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THE PERFORMANCE OF TUBERCULOSIS SPUTUM EXAMINATION AT DISTRICT HOSPITALS, KHON KAEN, THAILAND.

Keyword : tuberculosis, performance, sputum smear examination, district hospital

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บทคัดย่อ

สถานการณ์ : ห้องปฏิบัติการเวชศาสตร์ชันสูตรในโรงพยาบาลชุมชน จำนวน 19 แห่ง และในศูนย์วัณโรคเขต จังหวัดขอนแก่น ประเทศไทย

วัตถุประสงค์ : เพื่อประเมินพฤติกรรมการตรวจเสมหะเพื่อหาเชื้อวัณโรคโดยเจ้าหน้าที่ในห้องปฏิบัติการเวชศาสตร์ชันสูตรส่วนท้องถิ่น ในสถานการณ์ที่ปฏิบัติงานตามปกติ

วิธีการ : เป็นการศึกษาเพื่อสำรวจสถานการณ์ (Exploratory study) โดยได้ขอให้ห้องปฏิบัติการเวชศาสตร์ชันสูตรของโรงพยาบาลชุมชนจำนวน 19 แห่ง ส่งแผ่นสไลด์เสมหะที่ได้ทำการตรวจระหว่าง พ.ศ. 2533-2534 เป็นรายเดือน เพื่อไปทำการตรวจซ้ำโดยศูนย์วัณโรค แล้วเปรียบเทียบผลการอ่านแผ่นสไลด์ดังกล่าว ตลอดจนวิเคราะห์ถึงอิทธิพลของคุณภาพการเตรียมแผ่นสไลด์ต่อผลการอ่านแผ่นสไลด์

ผล : ในแผ่นสไลด์ตัวอย่างจำนวน 1,057 แผ่น พบว่าผลการอ่านแผ่นสไลด์ตรงกันระหว่างห้องปฏิบัติการเวชศาสตร์ชันสูตรของศูนย์วัณโรคเขต และของโรงพยาบาลชุมชน คิดเป็นร้อยละ 94 อย่างไรก็ตามพบว่าร้อยละ 39 ของจำนวนแผ่นสไลด์ทั้งหมดมีคุณภาพของการเตรียมแผ่นสไลด์ไม่ดี ในด้านคุณภาพของเสมหะ, การป้ายแผ่นสไลด์ หรือการย้อมแผ่นสไลด์ อนึ่ง ในกลุ่มของแผ่นสไลด์ที่มีคุณภาพเสมหะดี แต่มีคุณภาพของการป้ายแผ่นสไลด์ หรือการย้อมแผ่นสไลด์ไม่ดี พบว่ามีสัดส่วนของแผ่นไสลด์บวก แตกต่างอย่างมีนัยสำคัญทางสถิติ เมื่อเทียบกับกลุ่มของแผ่นสไลด์ที่มีคุณภาพการเตรียมดีทุกด้าน ทั้งนี้เมื่ออ่านโดยเจ้าหน้าที่ห้องปฏิบัติการเวชศาสตร์ชันสูตรของศูนย์วัณโรคเขตเช่นกัน คณะผู้วิจัยจึงตั้งสมมติฐานว่าเจ้าหน้าที่ห้องปฏิบัติการเวช-ศาสตร์ชันสูตรของโรงพยาบาลชุมชนและศูนย์วัณโรคเขต อาจผิดพลาดได้เหมือนกัน ในการอ่านแผ่น สไลด์ที่มีคุณภาพการเตรียมแผ่นสไลด์ไม่ดีดังกล่าวนี้

ดังนั้นสัดส่วนที่สูงของการอ่านแผ่นสไลด์ที่ตรงกัน จึงไม่ได้ประกันคุณภาพที่ดีของพฤติกรรมการตรวจเสมหะเพื่อหาเชื้อวัณโรคของห้องปฏิบัติการเวชศาสตร์ชันสูตรส่วนท้องถิ่น

สรุป : ไม่เพียงแต่สัดส่วนของการอ่านแผ่นสไลด์ที่ถูกต้อง (ตรงกัน) เพียงอย่างเดียวเท่านั้น แต่สัดส่วนของแผ่นสไลด์ที่มีคุณภาพการเตรียมดีทุกด้าน ก็เป็นตัวชี้วัดที่สำคัญอันหนึ่งของคุณภาพของพฤติกรรมการตรวจเสมหะเพื่อหาเชื้อวัณโรคของห้องปฏิบัติการเวชศาสตร์ชันสูตรส่วนท้องถิ่น

Abstract :

Setting : Nineteen district hospital laboratories and a reference Zonal Tuberculosis control Centre laboratory in Khon Kaen, Thailand.

