

Abstract

Two rounds of Taiwan Surveillance of Antimicrobial Resistance of Yeasts (TSARY) have been conducted in 1999 and 2002. The distribution of sources and *Candida* species has not been significantly different between these two surveillances. Urine was the most common sources, followed by sputum, blood, wounds. However, different species had different prevalence regarding different sources. Urine was the most common source for *C. glabrata* and *C. tropicalis*, sputum for *C. albicans* and blood for *C. parapsilosis*. The resistant rate to amphotericin B has increased comparing to that of the TSARY 1999 (2.5% vs. 0.5%), whereas, the resistant rate to fluconazole has decreased from 8.4% in 1999 to 1.9% in 2002. Nevertheless, the fluconazole susceptible rate of *Candida glabrata* has decreased from 77.6% in 1999 to 49.7% in 2002.

Of 162 *Candida tropicalis* isolates collected in TSARY1999, 23 (14.2%) of isolates were resistant to fluconazole. Clinically, the increase in the rate of fluconazole resistance in *C. tropicalis* is considerably important since *C. tropicalis* is one of the most commonly isolated non-*albicans* *Candida* species. The information regarding to the genetic background of the resistant and susceptible isolates may provide further knowledge about the distribution and origin of the resistance. To determine the genetic relatedness of the resistant isolates, we have performed pulsed field gel electrophoresis analysis of all 23 resistant isolates along with 13 susceptible ones. Interestingly, two distinguish pulsotypes were obtained. Furthermore, these two types were independent of sources and hospitals but associated closely with the susceptibility of fluconazole.

To investigate the mechanisms of fluconazole resistance of clinical *Candida albicans*, we have determined five known genes involved in drug resistance of 10 clinical fluconazole resistant isolates and one susceptible one. These five genes were *CDR1*, *CDR2*, *MDR1*, *CaERG11*, and *CaNDT80*. In the presence of miconazole, the expression of *CDR1*, *CDR2*, and *MDR1* of all resistant isolates was at least 3-fold higher than that of the control stain. The expression of *CaNDT80* of all but one resistant isolates was at least 1.5-fold higher than that of the control stain. Surprisingly, the expression of *CaERG11* of these resistant isolates was not significantly higher than that of the control strains.

Hence, periodic surveillance is needed to closely monitor the trends of susceptibility to antifungal drugs and for early detection of the newly emerging co-resistance to amphotericin B and fluconazole of *Candida* species, especially, of *C. glabrata*. The information gained from study the mechanisms of drug resistance may help us to design new effective antifungal drugs.

Keyword: TSARY, genetic relatedness, mechanisms of drug resistance