



Assessment of the Outcome of USG Guided Percutaneous Drainage of Liver Abscess with and Without Administration of Intra Cavitory Meropenem & Urokinase

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Abstract

Background: To evaluate the outcome of USG guided pigtail drainage of liver abscess with administration of intra cavitory meropenem and urokinase. Urokinase by its fibrinolytic action and meropenem with its time dependent local action enhances drainage of liver abscess.

Materials and Methods

- Pig tail (9 Fr/10Fr) inserted under USG guidance for all patients with liver abscess > 5 cm , pus to be drained from the liver abscess and sent for culture sensitivity.
- Instillation of intracavitory urokinase depends on the size of the abscess (2500 IU / cm of abscess diameter) on the 1st day , repeated at 8-hr intervals . Pigtail was clamped for 15 minutes and then unclamped.
- On third day if the organisms in the pus shows culture sensitivity positive for meropenem, 500 mg of meropenem administered inside the abscess , repeated two more times after one and two weeks since the first administration.

Results: The outcome of study is assessed by percentage of decrease in size of liver abscess at day 3,5,7,10 and 15 and the duration of hospital stay . It was found that using analysis of variance, p value is 0.032,chi square value 27.979 statistically significant difference exists.

Conclusion: Patients treated with intra cavitory drugs meropenem and urokinase had shorter hospital stay (Day 7 (min)-Day 15(max). Control patients had longer hospital stay (>15 days). Combination of urokinase with meropenem shortens the hospital stay

Keywords: Liver Abscess, Meropenem & Urokinase.

Introduction

Liver abscess requires appropriate diagnosis and early interventions, as they pose an important clinical problem. They are of two types – protozoal / amoebic and pyogenic liver abscess. Causative agent for amoebic abscess is Entamoeba histolytica, usually secondary to intestinal infection^[1]. Entamoebadispar, entamoeba moshkovskii, entamoeba bangladeshi

are the non pathogenic species closely related to the disease.

Hepatic diverticulum^[2] is the out pouching from the ventral foregut epithelium. Liver and intrahepatic biliary tree arises from anterior portion of the diverticulum. Based on Bismuth liver segments are defined based on their relationship with portal and hepatic veins^[4].For the liver abscess measuring >5cm, percutaneous

pigtail drainage is the treatment of choice, along with systemic antibiotics.

For the liver abscess measuring <5cm ,percutaneous needle aspiration is performed along with systemic antibiotics.

Fibrinolytic drugs like urokinase when administered inside the abscess cavity ,it reduces the viscosity of pus, there by enhances drainage.

Antibiotics like meropenem by time dependent local action causes speedy recovery. 2.3 cases per 100,000 people is the annual incidence rate^[5]

Risk factors include^[6] Diabetes, Liver cirrhosis, Hepatobiliary or pancreatic disease,etc

USG - Hypoechoic mass (arrowheads) with internal echoes produced by echogenic septa (arrow) and debris. Note the absence of internal Doppler signal. Confirmed case of a multimicrobial abscess double target sign^[9].

Fungal abscess

In immunocompromised patients presents in the form of microabscesses^[10]

Hydatid Cysts

. Liver is the most common site to be affected. Next common site is lungs. Causative organisms is the larval stage echinococcus granulosus tapeworm.^[11]

For liver abscess more than 5 cm, percutaneous drainage is the preferred method.^[12]

Only in case of peritonitis, abscess rupture, open surgical approach is preferred^[13]

Percutaneous needle aspirations⁽¹³⁾

For aspiration of pus, spinal needle of 18G is used. Under USG guidance, 5% lignocaine as local anaesthetic, the preferred site is infiltrated. With USG guidance abscess cavity is approached with spinal needle. Correct position is confirmed by pus aspiration. ⁽¹⁴⁾ Pus aspirated multiple times with needle in place till no further pus could be aspirated.

After that USG abdomen is performed to look for the residual size of the abscess cavity.

