

# Impact of introduction of sildenafil on other treatment modalities for erectile dysfunction: a study of nationwide and local hospital sales

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We assess the impact of introduction of sildenafil on alprostadil injection and penile implant surgery for the treatment of erectile dysfunction (ED) at our institution and in Taiwan. The data of national sales of sildenafil, alprostadil injection and penile implant were provided by industry companies. In the meanwhile, we analyzed the users of the above-mentioned three treatments at our institution. The national sales of sildenafil grew 136% from 0.8 million tablets in 1999 to 1.6 million tablets in 2002, while those of alprostadil injection dropped 33% after the marketing of sildenafil and of penile implant dropped 40% after the marketing of alprostadil injection and sildenafil. The market share of drugstores for sildenafil rose from 41% in 1999 to 72% in 2002. The trend of sales of sildenafil at our institution was similar to that of national sales from hospitals. Mean age of the sildenafil new users was becoming younger in the past 4 y ( $P < 0.001$ ). Of the new users of alprostadil injection and the recipients of penile implant, the commonest age group shifted from the range of 60–69 y before the launch of sildenafil to that of over 70 y after ( $P < 0.05$ ). In conclusion, the introduction of sildenafil has prompted more men as well as younger men with ED to seek treatment. Part of the roles of alprostadil injection and penile implants in this field are substituted by sildenafil and the commonest age group of their users becomes older than before.

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## Introduction

The approval of the first phosphodiesterase type-V (PDE-5) inhibitor, sildenafil citrate (Viagra<sup>®</sup>), by American Federal Drug and Food Administration in 1998 heralded a revolutionary change in erectile dysfunction (ED) therapy. Most would agree that when oral PDE-5 inhibitor fails, therapy may then proceed with medicated urethral system for erection (MUSE<sup>®</sup>), vacuum device, or alprostadil (prostaglandin E1) intracavernosal injection (ICI), while sexual counseling and education may be helpful in selected individuals.<sup>1</sup> Penile implant surgery is

regarded as the last resort when all other nonsurgical therapies fail.

In Taiwan, sildenafil has been on marketing in March 1999, alprostadil injection (Caverject<sup>®</sup>) in June 1995 and penile implant in 1985, while MUSE<sup>®</sup> was not approved here. Although apomorphine, a central-acting dopamine agonist, was approved in some countries, it has not been on marketing in Taiwan to date. Vacuum device is seldom used. The novel PDE-5 inhibitors, tadalafil and vardenafil, were not approved until late 2003. Therefore, oral sildenafil, ICI with alprostadil and penile implant surgery constituted the three mainstays for treatment of ED before 2003. It is our purpose to know their uses, especially regarding the impact of sildenafil on the use of other two forms.

## Materials and methods

The data of national sales of alprostadil injection from 1995 to 2002 and of sildenafil distributed from

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drug stores, private clinics or hospitals from 1999 to 2002 were provided by Pfizer Pharmaceutical Co., Ltd. The data of national sales of penile implant, including the products of American Medical System (AMS) and Dacomed, from 1993 to 2002 were provided by individual trading company. Although Mentor's products possessed one-third of market share in average after 1997, the contribution of Mentor's products was excluded from this study because its data before 1997 was not available.

Since more detailed information other than the number of national sales of three treatment modalities was unobtainable, we analyzed their sales, numbers and ages of the new users at our institution through a search of computer system. Owing to some delay, alprostadil injection was not available at our institution until late in 1998.

Data analysis was performed by descriptive statistics,  $\chi^2$ -test, ANOVA test. A *P*-value of 0.05 or less was considered statistically significant.

## Results

Table 1 shows the number of national sales of sildenafil, alprostadil injection and penile implant from 1993 to 2002. In the era before the introduction of sildenafil, the marketing of alprostadil brought about a 40% reduction in the sales of penile implant. Nevertheless, the sales of penile implant maintained a steady level from 1999 to 2002.

The national sales of alprostadil injection kept growing gradually at first, but dropped 33% in 1999, the year of sildenafil marketing, and then kept steady in the following years. The market share of alprostadil injection of drugstores, private clinics and hospitals in 1995 was 6, 58 and 35%, respectively, and in 2002 was 27, 24 and 49%, respectively.

Compared to those in 1999, the national sales of sildenafil increased 136% in 2002. The market share of national sales of sildenafil distributed from drug stores, private clinics and hospitals in 1999 was 41,

19 and 40%, respectively, and in 2002 was 72, 15 and 13%, respectively. The sales of sildenafil from drug stores increased markedly in a 4-y period. The sales of sildenafil from hospitals had a peak in 1999, decreased in 2000 and increased slightly in 2001 and 2002 and their shares in total declined yearly.

