Original Research
Medical Journal of the Islamic Republic of Iran. Vol. 22, No. 3, November, 2008. pp.120- 124

A novel bedside technique for differentiation of exudative from transudative pleural effusion

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Abstract

Background: At present, differentiation between exudative and transudative pleural effusion is based solely on laboratory measures and is time-consuming. A simple bedside method would be of great help to differentiate between these two types of effusions. We present a new method for this purpose assessed in 46 patients.

Methods: Standard laboratory tests and our method were tested using the same fluid samples in 46 patients with pleural effusion. A principal in physics called the capillary tube law (h=2a/rpg) was used to compare the samples. The imbibition of the fluid level less than 15mm signified exudate and greater than 15mm signified transudate.

Results: Our data shows that this method is 74% sensitive and 89.4% specific compared to the standard method when analyzed statistically by the chi-square and Kappa agreement (Cronbach's K) tests.

Conclusion: The capillary tube test has an acceptable validity for bedside diagnosis of exudative or transudative effusions.

Keywords: exudate, transudate, pleural effusion, CTT.

Introduction

Fluid accumulation in pleural or peritoneal spaces are either exudative or transudative; this classification is the first and most important step for etiologic diagnosis of effusions [1]. Many methods have been reported for this purpose. The gold standard test is Light's criteria which is based on total protein of the fluid (greater than 3gr/dl) and lactic dehydrogenase (more than 200/lit) or fluid protein/plasma protein ($\geq$ 50%) or fluid LDH / plasma LDH ($\geq$ 60%) designating exudate.

These are the classical and universal criteria for diagnosis. Some other accepted methods are total cholesterol level of fluid greater than 45mg/dl and also serum albumin /fluid gradient less than 1.2gr/dl designating exudates [1-8].

We introduced a new bedside method which is based on a simple physics formula (capillary tube law or h=2A/rpg).

Methods

Standard laboratory tests and our method were tested using the same fluid samples in 46 patients with pleural effusion. A principal in physics called the capillary tube law (h= 2A/rpg) was used to compare the samples. The imbibition of fluid level less than 15mm signi-

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Case no.	Pleural fluid Protein level (gr/dl)	LDH (IU/lit)	Fluid Protein/ plasma protein	Fluid LDH/ plasma LDH	Pleural fluid WBC	Pleural fluid RBC	Height of fluid in capillary tube (mm)
1	5.5	170	55%	6%	1100	970	14
2	4	250	5%	65%	2750	1360	16
3	4/5	210	7%	66%	1100	2150	12
4	5/4	130	6%	55%	2500	1200	14
5	6	270	85%	7%	2100	3170	15
6	5/5	190	5%	67%	1550	2120	17
7	6/5	230	75%	7%	1800	1900	13
8	6	220	8%	4%	1100	1300	12
9	3/5	190	65%	5%	1750	1250	16
10	5/5	350	7%	65%	3500	900	13
11	3/5	290	55%	6%	550	1550	14
12	4	200	52%	5%	1800	2100	16
13	4	250	65%	4%	1250	2500	15
14	3/5	420	55%	5%	1150	1340	15
15	5	270	55%	6%	1500	3500	14
16	6/5	390	8%	65%	3400	4750	11
17	6	350	75%	55%	2500	3100	13
18	6	331	7%	75%	1900	3300	13
19	5/5	140	65%	55%	1250	245	16
20	4/5	260	6%	65%	2850	2700	12
21	5	300	65%	7%	450	1100	15
22	3	110	33%	45%	1100	315	18
23	2	150	35%	4%	1240	1100	18
24	1/5	95	25%	3%	140	0	20
25	2/5	120	4%	45%	950	1200	23
26	2/5	180	4%	4%	1500	1450	17
27	2	110	25%	3%	1300	2120	18
28	2	80	3%	4%	150	0	24
29	3	120	45%	35%	1200	1250	17
30	2	140	3%	4%	1100	2450	16
31	2/5	160	35%	45%	3500	1500	14
32	2/5	75	3%	25%	1700	2100	21
33	1	80	25%	3%	200	0	20
34	2/5	130	25%	4%	540	250	19
35	3	190	45%	55%	1400	2100	14
36	3	150	4%	5%	2250	3200	15
37	2	100	2%	3%	2160	2100	22
38	2	90	35%	25%	340	2100	18
39	1	120	25%	35%	3200	1500	20
40	3	160	3%	45%	3250	4200	15
41	2/5	100	4%	3%	1150	1240	18
42	2/5	110	45%	35%	3100	3120	16
43	2	160	3%	45%	2350	1500	14
44	3	290	45%	5%	4300	4560	15
45	2/5	180	3%	33%	3210	1200	18
46	2	95	35%	35%	3190	1520	17

Table 1. Pleural fluid samples measured for the height of fluid inbibition in millimeters.

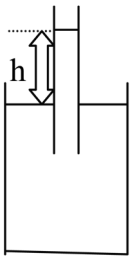

Fig. 1. The nonheparinized tube was inserted into the pleural fluid sample and measured for the height of fluid imbibition in millimeters.

fied exudate and greater than 15mm signified transudate. The capillary tube law or h=2A/rpg explains how the level of fluid in a capillary tube rises. In this formula "h" is the height of fluid in the capillary tube, " r" is the radius of the tube (surface area), "p" is the fluid specific gravity "g" is gravity, constant "A" is "water surface tension".