Percutaneous drainage

⁽¹⁵⁾ Using 10/12 Fr pigtail with modified seldinger technique, largest abscess locule is cannulated, pus aspirated to find the needle position.

The shortest length between the abscess with capsule of liver should be mentioned..

According to Liao et al the following are the predisposing factors for PCD failure - lack of cystic areas, presence of gas, size of abscess >7.3 cm, shortest distance between capsule of liver and the lesion (<0.25 cm)⁽¹⁶⁾.

Urokinase

It is a known fact that percutaneous drainage for multilocular abscess has got lower success rates. Many studies show that in empyema/loculated hemothorax,the drainage is enhanced by the injection of fibrinolytics into the pleural cavity. Urokinase causes increase in fibrin turn over, which is not associated with complications like bleeding/ altered coagulation factors . Also urokinase helps in liquefying thick pus and breaks the loculations there by enhances drainage. ^[17]The dose of urokinase is assigned based on the size of the abscess 3-5cm (25,000 IU),5-10 cm(50,000 IU), >10cm (1,00,000 IU). ^[18]Among fibrinolytics urokinase is the preferred drug . It is because of :

- ❖ No side effects/systemic effects
- ❖ It is a hydrolase enzyme, High level of fibrin is present in the pus. Within the pus urokinase retains the enzymatic properties, fibrin is split into smaller fragments. Urokinase splits the plasminogen to the active protease like plasmin .It degrades the fibrin^[19]

Meropenem

In large abscesses , there is poor penetration of systemic antibiotics into the abscess cavity .Volume of the abscess cavity is reduced by the percutaneous drainage, followed by administration of antibiotic into the abscess cavity. So the antimicrobial attains high concentration within the cavity .Half life of these drugs are increased by the proteins in the abscess fluid. Lack of vascularity^[20] also promotes the action of the drug

The efficacy of the antibiotic depends on the sensitivity of the bacteria to the antibiotic, acidic / anerobic conditions, half life of the drug. To achieve intra cavitory concentration above the minimal inhibitory concentration 500 mg of meropenem has to be instilled.

For time dependent antibiotics, half life of the drug is important, the antibiotic metabolism is by hepatocytes and depends on the protein binding capacity.

In closely spaced abscess, instillation of meropenem in one cavity, may diffuse through the inter abscess membrane into the second cavity. High concentration of meropenem is noted in the tissue surrounding the abscess because of the low protein binding capacity^[20]

Materials and Methods

Study Methodology

Study Design: Randomised Control Study

Study Period: From August 2018 – May 2019, for a period of 10 months

Study Population: Patients of both sexes attending the outpatient department and those admitted in the wards in Govt Royapettah Hospital and Government Kilpauk Medical College and Hospital, Chennai.

Inclusion Criteria

- ❖ All Liver abscess Patients > 5 cm for urokinase instillation
- ❖ Patients with meropenem sensitive liver abscess >5 cm for meropenem instillation
- ❖ Both male and female sexes included

Exclusion Criteria

- ❖ Liver abscess with Culture sensitivity negative for meropenem is excluded for instillation of meropenem.
- ❖ Coagulation impairment
- ❖ Hypersensitivity to meropenem / urokinase
- ❖ Refusal to take part in the study

Data Collection

Data collection was performed in the included study group using a standard questionnaire/ proforma

