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Effectiveness of infection control measures in controlling a nosocomial outbreak of multidrug-resistant tuberculosis among HIV patients in Italy

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SUMMARY

SETTING: Between October 1992 and February 1994, 33 cases of multidrug-resistant tuberculosis (MDR-TB) were diagnosed among patients infected by the human immunodeficiency virus (HIV) and hospitalised in an HIV ward in Milan, Italy. This outbreak was part of a much larger outbreak, begun in another hospital and probably transferred through a patient.

OBJECTIVE: To evaluate risk factors for transmission and the effectiveness of infection control measures.

DESIGN: 1) Active follow-up of exposed patients, 2) cohort study among HIV-infected patients exposed to MDR-TB cases before and after the implementation of control measures, 3) screening of close contacts of MDR-TB cases, and 4) molecular typing by restriction fragment length polymorphism (RFLP) analysis.

RESULTS: The risk of MDR-TB was higher in patients with lower CD4+ lymphocyte percentages and longer duration of exposure. No difference in the daily risk was observed for in-patients vs day-hospital patients or by room distance from an infectious case. Of the 90 patients exposed before the implementation of infection control measures (i.e., October 1992–June 1993) 26 (28.9%) developed MDR-TB, whereas none of the 44 patients exclusively exposed after implementation developed MDR-TB, despite the continuing presence of infectious MDR-TB cases in the ward.

CONCLUSION: Simple control measures were effective in significantly reducing nosocomial transmission among patients.

KEY WORDS: tuberculosis; *Mycobacterium tuberculosis*; multidrug resistance; outbreak; HIV infection; infection control measures; effectiveness

IN THE UNITED STATES, in recent years large outbreaks of multidrug-resistant tuberculosis (MDR-TB) have occurred involving institutional settings, mainly hospitals, where patients infected with the human immunodeficiency virus (HIV) were prevalent.[1–4] In Europe, nosocomial outbreaks of both drug-susceptible[5] and MDR-TB have been reported.[6–8]

Nosocomial transmission of TB has been associated with inadequate TB control programmes and facilities. To reduce the risk of transmission of TB in hospital, the US Centers for Disease Control and Prevention (CDC) has issued, and regularly updates, specific guidelines,[9] which include the implementation of infection control measures at different levels (i.e., administrative measures to reduce the risk of exposure, engineering control, and the use of personal respiratory protective equipment).

From October 1992 to February 1994, 116 TB cases of TB due to *Mycobacterium tuberculosis* strains resistant to seven drugs occurred among HIV-infected patients cared for in two large urban hospitals in Milan, Italy.[10] The outbreak began in 1991 in one hospital and was probably transferred to the other hospital through a patient. In this second hospital, all of the patients exposed during the outbreak period were actively followed up, a cohort study was performed to evaluate the risk factors for transmission and the effectiveness of infection control measures, and close contacts of MDR-TB cases in the community were screened. This report summarises the results of the follow-up investigation for assessing the efficacy of the infection control measures implemented and the impact of the outbreak on the community.

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MATERIALS AND METHODS

Case finding

A case of MDR-TB was defined as any patient admitted to Niguarda-Ca' Granda Hospital, a large general hospital in Milan, between October 1992 and March 1994 who had clinical signs and symptoms consistent with TB and an *M. tuberculosis* isolate resistant to at least isoniazid, rifampicin, streptomycin and ethambutol. Microbiology records of the hospital were reviewed to identify patients from whom *M. tuberculosis* had been isolated from January 1992 to March 1994 and to document the drug susceptibility patterns of the isolates from these patients. Medical records were reviewed to verify that the clinical course in these patients was consistent with TB. All patients cared for at the HIV ward during the epidemic period and subsequently hospitalised in other health care facilities were traced in April 1995 to identify additional TB cases and to collect available *M. tuberculosis* strains.

Epidemiological studies

To identify the individual characteristics and the type of care associated with an increased risk of MDR-TB, a cohort study was conducted among HIV-infected patients hospitalised in the ward implicated and whose hospital stay overlapped the infectious periods of MDR-TB patients in this ward.