We know that "r" and "g" are constants so the height of the fluid is dependent on fluid protein (p) concentration; the greater the protein (p), the lower the height (h) designating exudates. After thoracentesis aspirated fluid was tested simultaneously via standard criteria (protein concentration and LDH both for fluid and plasma) and at the same time with a nonheparinized microhematocrit capillary tube 75mm length, inner diameter 1.1-1.2 mm, outer diameter 1.5-1.6mm which is used as a standard tube for measurement of hematocrit. The nonheparinized tube was inserted into the pleural fluid sample and measured for the height of fluid imbibition in millimeters as shown in Figures 1 to 3, then the information was recorded (Table 1). For analysis of the data, calculation of sensitivity and specificity, and predictive value from ROC and changing several decision thresholds, we find that 15mm has optimal accuracy according to Tables 2, 3 and 4. Both criteria for exudative effusion are used in Table 2. Only total protein $\geq$ 3gr/dl is assessed in Table 3. LDH alone is assessed in Table 4.

Discussion

For diagnostic purposes, plural effusion is categorized as transudative or exudative. Transudative pleural effusion results from an imbalance of the Starling's forces which govern the movement of fluid in and out of the pleural space [9]. Congestive heart failure, cirrhosis of the liver, renal disease and hypoproteinemia are responsible for the majority of transudative effusions. Exudative effusions are secondary to protein clearance from the pleural space by the lymphatic system. The most common causes of exudative pleural effusions are infection, malignancy, immune inflammatory and pulmonary emboli. As a general rule transudative pleural effusions are a manifestation of systemic disease whereas exudative effusions are an indication of a pathologic process within the respiratory system.

To differentiate between these two types of effusions measurement of fluid protein level, lactic dehydrogenase (LDH), white blood cell count (WBC), glucose, pH and cholesterol are necessary.

	Height of fluid in capillary tube	
	≤ 15mm	> 15mm
(Exudates) Both test positive Pleural protein/ serum protein ≥ %50 + **p**leural LDH/serum LDH > %60	11	2
(Transudate) any other combination	11	22

Sensitivity = 11/13 = 84.6%
Specificity = 22/33 = 66.6%
K agreement (K) = 46%
PPV=11/22 = 50%
NPV=22/24 = 91.6%

Table 2. Comparison of both LDH and protein with CTT.

	Height of fluid in capillary tube	
	≤ 15mm	> 15mm
Exudates Pleural fluid protein ≥ 3gr/dl	20	7
Transudate Pleural fluid protein < 3gr/dl	2	17

Sensitivity = 20/27 = 74%
Specificity = 17/19 = 89.4%
K agreement (K) = 62%
PPV=20/22 = 90.9%
NPV = 17/24 = 70.8%

Table 3. Comparison of protein with CTT.

Most authors [2,5-8,10-17] believe that a pleural effusion is exudative when at least one of the following criteria is met:

1- Protein level of effusion ≥ 3g/dl,

2- Pleural fluid LDH ≥200 IU/lit or two-thirds of laboratory upper normal limit for LDH,

3- Pleural LDH / serum LDH ratio ≥ 0.6,

4- Pleural protein / serum protein ratio ≥ 0.5,

5- Glucose ≤ 60mg/dl,

6- WBC ≥ 1000mm^3,

7- Cholesterol level ≥ 48mg/dl,

8- Serum albumin-fluid albumin gradient ≤ 1.2g/dl,

9- Fluid cholesterol/serum cholesterol ratio ≥ 0.3.

Classically, having the first criteria the protein level ≥ 3gr/dl alone has 75% and 85% sensitivity and specificity, respectively [2,5], and for LDH alone, these values are 75% and 90%, if all three criteria, ie LDH and LDH/LDH ratio > 0.6 and protein/protein ratio > 0.5 are met the effusion is exudative with 99% and 98% sensitivity and specificity, respectively [2]. The above criteria misidentify approximately 25% of transudates as exudates [2]. If one or more of the exudate criteria are met and the patient is clinically thought to have a condition producing a transudative effusion, the difference between the albumin level in the serum and the pleural fluid should be measured; if this gradient is greater than 12g/lit (1.2 gr/dl) almost all such patients have a transudative pleural effusion. According to this simple physical method (CTT) which is bedside, rapid, cost effective procedure, if the height of fluid imbibition in the capillary tube is less than 15mm the fluid is exudative with 84.6% sensitivity and 66.6% specificity for both (Fluid protein/serum protein ratio + fluid LDH / serum LDH ratio) according to Table 2, and for protein concentration alone sensitivity is 74% and specificity 84.9% with 90.9% positive predictive value and 70.8% negative predictive value (Table 3). Regarding LDH alone 88% and 75% sensitivity and specificity respectively with 68% positive predictive value and 91.5% negative predictive value was calculated (Table 4).

Conclusion

The capillary tube test has an acceptable validity for bedside diagnosis of exudative or transudative effusions. Many criteria for differentiation of effusions are classically used. However, the most accepted are:

	Height of fluid in capillary tube	
	≤ 15mm	> 15mm
Exudates Pleural fluid LDH ≥ 200IU/lit	15	2
Transudate Pleural fluid LDH < 200IU/lit	7	22

Sensitivity = 15/17 = 88%
Specificity = 22/29 = 75%
K agreement (K) = 61%
PPV=15/22 = 68%
NPV = 22/24 = 91.6%

Table 4. Comparison of LDH with CTT.

1- Protein level of effusion $\geq$ 3gr/dl

2- Pleural fluid LDH $\geq$ 200 IU/lit or two-thirds of laboratory upper normal limit for LDH

3- Pleural LDH / serum LDH ratio $\geq$ 0.6.

Thus, we compared our data with these references.

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