Objective : To assess the performance of sputum smear examinations by peripheral laboratory technicians in their own work setting.

Design : Exploratory study. 19 district hospital laboratories were asked to submit monthly a sample of sputum slides that were examined during 1990 and 1991. These slides were reexamined by a reference laboratory technician. The reading results were compared and the influence of slide preparation on the reading result was analysed.

Results : In a sample of 1057 slides the agreement in reading results between the reference and peripheral laboratories was 94%. However, 39% of slides were not prepared well in sputum collection, smearing or staining. Among the slides with good sputum but with poor smearing or staining a significantly different proportion of positive slides were found compared with the well prepared slides when examined by the reference laboratory. The authors speculate that technicians in the district and reference laboratories make the same mistakes in reading these poorly prepared slides, so that a high agreement in results does not guarantee good performance.

Conclusion : Not only agreement in reading results but also the proportion well prepared slides is an important indicator for peripheral laboratory performance.

Kdyword : tuberculosis, performance, sputum smear examination, district hospital

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INTRODUCTION

The WHO strategy to improve case detection and cure rates in developing countries rests upon four cornerstones of national tuberculosis control programmes : a reliable sputum-smear microscopy service, registration of all tuberculosis patients, a secure drug supply, and supervision of programme activities at all levels (1). In developing countries tuberculosis is common but health care resources are limited and the major aim of tuberculosis control is to detect the infectious cases and render them rapidly non-infectious by modern short-course chemotherapy (2,3,4,5,6,7,8). In such a programme sputum microscopy is the mainstay of the diagnosis (9,10,11) since a skilful laboratory technician can detect the majority (80%) of infectious cases making use of this technique (12). The demonstration of the *Mycobacterium tuberculosis* in sputum by microscopy techniques is a clear indication of active tuberculosis (3,13). Sputum smear examination is not only vital for case detection and diagnosis but also for the follow-up of the response to chemotherapy (14,15,16). In areas where HIV infection is common it should be emphasized that the HIV epidemic does not change the strategy of tuberculosis control (17,18), and therefore the need for high quality microscopic sputum examination remains.

In Thailand the district hospital is the most peripheral health facility with a laboratory where sputum smear microscopy can be performed. A district hospital covers about 100,000 population. The quality control of these laboratories is carried out by the Regional Medical Science Centre. Four times per year two sputum test slides with a known bacterial load are sent to the peripheral laboratories

for staining and reding. Written feedback of the test results is given to the laboratories. In this system the performance in staining and reading under routine field conditions (high workload, lack of motivation, not well maintained equipment) cannot be assessed and the performance in sputum collection and smearing is not assessed at all.

The MURLEP project (19) in Khon Kaen province was a multidisciplinary health systems research project aiming at the development of tools for tuberculosis and leprosy control programme managers to easily assess the quality of the programme and to identify appropriate interventions to improve performance. In the framework of this project we studied the performance of sputum smear examinations of peripheral laboratory technicinas in their own work setting.

METHODS

During 12 months in 1990 and 1991 the 6th Zonal Tuberculosis Control Centre (TBZC), in its role as supervisory coordinator for 5 provinces in North-East Thailand, asked the district hospital laboratory technicians in Khon Kaen province to submit monthly the sputum slides they had prepared and examined from both TB suspects and patients registered on treatment, separately accompanied by the reading results. All 19 Khon Kaen Province district hospitals participated in this study. These slides (Ziehl-Neelsen stained) were reexamined by a senior laboratory technician of the TBZC, which is the reference laboratory for the Regional Medical Science Centre in sputum smear microscopy, within a month after the slide preparation at the district hospital. We regard the reading results of this laboratory technician as the gold standard. This technician was blinded about the reading results of the district hospital. He classified the qulaity of the sputum slide (sputum content, smearing and staining) accouding to the procedure described by Latini e.a. (20) : the sputum was classified as good (mucous or mucopurulent) or poor (mainly saliva) ; the smearing was good or poor (too thin or too thick or uneven thickness) ; the staining was good or poor (precipitate, too red). The reading was done according to national standards which are the same as recommended by the International Union Against Tuberculosis and Lung Diseases (21). The slides were grouped in poositives and negatives. A slide is negative when no AFB are found in 100 oil immersion fields. A Slide is positive whe the reading result is 1+, 2+ or 3+. Doubtful slides are excluded. The results of the reference laboratory were compared with the district hospital laboratory results. The analysis consisted of determining agreement and the positive predictive value and the negative predictive value of the district hospital results. The findings were communicated to the technicians through the provincial control programme.