The following definitions were used: 1) infectious period for each MDR-TB case: the interval from 2 weeks before collection of an acid-fast bacilli (AFB) smear-positive sputum until the first negative *M. tuberculosis* culture or last contact with the HIV ward. 2) Infectious MDR-TB patient-day: any day during which an infectious case was present in the HIV ward. 3) Susceptible period: for non-cases, the time between first admission and last discharge; for cases, this was truncated at 5 weeks before the day of collection of the first positive specimen (culture or microscopy). The specific period of 5 weeks was based on an estimated delay of 2 weeks between onset of symptoms and obtaining a first positive specimen (diagnostic delay) plus an estimated minimum of three weeks of incubation.[11] 4) Patient-day of exposure: any day (within the susceptible period), in which a patient was present on the same floor as an infectious MDR-TB case. 5) Incubation period: the interval between the midpoint of the exposure period (first and last exposure to an infectious MDR-TB patient) and 2 weeks before the first positive culture.

Despite the fact that many hospitalised patients were seen in the hospital's out-patient HIV clinic, only three infectious MDR-TB patient-days occurred in that clinic. Moreover, not all visits to the HIV clinic were recorded. Therefore, out-patient exposures were excluded from further analysis. Overall, 244 HIV-infected patients were exposed as in-patients. Seventy-three were excluded from the cohort analysis: 36 patients who survived less than 4 months from their first day of exposure, seven MDR-TB cases with known exposures to other cases both outside and within the HIV ward, seven patients who developed TB but for whom the antibiotic susceptibility pattern was unknown, and 23 patients who were lost to follow-up after discharge and for whom it was thus not possible to retrieve the medical history through active surveillance.

Medical and nursing charts were reviewed to retrieve information on patients' demographic and clinical characteristics, the room(s) in which they were hospitalised, type of hospitalisation (in-patient or day-hospital), prior contacts with MDR-TB cases in other facilities, and clinical outcome. Dates of pentamidine administration were not available at the time of the survey. Incidence rates per 100 patients and rates per 1000 patient-days of exposure were calculated both for the periods before and after 30 June 1993, the date by which the strict infection control measures that were introduced in May had been fully implemented (see below). To identify the patients' hospitalisation characteristics associated with the risk of developing MDR-TB, relative risks comparing incidence rates for exposed and non-exposed patients were calculated, including only those patients exclusively exposed before 30 June 1993.

Laboratory methods

Microscopy (Ziehl-Neelsen stain) and culture on International Union Tuberculosis Medium (IUTM medium) were performed at the hospital laboratory. A regional reference laboratory performed species identification (biochemical tests plus DNA probe) and antimicrobial susceptibility using the proportional method on solid medium. An independent laboratory performed restriction fragment length polymorphism (RFLP) using IS*6110* probe with standard methods,[12] on *M. tuberculosis* isolates still available at the time of investigation. Polymerase chain reaction (PCR) for identification of *M. tuberculosis* from clinical specimens became available in the hospital in May 1993.

Facility and infection control measures

The HIV ward (17 rooms, 2–3 beds per room) is located on two different floors of a free-standing building of Niguarda hospital in Milan. The first floor has three day-hospital rooms and a room for inhalation therapy (aerosolised pentamidine). These rooms are contiguous with the in-patient rooms. The out-patient clinic is located on the ground floor and has a separate entrance. All in-patient rooms have anterooms and independent bathrooms. The building has no air-conditioning system and no air filtration/decontamination equipment. Until recognition of the outbreak, patients with an AFB smear-positive sputum and/or treated with full course of antituberculo-

sis therapy were isolated in any available room in the ward, either alone or, on occasion, with other TB patients under treatment. Compliance with isolation procedures was not complete, and prohibition of TB patients from moving outside their rooms was not always followed. Bronchoalveolar lavage was usually performed in the patient's room. Patients were transported to other hospital departments for X-rays and other diagnostic procedures.

No routine policy was in place for the periodic screening of health care workers (HCW), who by Italian law are required to be vaccinated with the bacille Calmette Guérin (BCG).

After recognition of the outbreak, strict AFB isolation precautions were initiated in May 1993 for all patients with respiratory disease or fever. These measures consisted of placing the patients in single rooms, with doors always closed, and strict control of patient adherence to isolation. The measures also called for limitation of transportation outside the room or building for diagnostic purposes and use of surgical masks during transport. Respiratory protection (i.e., surgical masks) was mandatory for persons entering all patient rooms. Finally, day-hospital admissions were restricted to patients without acute respiratory symptoms and/or fever. Pentamidine administration was discontinued. All of these measures had been fully implemented by June 1993.

