Risk of Bacteraemia in Splenectomised Cirrhotic Patients after Elective Oesophageal Injection Sclerotherapy

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Abstract: Injection sclerotherapy still predominant in many Egyptian endoscopic units and is usually associated with transient bacteraemia in up to 30 % of upper GI endoscopies .The risk of bacteremia is more common in cirrhotic patients scheduled for injection sclerotherapy. The splenectomised cirrhotic patients are more susceptible to this risk. We aimed to estimate the prevalence of bacteremia in splenectomised cirrhotic patients who underwent injection sclerotherapy in our unit. Patient and Methods: A prospective observation study was conducted in our endoscopy unit, Internal Medicine department, Zagazig University Hospital, Egypt, over a period of six months from December 2009 to May 2010. One hundred and forty cirrhotic patient (78 male and 62 female were included in this study and were classified into two groups (according to absence or presence of the spleen); patient group; included 80 splenectomised cirrhotic patient and control group that included 60 non-splenectomised cirrhotic patient (35 male and 25 female). All patients were cirrhotic (Child A and B), and they were referred for scheduled elective endoscopic injection sclerotherapy. High sensitive CRP (*Hs-CRP*) and blood culture 10 minutes before and 20 minute post-endoscopy were taken for all patients. Presence or absence of bacteraemia was detected and recorded. Results: No positive blood cultures were detected before the endoscopy for all patients. 20 patients (14.3%) of the whole participants had positive blood culture after injection sclerotherapy; 3 of them (5%) were in non-splenectomised patients (control group) and 17 (21.25%) were in splenctomised patients (patients group). Positive blood cultures were more frequent in Child B patients compared to Child A (13 vs. 7) in both splenctomised and non-splenectomised patients with statistically significant difference. *Hs-CRP* was significantly elevated in Child B patients compared to Child A patients (P=0.018), moreover, *Hs-CRP* was highly elevated in positive culture cases regardless the Child status of the patients. Six types of micro-organisms were isolated in our study; Actinomyces (3), Candida Albican (2), H. Influenza (3), Alpha Haemolytic Streptococci (4) and Coagulase Negative Staphylococci (4) and Streptococcus Viridian (4). Conclusion: Prevalence of bacteraemia was higher in the injection sclerotherapy splenectomised cirrhotic group compared to non- splenectomised cirrhotic group, and in Child B patients more than Child A ones.

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1. Introduction:

The risk of infection after upper gastrointestinal (GI) tract endoscopy has been found to be infrequent (1); however, invasive endoscopic procedures can lead to various complications including remote bacterial infection (2).

The most common systemic complication of the upper endoscopic procedure is fever which is usually transitory and results from mucosal inflammation not related to infection, however, there are considerable reports of serious bacterial complications such as; brain, perinepheric abscesses, bacterial peritonitis and bacterial endocarditis(3).

Transitory bacteraemia is a frequent event after injection sclerotherapy and can occur following minor trauma even after diagnostic upper GI endoscopy. Most transient bacteraemias don't cause symptoms and have no clinical significance; however, they become important in immuno-deficient patients and in those at risk for the developing of bacterial endocarditis (4).

Bacteraemia after endoscopic injection sclerotherapy is depending on multiple factors including ; the duration of the procedure, size of the injection needle ,device contamination, inappropriate disinfection and insufficient mechanical cleaning of the devices (5).This is in addition to host factors that may predispose to bacteraemia like advanced liver cell failure, renal cell failure, diabetes mellitus, elderly patients and in patients with defective immunological response as in immuno-compromised patients like transplant recipients and patients on immunosuppressive drugs and splenectomised patients(6).

The spleen plays a vital role in the host's protection against invading microorganisms and bacterial clearance after injection sclerotherapy (7). Splenectomy significantly increases both the febrile response to bacterial lipopolysaccharide (LPS) and

the uptake of LPS by Kupffer cells. Although, splenectomised patients get proper vaccinations for capsulated gram negative bacteria, yet they still at high risk of bacteraemia following any invasive procedure including, upper GI endoscopy (8).