Methodology

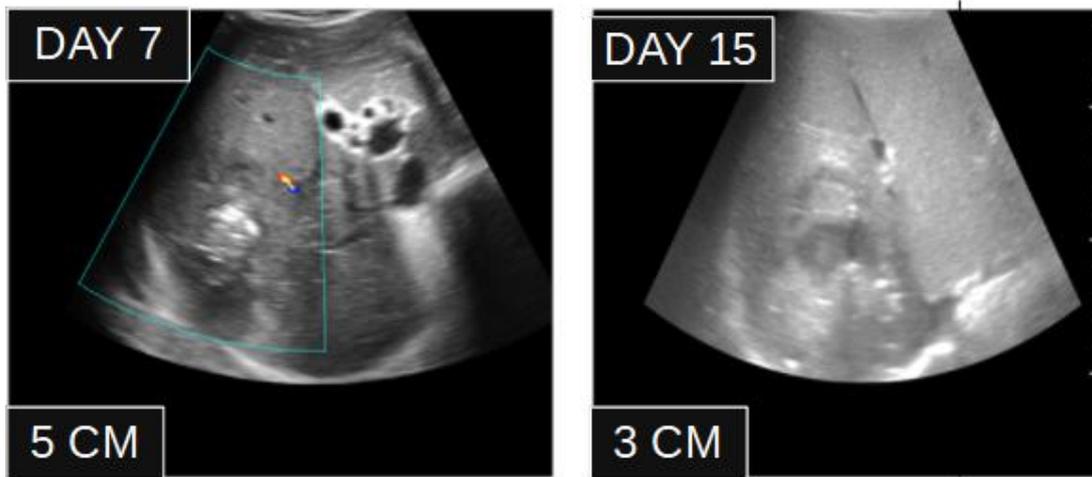
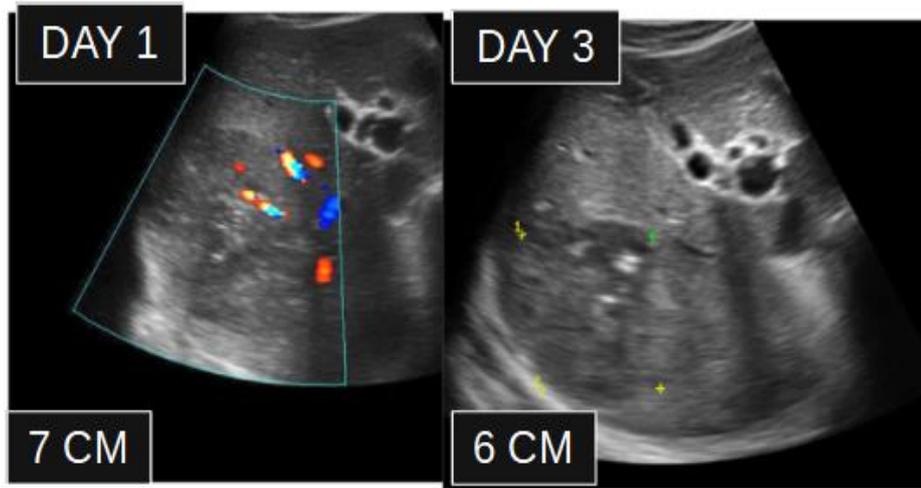
- ❖ All patients presenting with liver abscess >5 cm
- ❖ Pigtail catheter (9Fr/10Fr)
- ❖ Urokinase used as abscess-cavity irrigant.
- ❖ Meropenem.
- ❖ After explaining the details of the procedure, informed consent will be obtained from the patient. Under strict aseptic precaution, under local anaesthesia skin incised using 11size blade. pig tail (9Fr/10Fr) inserted under USG guidance for all patients with liver abscess > 5 cm, pus to be drained from the liver abscess and sent for culture sensitivity. Pig tail catheter is fixed to the skin by 3-0 silk.
- ❖ Instillation of intracavitory urokinase to be done on the first day for all patients with liver abscess > 5 cm. Dose depends on the size of the abscess (2500 IU / cm of abscess diameter) Urokinase dissolved in 10 ml of normal saline was instilled and pigtail is clamped for 30 minutes so that gravity drainage could occur. Patient is followed up by USG.
- ❖ On third day if the organisms in the pus shows culture sensitivity positive for meropenem, 500 mg of meropenem followed by 10 ml of normal saline administered inside the abscess. Patient is followed up by USG.

Case – 1

A 48 year old diabetic patient with complaints of right hypochondrial pain, USG showed well defined heteroechoic collection in right lobe segments.

On day 1 abscess size is 7cm, after draining pus urokinase given.