Investigation of household contacts

The results of the screening conducted by local public health personnel on household contacts of MDR-TB cases were collected. In June 1994, unscreened contacts were identified and screened with the Mantoux test (5 tuberculin units [TU] of purified protein derivative [PPD]). Mantoux negative contacts were followed up at 3 and 6 months; positive contacts were clinically and radiographically examined both initially and after 6 months. HIV testing was offered when appropriate, and in these cases anergy testing was carried out along with Mantoux testing.

Screening of HCWs

Because periodic tuberculin screening had not been in place before the recognition of the outbreak, skin test conversion could not be determined. Exposed HCWs were screened with Mantoux in June 1993 and once again in 1994. Skin test positive persons and converters were evaluated by chest X-ray.

Statistical analysis

A programme written in Clipper 5.0 was used to calculate the number of patient-days of exposure and infectious MDR-TB patient-days for each patient in the cohort. Data were analysed using Epi Info (Version 6, CDC). Categorical variables were analysed using the χ^2 or Fisher's exact two-tailed tests. Continuous variables were compared using the Kruskall-Wallis test for two groups. Relative risks (RR) and 95% confidence intervals (95%CIs) were calculated.

RESULTS

Case characteristics and description of the outbreak

Between October 1992 and March 1994, 49 patients hospitalised in the HIV ward were identified as having culture-confirmed TB, 29 of whom (59.2%) met the case definition of MDR-TB. No MDR-TB isolate was identified either in patients admitted to other hospital wards or during the first months of 1992 in the hospital under study. Four additional MDR-TB cases were diagnosed in other hospitals, in patients previously hospitalised in the HIV ward, three of whom were identified through active surveillance. Case characteristics have been described in detail elsewhere.[10]

The index case was admitted to the second floor of the hospital on 24 August 1992, with fever and cough. Due to slow growth, *M. tuberculosis* was identified only in February 1993 in a specimen collected at the end of October 1992; the drug sensitivity test results were available in March 1993. The patient died on 10 December 1992. He had had no prior TB diagnosis or treatment and no previous contact with the HIV ward. From 9 July to 17 August 1992, he had been hospitalised in another HIV ward in Milan, where MDR-TB cases occurred during 1992.[10]

Of the 33 cases, 26 had previous exposures in the HIV ward only, whereas seven had no known exposure or had multiple exposures. Of these seven patients, three (including the index case) had been exposed to MDR-TB in the other hospital where the outbreak occurred,[10] one had no known previous contact with the HIV ward and had been in prison in the 6 months before diagnosis, two were HIV-positive partners of MDR-TB patients, and one was exposed to MDR-TB both at Niguarda hospital and, for a longer period of time, in a hospital outside Milan. The incubation periods ranged from 31 to 218 days (median 90 days, mean 102.0, SD 43.6). Among the 26 cases with exposure in the HIV ward only, the median interval between the first observed exposure to an MDR-TB case and the date of death was 241 days (range 132–939). All 33 cases died.

Cohort study

Overall, 171 patients were included in the cohort study, including the 26 cases (15.2%) who had been exposed in the HIV ward only and 145 HIV-infected patients who did not develop MDR-TB. The median length of hospitalisation was 39 days. Neither age nor sex were associated with an increased risk of MDR-TB. MDR-TB case patients had a significantly lower CD4+ lymphocyte percentage than patients who did not develop MDR-TB (median 1.85%, range 0.1–9 vs median 7.45%, range 0–45.5; Kruskall-Wallis test 12.7, *P* value 0.001).