RESULTS

A total of 1057 slides were received from the 19 district hospitals and checked at the TBZC. Compared to the number of reported in the 6th Zonal Tuberculosis Control Centre Annual Report this is about 20% of the slides made during the year. In the beginning of the year the laboratory technicians were not yet accustomed to keep the slides, later they kept only the slides they thought had good quality. The selection bias in our slide population most likely leads to better results than in the whole population of slides made during the year.

The quality of slide preparation

The findings on quality of preparation are described in Table 1. About one-third were not good in one or more of the 3 stages of preparation. 15% of all slides contained only saliva, and are therefore completely unsuitable for finding bacilli. This may be

caused by the fact that also sputum specimens of patients on treatment, who may not easily cough up sputum any more, were taken. 647 (61%) slieds were determined as "well prepared slides" which were good in all steps of sputum collection, smearing and staining. So 39% of all sildes were poor at least in sputum collection, smearing or staining.

This table also shows the negative effect of a poorly conducted step in slide preparation on the following step. The effect of poor sputum collection on smearing is large : 96% of the poor sputum slides are poorly smerared, against 16% of the good sputum slides. The effect of poor smearing on the following step, staining, is less but still considerable : 26% of the poorly smeared slides is poorly stained against 13% of the well smeared slides ($p<0.001$).

Quality of slide reading

Comparison of reading results between the district hospital laboratory and the TBZC (reference laboratory), shows a very good agreement, see table 2, section A.

In order to assess whether reader agreement was influenced by the quality of slide preparation, we tested the agreement in three different subgroups : B. Well prepared slides (all 3 qualities good, n=647), C. Slides with good sputum but poor smearing and/ or staining (n=250) and D. Slides with poor sputum and poor smearing and/or staining (n=160), see table 2; section B,C and D.

For all subgroups the agreement remained about the same as for the group of all slides : 93%-94%, just as the negative predictive value of the district hospital results. However, the positive predictive value was smaller the slides with poor sputum and poor smearing and/or staining (group D).

It seems that if a slide is prespared badly the reference lab technician cannot read it much better than the DH lab technician. We therefore compared the percentage positive slides between the subgroups of slides as read by the reference laboratory, see figure 1.

The 40% positive slides in the group of well prepared slides (group B) served as the reference percentage for the subgroups of slides. Since smear preparation should not change the reading outcome this percentage should be found in all other groups. When we compare this percentage positive slides with that of group D it becomes clear that poor sputum collection is related to a very low percentage positive slides (significant difference, $p<0.001$). This is to be expected since few AFB will be present in saliva specimens. Although this low percentage positive smears may have come from follow-up patients who are almost cured, it may also indicate missed diagnoses when the laboratory technician is not keen on obtaining a good sputum specimen from a coughing patient.

When the slides contain good sputum but smearing and/or staining is poor (group C) we see a higher percentage positive slides ($p<0.05$). Further differentiation shows that poor staining (groups E and G) causes far more slides to be read as poositive (51% and 61%, $p<0.05$) but that the combination poor smearing and good staining (group F) gives 40% positive slides, not different from the "true percentage"

DISCUSSION

In the 1057 slides the agreement in reading results between the reference and peripheral laboratories was 94%, but 15% of the slides did not contain good sputum (saliva) and 39% of the slides were poorly prepared by the district hospital laboratory technicians. Among the slides with good sputum but with poor smearing or staining a significantly different proportion of positive slides were found when compared with the well prepared slides when examined by the reference laboratory.

We concluded that technicians in the district and reference laboratories make the same mistakes in reading these poorly prepared slides, so that a high agreement in results does not guarantee good performance.

The sample of 1057 slides may not have been representative of all slides made during the year. The laboratory technicians most likely kept more positive slides and more slides that were well prepared. Since we aimed to look at the performance of the district hospital technicians we assessed their performance in determining slides as positive separately from their performance in determining slides as negative in our sample of 1057 slides. In this way the possible bias in our sample did not influence the performance assessment outcome.