Table 2 lists the annual number of new users and sales of sildenafil and of alprostadil injection and the number of recipients of penile implant at our institution from 1993 to 2002. The sales of sildenafil displayed a surge in 1999, declined in 2000 and grew slightly afterwards. The change in the number of new users of sildenafil and alprostadil injection showed a similar pattern. The sales of alprostadil injection at our institution almost doubled from 1999 to 2002. The change of sales of penile implant at our institution was parallel to that of the national data.

In a 4-y period from 1999 through 2002, there was a total of 2139 new users of sildenafil and of 269 alprostadil injection new users and of 48 penile implant recipients and their mean age in years with a standard deviation (range) was  $62.8 \pm 12.5$  (23–89),  $62.5 \pm 15.9$  (25–89) and  $65.6 \pm 12.9$  (44–80), respectively, without a significant difference among them (ANOVA test, *P* = 0.2914). Mean age of the sildenafil new users in each year is presented in Figure 1 that demonstrates a significant trend of becoming younger (ANOVA test, *P* < 0.001). The age distribution of sildenafil new users in 1999 and 2002 is shown in Figure 2 ( $\chi^2$ -test, *P* < 0.001). The percentage of age younger than 50 y of sildenafil new users in 1999 and 2002 was 10 and 24%, respectively.

The commonest age group of the new users of alprostadil injection moved from the range of 60 to 69 y in 1998 to that of over 70 y in 2002 ( $\chi^2$ -test, *P* < 0.01, Figure 3). In the meanwhile, the commonest age group of penile implant recipients during years of 1993–1998 was 60–69 y while that of those during years of 1999–2002 was over 70 y ( $\chi^2$ -test, *P* < 0.05, Figure 4).

## Discussion

The introduction of sildenafil has made it possible to treat men with ED by an oral agent with a high efficacy and a good tolerance.<sup>2,3</sup> The manufacturer claimed that sildenafil had worked for 20 million men worldwide till 2003. A report showed the number of prescriptions of sildenafil increased 87% from 7.5 to 14 million from 1998 through 2001 in the USA.<sup>4</sup> The growing sales of sildenafil in Taiwan followed this trend too.

The data from the UK National Health Service (NHS) showed the number of men presenting with ED increased two-fold between 1997 and 2000 after the marketing of sildenafil.<sup>5</sup> We did not have the national number of subjects who received sildenafil

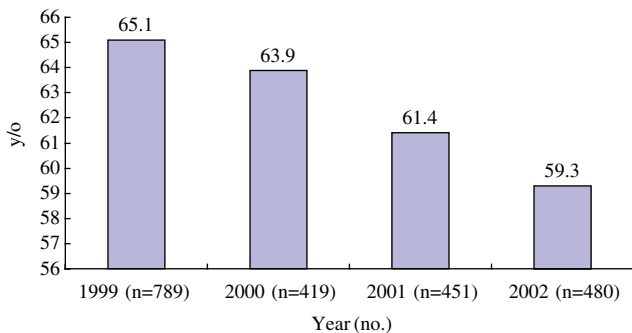
**Table 1** National sales of sildenafil, alprostadil injection and penile implant in Taiwan from 1993 to 2002

Year	Sildenafil (tablets)	Alprostadil injection (syringes)	Penile implant (sets)
1993			194
1994			194
1995		5193	180
1996		10666	181
1997		15537	146
1998		17272	111
1999	1085116	10867	95
2000	1268472	11146	102
2001	1691632	11177	99
2002	2566512	11444	123

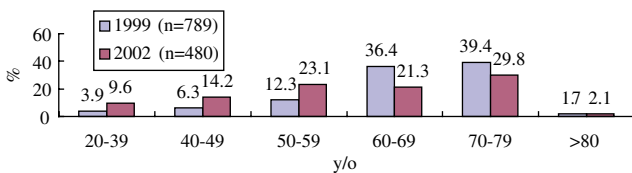
**Table 2** Number of new users and sales of sildenafil, alprostadil injection and recipients of penile implant at our institution from 1993 to 2002

Year	Sildenafil		Alprostadil injection <sup>a</sup>		Penile implant recipients (no.)
	New users (no.)	Sales (tablets)	New users (no.)	Sales (syringes)	
1993					20
1994					25
1995					13
1996					22
1997					24
1998			55	175	6
1999	789	6828	88	681	8
2000	419	5310	58	836	16
2001	451	5841	58	1201	9
2002	480	6059	65	1344	15

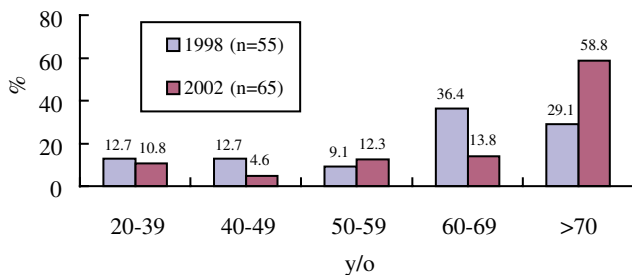
<sup>a</sup>Available since August 1998.