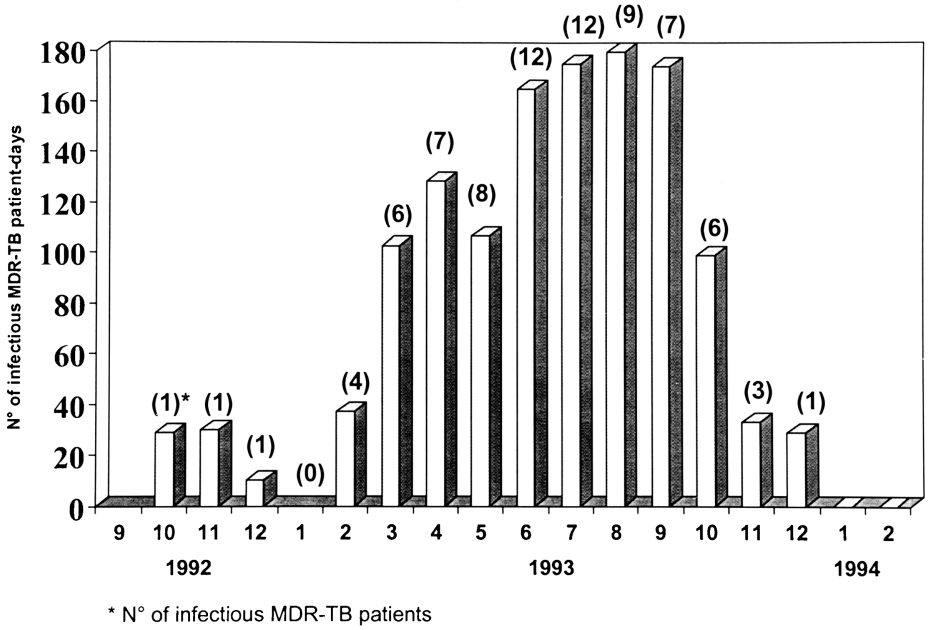

Figure Number of infectious MDR-TB patient-days per month, October 1992–December 1993 (only patients exposed exclusively before 30 June 1993).

Among the 90 patients exposed from October 1992 to June 1993 (2455 patient-days), 26 (28.9%) developed MDR-TB (10.6/1000 patient-days).

None of the 44 patients exposed exclusively after 30 June 1993 (654 patient-days), when infection control measures were already fully implemented, subsequently developed MDR-TB, despite the continuing presence of several infectious MDR-TB cases in the ward (Figure). Furthermore, no MDR-TB cases were observed among the 37 cases exposed both before and after 30 June 1993 (1839 patient-days). When including these 37 patients to estimate the MDR-TB rate before implementation of the infection control measures, the incidence rate is 20.5% (6.1/1000 patient-days).

The factors associated with an increased risk of MDR-TB were further analysed in the group of patients exposed only before 30 June 1993. The risk of MDR-TB was significantly higher in patients with longer duration of exposure: the median length of exposure to infectious patients among MDR-TB cases was 40 days (range 6–113) compared to 9 days (range 1–83) for those who did not develop MDR-TB (Kruskall-Wallis 16.6; $P = 0.00005$). The cumulative incidence of MDR-TB was significantly higher in those exposed as in-patients compared to those exposed in the day-hospital only, but the incidence per 1000 patient-days of exposure was the same (Table). Most of the 33 patients attending only the day-hospital had a short duration of exposure: of the 27 with $\leqslant 5$ days of exposure, none developed MDR-TB, whereas among the six patients exposed for more than 5 days, three developed MDR-TB (Fisher's exact test $P = 0.004$). Among in-patients, the MDR-TB rate/100 patients appeared to be twice as high (33.8%) among patients whose hospital rooms were located within two rooms of an infectious case than among those whose rooms were further away (16.0%), but this difference was not significant; rates per 1000 patient-days of exposure were the same in the two groups.

Table Frequency of MDR-TB by hospitalisation characteristics

Risk factors	No. of patients	Incidence rate/100 patients	Relative risk (95% confidence interval)	No. of patient-days	Incidence rate/1000 patient-days	Relative risk (95% confidence interval)
Type of admission						
In-patients only	32	37.5	4.13 (1.28–13.26)	1020	11.8	1.07 (0.30–3.81)
In-patients and day-hospital	25	44.0	4.84 (1.51–15.53)	1170	9.4	0.86 (0.24–3.08)
Day-hospital only	33	9.1	1.0	274	10.9	1.0
Distance from infectious cases						
0–2 rooms	65	33.8	2.12 (0.81–5.53)	1969	11.2	1.38 (0.48–4.01)
>2 rooms	25	16.0	1.0	495	8.1	1.0