With the recent advances in surgical treatments in chronic hepatic disorders, the indications for splenectomy in hepatic disorders have greatly expanded. In country like Egypt which is considered an endemic area for chronic HCV and Schistosomiasis infections , splenectomy usually with vaso-ligation is a common surgical practice especially when intractable pancytopenia develops .These splenectomised patients usually attend endoscopic units for follow up reappearance of oesophageal varices and become eligible for upper GI injection sclerotherapy for eradication of varices, if any.

In the context of splenectomy and immunological deficits of liver cirrhosis, cirrhotic patients with splenectomy eligible for injection sclerotherapy are at great risk for permanent bacteraemia post-endoscopy. We aimed to assess this risk after upper elective injection sclerotherapy in cirrhotic patients with splenectomy in our unit.

2. Patient and Methods

This prospective observation study was conducted in the endoscopy unit, Internal Medicine Department, Zagazig University Hospitals, Egypt, over a period of six months from December 2009 to May 2010.

140 cirrhotic patients were included in this study; 80 splenctomised patients as patient group and 60 non-splenctomised patients as control group. Patients participated in this study were all cirrhotic patients with *Child (A)* and *(B)* classification who attend our unit for elective injection sclerotherapy.

The exclusion criteria were:

- Advanced liver disease (*Child C*).
- Patients with any clinical or laboratory evidence of any febrile disease.
- History of antibiotic intake in the last week.
- Advanced respiratory or cardiac disease as well as renal failure patients.
- Any patient under immunosuppressive drugs.

The purpose and details of the study were explained for each patient, oral and written consent were taken from all patients and the patients who refused consent were excluded from the study.

All the participants were subjected to detailed history taking and bedside physical clinical examination complemented with routine investigations that included; urine analysis, CBC, serum albumin, hepatic transaminases, total and direct bilirubin, PT and INR , serum creatinine ,blood urea and real time abdominal ultrasound aiming to exclude unfit patients and put the patients into their *Child's* classification category.

Patient preparation prior to elective injection sclerotherapy endoscopy was only over-night fasting and the procedure was done at 9:00 AM. After putting in the left lateral position, patient was connected to a monitoring pulse-oximeter then Midazolam Hydrochloride (Mediathetic, Amoun Pharmaceutical Company, Egypt) in weight- based dose (70 micg /Kg) was administrated in a pre-settled IV cannula 3 minutes before the procedure. The endoscopy was done using Olympus GIF3W gastroscopy (Olympus Optical, Tokyo, Japan).Size and numbers of the gastroesophageal vaices were noticed and recorded ,injection sclerotherapy was done using sclerosant material ethanolamine Oleate 5%(EPICO pharmaceutical company, Egypt), 3~5 ml was used for each varix and a total of 10~25 ml was used for each endoscopic session. The oesophageal varices were injected tightly intravariceally using sterile 21 French size sclerotherapy needle (Wilson-cook, USA).

Blood cultures were taken for all patients 10 minutes before the endoscopy and 20 minute after finishing of the injection sclerotherapy. After reparation of the skin with 70% isopropyl alcohol, five millilitres of venous blood were drawn, the taken blood samples were then inoculated into 45 ml tryptic Soya broth media(Oxoid\®).The blood culture was incubated aerobically and anaerobically at 37 °C for seven days. All isolates were identified and recorded (12).

Plasma of 2 ml centrifuged blood was used to measure of *Hs-CRP* using high sensitivity C - reactive protein ELISA kit (Biometrica, USA) results above 3mg/dl was considered as positive reading.

Follow up of the patients:

All patients were followed and traced by telephone for any symptoms or signs of infection for 5 days post-endoscopy and confronted for clinical examination and necessary labs if needed.

Statistical Methods:

Data were analysed by Statistical Package for Social Science (SPSS) version 14 (SPSS, Chicago, USA).Results were expressed as means and standard deviation (SD) of the means. Differences between groups were analysed by using either the chi -square test or Student's t-test and non-parametric (Mann–Whitney test) for comparison between two groups or the analysis of variance (ANOVA) test for multiple group comparison. The p value was considered significant at $p < 0.05$.

3. Results

Our study included 140 cirrhotic patient (78 male (55.7%) and 62 female (44.3%) with mean age (43.3 ± 9.2 year), they were classified into two groups; the patient group included 80 patient (43 male and 37 female) and control group included 60 patients (35 male and 25 female). Both sex and age were matched in our study groups.