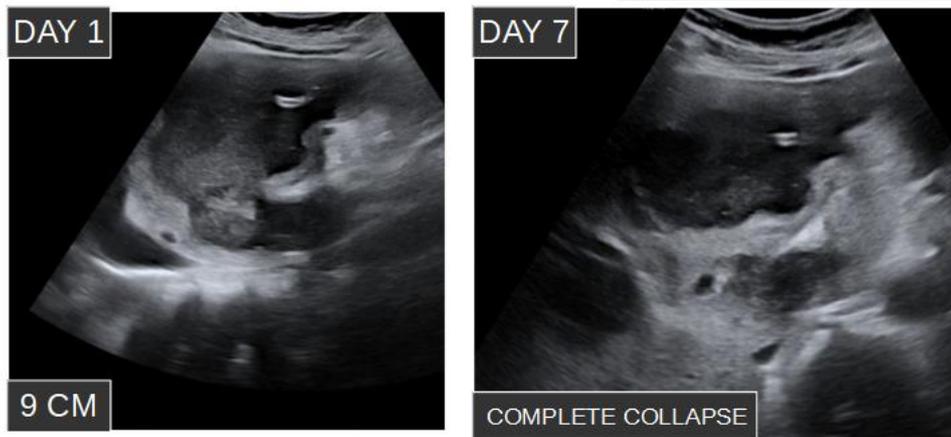
Day 3 size of the abscess is 6cm. pus culture showed sensitivity to meropenem, but intra cavitory meropenem not given to the patient, the routine systemic antibiotics given to the patient. Day 15 the size is 3 cm. Pigtail is removed on 15th day.



Case - 2

A 65 year old male patient with continuous fever for 10 days, USG showed hypoechoic collection, pigtail inserted, On day 1 abscess size is 9cm, after draining pus, urokinase given. On day 3, pus

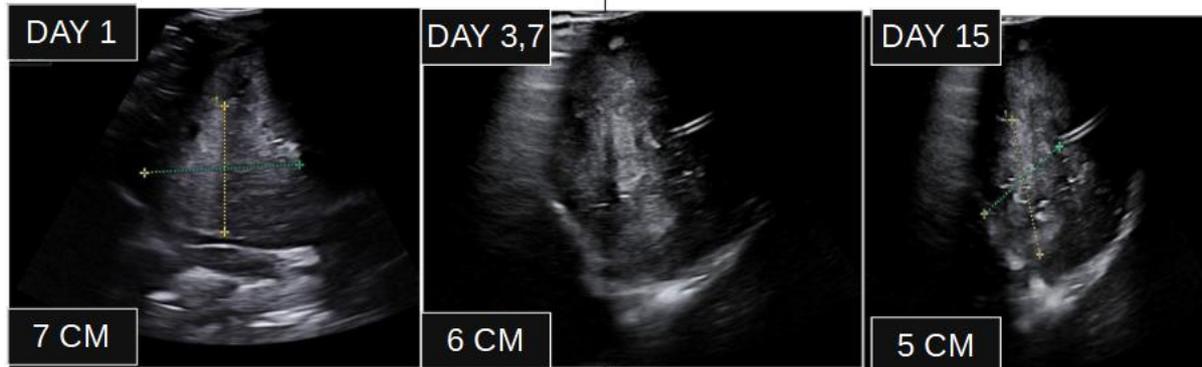
culture showed sensitivity to meropenem, so intra cavitory meropenem given to the patient. Day 7 complete collapse of abscess cavity. Patient discharged.



Case - 3

A 40 year old diabetic patient with c/o right hypochondrial pain and fever, USG showed well defined heteroechoic collection in right lobe. On day 1 the size is 7 cm .pigtail inserted. No intracavitary drugs given. But the patient will be routinely getting systemic antibiotics from ward.

On day 3, the size is 6 cm. pus culture sensitivity positive for meropenem. But no intra cavitory meropenem given. Day 7 the size is still 6cm. Day 15 the size is 5cm. the patient got discharged at 18 th day as the size turned 3cm on day 18.

