial-volume effects. This hybrid imaging is technically more challenging and complex but provides useful information for some procedures along with patient examinations (14). All these benefits help in diagnosis and tissue biopsy procurement. The integration of hybrid imaging device such as SPECT/CT in this study has helped to localise and characterise the lesion, and differentiate between infection, benign lesion and also malignancy.

SPECT/CT has added slight contribution to the final diagnosis and has increased the specificity of study by 28.6% by accurately providing additional information on the anatomy in those with positive scan. The specificity of SPECT/CT to detect infection was 100% as compared to planar imaging which was 71.4%. Strong agreement was seen between SPECT/CT and the ability to diagnose infection in our study with a Kappa value of 0.9. Horger et al. (15) demonstrated the capability of SPECT/CT to change the interpretation by 28% in 27 suspected OM patients with suspicious foci. SPECT/CT was contributory in 48% patients to detect the accurate anatomical site and all foci of uptake seen on planar scan was correctly localised. The differentiation between septic arthritis, OM and infection involving soft tissues were correctly made by SPECT/CT imaging. In this study, besides being able to accurately locate the anatomical sites of infection and the extent of the infection, SPECT/CT was also able to change the management in two patients. On the planar imaging, there was no infectious sites detected, however on SPECT/CT we were able to locate the uptake in the bowel wall which was in keeping with the clinical history and final diagnosis of bowel infection. In another patient, planar image showed heterogenous uptake at the pelvic region whereby SPECT/CT image have helped to localise anatomically the uptakes which were actually from pelvic masses, likely due to underlying inflammation within the masses. There was limitation in Tc99m-besilesomab as seen in one of the patient whereby SPECT/CT missed to detect infection in the urinary tract due to physiological excretion of the tracer in the urine. One of the patient in this study showed diffuse uptake at bilateral lungs. Localisation of infection in lungs can be difficult because of cardiac blood pool activity, pulmonary blood background and margination of leucocyte along small pulmonary vessels making the interpretation of lung imaging difficult. A negative scan would exclude lung infection with high confidence despite all the limitations (16). Another example on how SPECT/CT help in localising and characterising the lesion is seen in our study whereby planar image showed focus of increased tracer uptake at the right ankle region. We were able to interpret better by localising the infection to the talocrural and subtalar joints, and establish the extent of lesion by performing SPECT/CT.

The reason for high sensitivity and specificity of SPECT/CT in this study could be due to the fact that the patients who were referred for this scan were those that had been thoroughly investigated and the suspicion of having infection was high in these patients. Therefore the sensitivity and specificity in this study was rather high as compared to other studies reported earlier. Few other studies had demonstrated the benefit of SPECT/CT as compared to performing planar imaging alone (17). Filippi and Schillaci showed the ability of SPECT/CT to provide additional anatomical information on all patients with positive scan results (64.2%), and added a significant contribution in 35.7% of these patients with regard to the final diagnosis.

CONCLUSION

Indeed, the addition of SPECT/CT has increased the specificity and sensitivity of the imaging, helped in accurately localising the lesion and defining the extent of involvement. The most important outcome derived from the alteration in patient management clinically by detecting or excluding infection as this could prevent from unnecessary usage of prolonged antibiotics in patients and prevent the emergence of antibiotics resistance. Despite the superiority of SPECT/CT as compared to planar imaging, it should be kept in mind that in infection imaging, infection in the area with normal physiological uptake could be missed even by SPECT/CT due to the high physiological uptake in these areas such as the urinary system, liver and spleen. In these cases, correlation with investigations such as cultures, blood investigations and other imaging is required.

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