83 (59.3%) of all patient were of *Child A* and 57 (40.7%) of *Child B*. On looking to *Child* status of both groups, we found that control group included (33 patients with *Child A* and 27 patients with *Child B),* while patient group included (50 patients with *Child A* and 30 patients with *Child B*). *Child C* patients were excluded from the start. We didn't found statistical difference in *Child* classification distribution among both groups (Table 1).

Eighty patient (100%) in the patient group had varices; 46 (57.4%) had grade II varices, 27 (33.8%) had grade III and only 7 (8.8 %) had grade IV. In the other hand, control group, we reported 60 patient (100%) had varices; 25 (41.7%) had grade II varices, 20 (33.3%) had grade III and 15 (25. %) had grade IV varices with statistically difference between both groups. Moreover, No significant different was reported regarding size of OV between both groups (Table 1).

Regarding serum *Hs-CRP*, no statistically significant difference was found between both group either 10 minute before or 20 minute after the endoscopy, but we noticed a significant high *Hs-CRP* in positives blood culture cases. Moreover, on correlation of Hs-CRP with *Child* status of the patients in both groups, we find statistically significant difference (p=0.018) (Table 2, 3)

No positive blood cultures were detected before the endoscopy in both groups, however, post-endoscopy, we diagnosed 20 cases of positive blood culture (14.3%), 3 of them (15%) were in the control group and 17(85%) in the patient group with statistically significant difference (p=0.006) and OR(1.36) (Table 4).

Positive blood cultures were common in *Child B* patients (13 patient) than in *Child A* patients (7 patients) with statistically significant difference (p=0.021) table (3). Six micro-organisms were isolated from +ve blood cultures cases (Table 4, 5).

4 patients of +ve blood culture -all were splenectomised cirrhotic- showed high fever and rapid clinical deterioration on follow up, 2 of them needed hospital admission where they received IV antibiotic combination according to culture and sensitivity with remarkable clinical improvement within 3 days. They stayed for one week and discharged in a stable clinical condition. No deaths were reported in our study.

Table (1): General characteristics of study groups

item	*Control group*	*Patient group*	*X2*	*p*	OR
Age in years (mean (SD)	***43.7(8.6)***	***43 (9.7)***	***0.39***	***0.68***	
Gender: N (%)					
Male	***35(58.3%)***	***43(53.8%)***	***0.29***	***0.58***	
Female	***25(41.7%)***	***37(46.2%)***			
Child Classification: N (%)					
A	***33(55.0%)***	***50(62.5%)***	***0.8***	***0.37***	
B	***27(45.0%)***	***30(37.5%)***			
OV Size: N (%)					
2	***25(41.7%)***	***46(57.4%)***			
3	***20(33.3%)***	***27(33.8%)***	***7.46***	***0.02***	**1.36**
4	***15(25.0%)***	***7(8.8%)***			(0.6-3.11)
Blood culture :					
-ve	***57(95 %)***	***63(78.7%)***	***7.39***	***0.006***	**3.66**
+ve	***3(5%)***	***17(21.3%)***			(1,28-12.45)

Table (2): Serum hs-CRP in both study groups.

Variable	**Child Classification**		**t**	**p**
	A	**B**		
hs-CRP(mg/dl)	9.5±7.6	13.4±11.3	2.38	0.018

Table (3): Serum hs-CRP (mg/dl) before and after the endoscopy.

Time	Control group	Patients group	t	p
10 minutes before endoscopy	10.1 ±7.78	18 ±10.5	1.07	0.28
20 minutes after endoscopy	7.76 ±1.7	6.7 ±1.6	0.28	0.27

Table (4): Isolated micro-organisms in culture-positive cases.

Organism	Total (N %)	Control group (N %)	Patients group (N %)
Actinobacter	**3(15 %)**	**0(0 %)**	**3(15 %)**
Candida Albican	**2(10 %)**	**0(0 %)**	**2(10%)**
H. influenza	**2(5%)**	**1(5 %)**	**1(5 %)**
Streptococcus V.	**4(20 %)**	**0(0 %)**	**4(20 %)**
Coagulase -ve Staph	**5(25 %)**	**1(5 %)**	**4(20 %)**
Haemolytic Streptococcus	**4(20 %)**	**1(5%)**	**3(15%)**
	20 (100%)	**3(15 %%)**	**17(85 %)**

Table (5): Child classification according to blood culture.