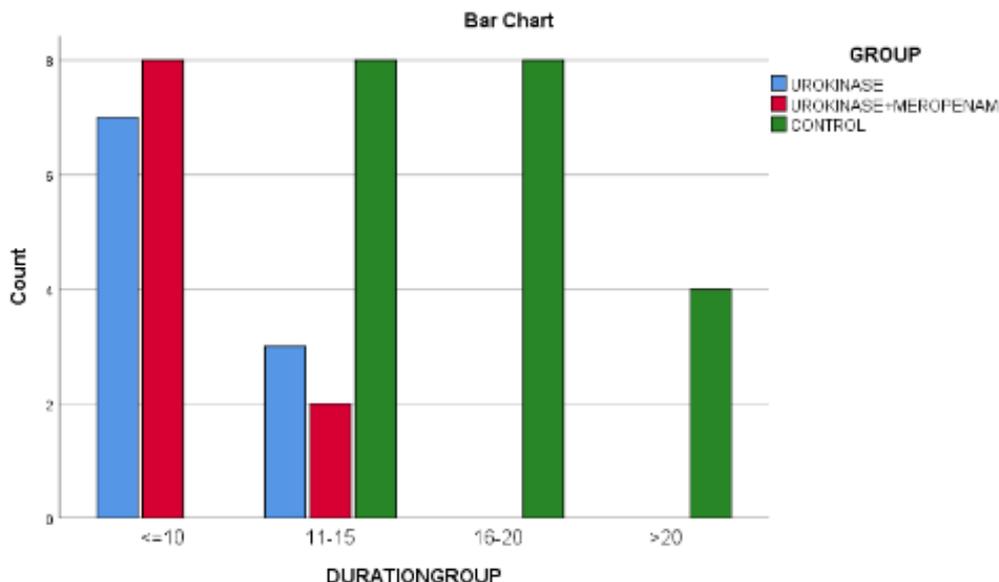


Statistical Analysis & Results

The Data was entered in a excel worksheet and double checked.IBM SPSS version 22 software is used for statistical analysis.

Difference in size of liver abscesses between cases and controls are not statistically significant with chi square value of 0.137 and P value of 0.069. .Hence different size of abscesses between cases and controls does not provide selection bias.

Comparison of Duration of Hospital Stay between Cases and Controls



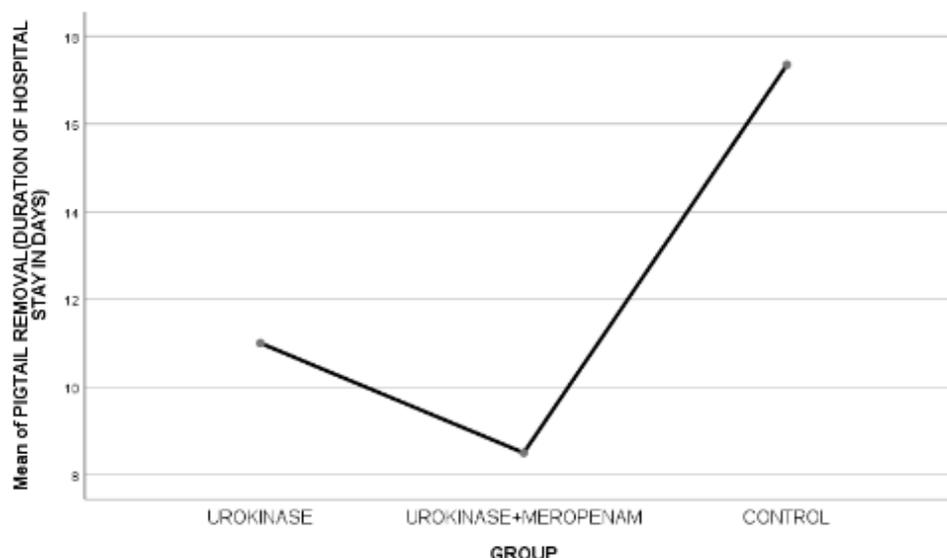
From the above bar chart, we infer that usage of urokinase and combination of urokinase with meropenem shortens the hospital stay, patients treated with these intra cavitory drugs had shorter hospital stay (<15 days). Control patients had longer hospital stay (>15 days).