Household contacts

Of the 90 household contacts identified, 84 (93.3%) were screened either routinely or during investigation and 68 (75.6%) completed the scheduled 6-month follow-up. Five of the 84 screened contacts were HIV-positive and all of them were successfully followed-up at 6 months. Three of the five were found to have MDR-TB (including cases 31 and 33 in the Figure) and one had a documented skin test conversion. Among the 63 HIV-negative contacts successfully followed, one MDR-TB case was observed in the initially Mantoux-negative partner of an MDR-TB case. Moreover, three skin-test conversions occurred (8.3% of the 36 initially negative contacts): two were 2-year-old children and one was an elderly woman.

Surveillance of HCWs

No case of TB disease was diagnosed among the 108 exposed HCWs. Of 55 HCWs who consented to Mantoux testing, 22 (41.8%) were positive in June 1993. Three skin-test conversions were observed among the 26 HCWs retested in 1994.

Laboratory results

Among the 33 case-patients, all *M. tuberculosis* isolates were resistant to four of the first-line antituberculosis drugs isoniazid, rifampicin, streptomycin and ethambutol. Isolates from 28 patients (84.8%) were tested against six additional drugs. Two were resistant to pyrazinamide, another first-line drug, all were resistant to amikacin, kanamicyn, and teryzidon, 23 (82.1%) were resistant to cycloserin, and 17 (60.7%) to ofloxacin. Time from specimen collection to the availability of results of drug susceptibility patterns was 4–6 months.

For the 33 MDR-TB cases, 27 *M. tuberculosis* isolates were available for RFLP typing (22 with prior exposure in the HIV ward only, two exposed in the HIV ward and in another hospital, the two partners, and the patient who had been incarcerated); of the 20 non-MDR-TB cases diagnosed in the HIV ward in the same period, four *M. tuberculosis* isolates were available. MDR-TB isolates showed an identical pattern in all 22 hospitalised cases, in the two partners, and in the patient who had been incarcerated. The strain of the index case was not available for RFLP typing. The four non-MDR-TB patients showed different RFLP patterns.

DISCUSSION

The MDR-TB outbreak discussed in the present paper was part of a much larger outbreak which began in another hospital in Milan in 1991 and whose general features have been described elsewhere.[10] Given the availability of data on exposure (such as hospital rooms), it was possible to conduct a cohort study in this hospital to evaluate the factors associated with TB transmission and the effectiveness of the infection control measures adopted.

There are both similarities and differences between this and other previously described nosocomial MDR-TB outbreaks. As in all previous outbreaks, the nosocomial transmission was strongly suggested by all the epidemiological and laboratory evidence; all the cases were HIV-infected and had lower CD4+ T-lymphocyte counts than other HIV-infected patients who were exposed but who did not develop the disease; the incubation period was brief, and the fatality rate was extremely high, with a short survival time.[1]

In contrast with previous outbreaks, however, the incidence rate among patients exposed before the implementation of infection control measures was particularly high.[13–15] Several factors may have contributed to aggravating transmission within the ward: facilities for respiratory isolation were not adequate and compliance of patients with infection control measures was not complete; considerable delays occurred in drug susceptibility testing; the periods of exposure (i.e., hospital stays) were long; and finally, the high proportion of patients with very low CD4+ counts contributed to the dimension of the outbreak.

The cohort study showed that the risk of MDR-TB transmission was higher in patients with longer duration of exposure to infectious patients and that the risk per patient-day of exposure to an infectious case was similar both in the ward and in the day-hospital. However, fewer patients acquired the disease in the day-hospital compared to the HIV ward, since most of the patients in the day-hospital only had short exposures. In other outbreaks, distance from infectious patients was associated with a significant increased risk of infection[13–15] as a consequence of the airborne spread of infectious droplet nuclei in the common spaces. In the present outbreak, among patients exposed to the index case, the incidence rates were higher among patients in adjoining rooms, although paradoxically high rates were also seen in patients who were hospitalised in the most distant rooms. The lack of a distance effect may have been due to the inadequacy of facilities for respiratory isolation and to the poor compliance of patients with the movement limitations in the ward. An additional factor was that after the first few months of the outbreak, a large number of infectious cases was present in the ward at any given time, resulting in a highly diffuse exposure to infectious cases.