The saliva specimens might have been collected from patients in the follow-up phase of treatment, who often do not cough much any more and cannot easily produce sputum. From our study it is clear that it is rather meaningless to examine saliva specimens. Labooratory technicians should be trained and be supervised to collect good sputum specimens. Similar conclusions were made in Roelsgaard's, da Costa Santiago's and Pollak's study (22,23,24).

The effect of poor smearing on the reading result

We found poor smearing mainly among saliva specimens (Table 1), which is understandable : when there is no sputum one connot smear it well. Among good sputum slides we found that poor smearing caused some more slides to be read as positive than among well prepared slides (Figure 1). So, poor smearing is associated with false positive reading.

The effect of poor staining on the reading result

We found that not only poor smearing but also poor staining caused more slides to be read as positive (Figure 1). So there are false positives among these slides. Apparently the poor staining causes more material to be stained red and falsely to be judged as acid fast bacteria by the laboratory technicians. This finding is similar to Latini's (20), who found an excess of false positive slides among poorly stained slides.

Agreement in reading results

The overall agreement between the district and reference laboratories was high (93-94%), whether the slides were well prepared or not (Table 2). The disagreement concerned mainly the PPV (87%) and not the NPV (99%). Latini (20) and Boulahbal (25) reported a similar reading agreements (98% and 95%). These relatively good agreements in reading results may be misleading because we have shown above that poorly prepared slides cause an excess of positive slides, also when examined by the reference laboratory technician. We conclude that poorly prepared slides cannot be read well neither by the peripheral laboratory technician, nor by the reference laboratory technician.

In group C (good sputum but poor smearing and/or staining) the district hospital laboratory diagnosed 51% of the slides positive (Table 2). This is 11% more than the "true" percentage of 40% positive among well prepared slides, as determined by the reference laboratory. This 11%, from 250 slides with good sputum but poor smearing and/or staining, translates into 28 probably false positive slides. Since it may be that two of these slides refer to one patient we can speculate that among these patients at least 14 were wrongly diagnosed and put to treatment for tuberculosis. It is often argued "better safe than sorry". But over diagnosis obviously

causes problems : Toman's statement speaks for itself (26) : "Man hours, drugs, films and finances are wasted on false positives, while the source of infection remains undetected and untreated. The effect on tuberculosis control is probably the same as underdiagnosis with the difference that such programmes cost more".

The method as presently used by the Regional Medical Science Centre in Thailand, which only checks staining and reading skills of laboratory technicians under "examination" circumstances dose not seem adequate. Since it would cause a too heavy workload for the reference laboratory to reexamine all slides, we have developed a suitable slide sampling method per district hospital laboratory, which indicates whether performance is acceptable or not. This system is described in a sepatate paper.

Recommendations for quality control of peripheral laboratories are :

- Take regularly a sample of all slides kept for reexamination by the reference laboratory (27, 28).
- Do not accept high agreement in slide reading result alone for good performance, since even experienced technicians cannot judge poorly prepared slides.
- The proportion well prepared slides is the first indicator for peripheral laboratory performance. The second indicators is the proportion correctly diagnosed slides, preferably among well prepared slides only.
- Supervisors should give clear feedback on the quality control results, stressing good slide preparation practices.

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Table 1. The distribution of 1057 district hospital laboratory sputum slides according to the 3 preparation qualities, as determined by the reference laboratory.

	all slides : 1057							
Sputum collection :	good 897 (85%)				poor (saliva) 160 (15%)			
Smearing :	good 750 (84%)		poor 147 (16%)		good 7 (4%)		poor 153 (96%)	
Staining :	good	poor	good	poor	good	poor	good	poor
	647 (87%)	103 (13%)	109 (74%)	38 (26%)	7 (100%)	0 (0%)	84 (55%)	69 (45%)

Table 2. Comparison of slide reading of all slides and different subgroups, between the district hospital laboratory and the reference laboratory (RL).

	Results of district hospital laboratory					
	positive slides			Negative slides		
	No.	confirmed By RL	PPV	No.	confirmed by RL	NPV
B. Good sputum, smearing and staining (well prepared slides)	292	255	87%	355	351	99%
C. Good sputum, poor smearing and/or staining	128	116	91%	122	120	98%
D. Poor sputum, poor smearing and/or staining	18	9	50%	142	140	99%
A. All slides	438	380	94%	619	611	99%

* PPV : Positive predictive value

** NPV : Negative predictive value

Figure 1. Percentages positive slides in different subgroups as determined by reference laboratory :