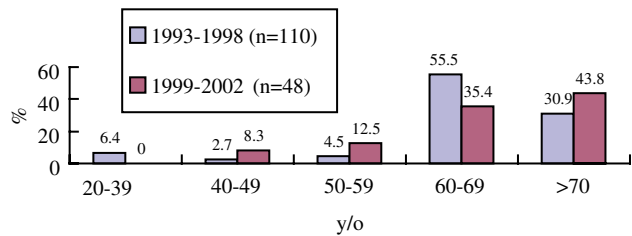
**Figure 1** Mean age of sildenafil new users at our institution from 1999 through 2002; ANOVA test,  $P < 0.001$ .



**Figure 2** Age distribution of sildenafil new users at our institution in 1999 and 2002;  $\chi^2$ -test,  $P < 0.001$ .



**Figure 3** Age distribution of alprostadil injection new users at our institution in 1998 and 2002;  $\chi^2$ -test,  $P < 0.01$ .



**Figure 4** Age distribution of subjects undergone penile implant surgery at our institution in 1993–1998 and 1999–2002;  $\chi^2$ -test,  $P < 0.05$ .

prescriptions. However, the tremendously uprising figures of national sales of it implicated an increasing number of Taiwanese men with ED sought treatment.

To assess the change of the number and age of users, the users of the three treatment modalities at our institution were analyzed. The mean age of the new users of sildenafil was becoming younger in a 4-y period. A study in the USA also showed that mean age of men who received prescriptions with sildenafil in 2001 were younger than that of those in 1998.<sup>4</sup> These indicated a global change that more younger men with ED were willing to seek treatment in the era of oral pharmacotherapy.

Our national sale of alprostadil injection rose gradually in the first 4y since marketing, but dropped by 33% after the launch of sildenafil. Similar condition was observed in the USA where the number of prescriptions for alprostadil injection decreased by 33% from 1998 through 2001<sup>4</sup> and in the UK where the cost for managing ED in NHS the ICI occupied 26.6% in 1997 and became negligible in 2000.<sup>5</sup> A study in Italy demonstrated that men with ED who were switched from stable ICI therapy to sildenafil expressed greater overall treatment satisfaction, better ease of use, naturalness of

erectile process, and intention to continue treatment with sildenafil.<sup>6</sup>

The satisfaction to sildenafil treatment correlated with ED severity.<sup>7</sup> Jiann *et al*<sup>8</sup> observed that the milder the severity of ED, the better the response to sildenafil. The normal aging process and age-related risk factor accumulation contribute to the increased prevalence of ED in the elderly.<sup>9</sup> According to the Massachusetts Male Aging Study, the prevalence and severity of ED were positively correlated with age.<sup>10</sup> Our study showed that the sales of penile implant did not increase in spite that more men with ED sought for treatment after the introduction of sildenafil. However, both the consumption of alprostadil injection and penile implant remained steady from 1999 to 2002. It implies that both of them play important roles for cases refractory to oral medication. It was also observed that the commonest new users of ICI and recipients of penile implant became the men aged over 70 y who were believed to have more severe ED.<sup>9</sup>

When sildenafil was just launched, people worried about the side effects including even death, and their concerns were sensitized by the mass media. Therefore, initially, men with ED were more likely to visit hospitals for the prescriptions of sildenafil for safety concern. As the experience of using sildenafil increased, the fear vanished gradually. We inferred that was why there was a surge of its sale in hospitals in the first year of launch, and later the drug stores exhibited a rapidly increasing market share year by year in Taiwan. A prior study revealed that the refill rate of sildenafil was only 58.6% in spite of the response rate being 72.0%.<sup>8</sup> Over-the-counter obtaining of sildenafil for the sake of convenience or other reason is overwhelming in Taiwan despite of its illegality. This gives rise to concerns that the associated diseases of ED may be neglected and further treatment options may not be offered to them when oral form fails.

A methodological limitation in this study was that, although the trends of sales of sildenafil and penile implant at our institution were similar to their counterparts of the whole island, the demographic data of users from a single medical center and the relatively small number might not exactly represent all the users. Another drawback was that the national data of penile implants excluding Mentor's products could not present the real number. However, the aim of this study was to assess the trend of change of sales, and we assumed the neglect of Mentor's share would not bias our

interpretation since it used to have a steady market share. As more oral agents are available and a longer time to observe, the changing trend of the uses of these treatment modalities will turn out more clearly.

## Conclusions

Sildenafil has attracted more men and younger men with ED to seek help and is the most popular form of therapy so far. The use of sildenafil increased tremendously ever since its marketing but its success did not promote the use of alprostadil injection and penile implant in this field. This indicates that an effective oral pharmacotherapy agent is what most ED patients want. Although the need of injection and surgery decrease in the era of sildenafil, they are more frequently used for men aged over 70 y and their roles in the treatment of ED cannot be overlooked.

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