The long follow-up period (up to April 1995) and the active search for patients who, after being exposed during the outbreak period, moved or were admitted to other hospitals, allowed us to evaluate whether the intervention reduced the risk of person-to-person nosocomial transmission of TB. No further cases were detected that could be traced to exposure in the HIV ward after 30 June 1993, although several

infectious MDR-TB patients were present in the ward. No MDR-TB case was diagnosed in the HIV ward after February 1994. These results provide evidence that implementation of an increased index of suspicion for TB, rapid diagnostic techniques, appropriate isolation of patients, prohibition of patients under TB isolation from leaving their rooms, and restriction in day-hospital admissions, even in the absence of engineering control measures, greatly decreased patient-to-patient MDR-TB transmission in this outbreak. Furthermore, more aggressive treatment regimens (five- or six-drug combinations) used in later patients may have resulted in decreased infectivity, although this could not be confirmed because complete follow-up of smear conversions was not always performed.

Rigorous application of administrative and source control measures has been shown to be effective in reducing nosocomial transmission in several other MDR-TB outbreak investigations.[1,16] However, one important limitation of our study is the lack of data concerning patient-to-HCW transmission. In the present outbreak, in fact, no MDR-TB case was observed among exposed HCWs, but the rate of infection among HCWs could not be assessed. In Italy, as well as in several other European countries, HCWs are required to be vaccinated with BCG on starting employment, and thus periodic skin test screening is not conducted, making it difficult to identify skin test conversions. Given this important limitation, we can only say that the simple measures adopted were probably effective in stopping TB transmission to patients, while we cannot draw conclusions regarding the risk of infection among HCWs. Stroud et al.,[15] who evaluated the impact of infection control measures at Roosevelt Hospital in New York City, demonstrated that the risk of patient-to-patient transmission was greatly reduced or prevented before negative pressure was achieved in all isolation rooms, whereas only the introduction of negative pressure and protective barriers allowed patient-to-HCW transmission to be prevented.

A special feature of the present investigation is the availability of results of the investigation of household contacts of MDR-TB cases. These data may be useful in quantifying, at least in part, the impact of a nosocomial MDR-TB outbreak in the community. The observed active disease rate was 4%, which is considerably higher than expected. According to Etkind,[17] in fact, on average 1% of identified persons in close contact with a TB case will already have progressed to active disease. The higher rate of progression can be attributed to the fact that the prevalence of HIV infection among household contacts was quite high, as demonstrated by the fact that three of the four secondary cases were HIV-positive. Rodrigo et al. have recently reported that the risk of generating secondary cases changes according to the social characteristics of the index case: the risk is significantly greater when the index case is an intravenous drug user (IDU).[18] Thus, the occurrence of a nosocomial MDR-TB outbreak can have a greater impact than that determined only on the basis of transmission inside the hospital. The expected impact on the community of IDUs co-infected with MDR-TB and HIV is probably greater due to the characteristics of the environment in which they live.

The present report points out that the transmission of MDR-TB among HIV patients in institutional settings should be considered a serious threat. Several factors can contribute to an increasing risk of MDR-TB outbreaks in Europe: 1) the increasing number of HIV-infected IDUs developing active TB[19–21] who are also at risk of poor compliance with antituberculosis therapy;[22] 2) the increasing incidence of TB in many areas[21] and the high prevalence of HIV infection among persons in some institutional settings; and 3) the inadequacy of infection control practices and isolation facilities in many institutional settings.

The mobility of HIV-infected patients, both within and between hospitals and health care facilities, can increase the potential for nosocomial TB transmission in different institutions. MDR-TB is a serious threat, but drug-susceptible TB is transmitted under the same conditions, and unrecognised transmission is probably occurring in other institutions. Moreover, hospitals seem to be poorly prepared to face a dramatic increase of infectious TB cases among HIV patients: isolation facilities are not adequate and renovations are costly. The results of this investigation suggest that the implementation of rigorous infection control was effective in controlling the outbreak; however, if MDR-TB is expected to increase, it will be necessary to assure adequate isolation of patients.