With chi square value 27.979 and p value <0.05, these values in the table are statistically significant. Usage of intra cavitory urokinase and meropenem significantly decreases duration of hospital stay.

On day 3,7,10,15, the percentage of decrease in size of the liver abscess is significantly greater for the group taking urokinase and meropenem than

the other two. So combined drugs promote easy drainage of liver abscess.

Analysis of the date of Pigtail Removal (Duration of Hospital Stay in Days) Means Plots



The mean date of pigtail removal for the combined urokinase and meropenem group is (8.50 days) which is elevated than for urokinase alone (11.26 days) and control group (17.35 days). By using analysis of variance, P value < 0.05, the combination of urokinase and meropenem causes statistically significant difference in pigtail removal, causing speedy recovery compared with other two, urokinase statistically differs compared with control.

Discussion

Distribution of age, lobe, size and co morbidities like pancreatitis, cholelithiasis, etc. among cases and controls are not showing statistically significant difference between cases and controls. Hence eliminates bias.

In our study the percentage of decrease in size of the liver abscess is significantly greater for the group taking urokinase and meropenem than the other two on day 3,7,10,15,

Percentage of decrease in size of abscess is significantly greater for urokinase group compared to the control group. So combined drugs promote easy drainage of liver abscess.

By using analysis of variance, P value < 0.05, the combination of urokinase and meropenem causes statistically significant difference in pigtail removal, causing speedy recovery compared with other two. Urokinase group statistically differs from control group.

So, we infer that usage of urokinase and combination of urokinase with meropenem shortens the hospital stay, (<15 days). Control patients had longer hospital stay (>15 days).

With chi square value 27.979 and p value <0.05, these values in the table are statistically significant. Usage of intra cavitory urokinase and meropenem significantly decreases duration of hospital stay.

In a study **volgelzang et al**⁽²¹⁾ proved the effect of intra cavitory fibrinolytics in post op intra abdominal hematomas. All the loculations and fibrinous adhesions may delay the complete drainage.

Lahora et al⁽²²⁾ proved the safety of urokinase, he stated that the drug causes increase in fibrin turnover, which is not associated with complications like bleeding/ altered coagulation factors.

Park et al⁽²³⁾ showed that urokinase acts by reducing the viscosity of purulent material and there by enhance the flow through the catheter.

According to the study of **Bouros et al**⁽²⁴⁾ the intra pleural instillation of urokinase (50,000 U in 100 ml of 0.9% saline solution) significantly increased the drainage of loculated pleural effusion and parapneumonic effusion.

Urokinase also helps in drainage of multilocular liver abscess, but the success rate is less when compared to the simple abscess without loculations^(25,26)

The safety of the drug urokinase in liver abscess is proved in the studies by oh jh, Yoon y⁽²⁷⁾.

Further studies by Lee KS proved the safety of urokinase in empyema⁽²⁸⁾

Urokinase in loculated pleural effusions enhances drainage⁽²⁹⁾

Few studies show that intra cavitory antibiotics in brain abscess reduced the duration of systemic antibiotics.⁽³⁰⁾

Similar concept is used in our study, intra cavitory administration of meropenem reduced the hospital stay.

Conclusion

Image guided percutaneous drainage of liver abscess has replaced open surgical drainage. Addition of Urokinase on the same day of pigtail insertion and meropenem on third day enhances drainage of liver abscess.

With the follow up of patients with ultrasound on day 3,7,10,15, it was found that image guided percutaneous drainage of liver abscess with combination of intra cavitory urokinase with meropenem shortens the hospital stay

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