Variable	Child classification		X2	p	OR
	A	B			
Blood culture :					
-ve	74(91.36%)	46(78.0%)	5	0.021	2.99
+ve	7 (8.64%)	13(22.0%)			(1.01-9.09)

4. Discussion:

Risk of bacterial translocation during upper GI endoscopy is high even without mucosal trauma. During oesophageal varices injection sclerotherapy in cirrhotic patients, this risk becomes high and constant especially in splenctomised cirrhotic patients (3).

To study this risk of bacteraemia after injection sclerotherapy and compare this in splenectomised and non-splenectomised cirrhotic patients, 140 cirrhotic patients were enrolled in this study. Hs-CRP measurement and blood samples for blood culture 10 minutes before and 20 minute after the endoscopy.

No positive blood cultures were detected before the endoscopy in both groups .Post- endoscopy, we diagnosed 20 case of positive blood culture (14.3%), 3 of them (15%) were in the control group and 17(85%) in the patient group.

Many previous reported discussed the risk of bacteremia after different endoscopic procedures with wide range of variations ranging from 3 up to 50 % (18.19.20) .Moreover , a considerable number of papers compared this risk between oesophageal band ligation and injection sclerotherapy with little risk in band ligated cirrhotic patients (13).

This variation in the different studies simply reflect many variables that include; type of participants ,size of varices ,changes in patient response and defective phagocytic capacities that usually present in patients with liver cirrhosis and the absence of splenic clearance of bacteremia add more risk for permanent bacteremic seeding after injection sclerotherapy(18), in addition to other factors that may contribute to this variation which including ; procedure duration, size and length of injection needle, volume of injected material and of course the disinfection process of the endoscopy(19) .

The incidence of bacteremia in cirrhotic non-splenectomised patient after injection sclerotherapy is compatible with many reports (1718, 19&20). In our study we reported 17 (21.3%) cases with +ve blood culture in splenectomised cirrhotic patients. This slight high incidence of bacteremia in this patient category reflect a combination of defective immunological response and reduced phagocytes activity that are commonly seen in cirrhotic patients, in addition to, absence of the splenic clearance of the bacteria that let the injected bacteria to be permanently seeded in remote areas of the circulation. As we know, no reports assess this risk in splenectomised cirrhotic patients

Different types of microorganisms isolates have been reported in the different centres by many authors [16, 19&21].In our study we isolate six types of microorganism namely; *Actinobacter H. Influenza, Streptococcus V., Coagulase -ve Staph and Haemolytic Streptococcus.*

In our study, we found more positive blood cultures in *Child B* cirrhotic patients more than in Child A patients, these results were reported by many authors (13, 14, 15,16,17,18 & 19). This predilection in Child B cases represents marked immunological and phagocytic defects and more porto-systemic collaterals that enable bacteria to bypass the reticulo-endothelial system.

Similar results of overt clinical infection after elective injection endoscopic sclerotherapy like, Chen et al. [17] reported on a patient mortality due to sepsis after injection sclerotherapy, also, Stiegmann et al. [21] reported one case of pneumonia following injection sclerotherapy.

In our study, four patients - all in splenctomised group- had clinical signs of infection on follow up, 2

of them were hospitalized, one of them had pneumonia and the other had septicaemia , no death was reported and the two patients were discharged from the hospital after 8 days.

In conclusion, the rate of bacteremia in splenectomised cirrhotic patients after oesophageal injection sclerotherapy is higher than cirrhotic non-splenectomised cirrhotic patients. Band ligation should replace injection sclerotherapy in this category of patients. Those patients may need strong parental antimicrobial combination coverage before the endoscopy apart from they received vaccinations or not, however this recommendation needs more work up on these unique types of patients especially in Egypt.

Conflict Of Interest

No grants were received and none of the authors have any financial interest or any conflict of interests. All the authors have read and approved the manuscript.

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