In conclusion, preventing institutional transmission of MDR-TB among HIV-infected individuals should be considered as a public health priority in European countries also, as should improving awareness of TB in all institutions caring for HIV patients and monitoring compliance with recommended infection control practices. Moreover, efforts should be focused on developing guidelines that take into account the scarcity of European hospitals capable of meeting the CDC standard for isolation rooms. A good example is represented by the guidelines recently issued in the United Kingdom, which specify minimum requirements for the isolation of patients, reserving negative pressure rooms for specific high-risk patients with suspected or proven TB.[24]

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RÉSUMÉ

CADRE : Entre octobre 1992 et février 1994, 33 cas de tuberculose à germes multirésistants (MDR-TB) furent diagnostiqués chez les patients infectés par le virus de l'immunodéficience humaine (VIH) et hospitalisés dans une service VIH à Milan. Cette éclosion faisait partie d'une éclosion beaucoup plus étendue dont le point de départ était situé dans un autre hôpital et qui fut probablement transmise par l'intermédiaire d'un patient.

OBJECTIF : Evaluer les facteurs de risque de transmission et l'efficience des mesures de contrôle de l'infection.

SCHÉMA : 1) Suivi actif des patients soumis au risque ; 2) étude de cohorte parmi les patients infectés par le VIH, exposés aux cas de MDR-TB avant et après la mise en œuvre des mesures de contrôle de l'infection ; 3) dépistage des contacts étroits des cas de MDR-TB ; et 4) typage moléculaire par analyse du polymorphisme de longueur des fragments de restriction (RFLP).

RÉSULTATS : Le risque de MDR-TB est plus élevé chez les patients dont les décomptes lymphocytaires CD4 sont plus bas et dont l'exposition au risque fut plus longue. Aucune différence n'a été observée en ce qui concerne le risque quotidien pour les patients hospitalisés vis à vis des patients de l'hôpital de jour ou en rapport avec l'éloignement de la chambre par rapport au cas contagieux. Une MDR-TB s'est développée chez 26 (28,9%) des 90 patients exposés avant la mise en œuvre des mesures de contrôle de l'infection (c'est à dire entre octobre 1992 et juin 1993), alors que la MDR-TB n'est apparue chez aucun des 44 patients exposés exclusivement après cette mise en œuvre, malgré la présence persistante de cas de MDR-TB contagieux dans le service.

CONCLUSION : Des mesures de contrôle simples sont efficaces pour réduire la transmission nosocomiale de manière significative parmi les patients.

RESUMEN

MARCO DE REFERENCIA: Entre octubre de 1992 y febrero de 1994 fueron diagnosticados 33 casos de tuberculosis multirresistente (MDR-TB) en pacientes positivos al virus de la inmunodeficiencia humana (VIH) hospitalizados en un centro de VIH en Milán. Este brote fue parte de otro brote mucho mayor, que se inició en otro hospital y que probablemente se trasmitió a través de un paciente.

OBJETIVO: Evaluar los factores de riesgo para la trasmisión y la eficacia de las medidas de control de la infección.

MÉTODO: 1) Seguimiento activo de los pacientes expuestos ; 2) estudio de las cohortes entre los pacientes VIH positivos expuestos a los casos MDR-TB antes y después de la implementación de las medidas de control ; 3) catastro de los contactos íntimos de los casos MDR-TB ; y 4) tipificación molecular por el análisis de polimorfismo de restricción de longitud de fragmentos (RFLP).

RESULTADOS: El riesgo de MDR-TB era mayor en los pacientes con porcentajes más bajos de linfocitos CD4 y mayor duración de la exposición. No se observó diferencia en el riesgo diario entre los pacientes hospitalizados y los atendidos en el hospital de día, ni en la distancia a la sala de hospitalización de un caso contagioso. De los 90 pacientes expuestos antes de la implementación de las medidas de control de la infección (a saber, octubre 1997 a junio 1993) 26 casos (28,9%) desarrollaron MDR-TB, mientras que ninguno de los 44 pacientes expuestos exclusivamente después de implementar las medidas desarrolló MDR-TB, a pesar de la presencia permanente de casos contagiosos de MDR-TB en el servicio.

CONCLUSIÓN: Las medidas simples de control fueron efectivas para reducir significativamente la trasmisión intrahospitalaria entre los enfermos.