

## The economic value of extemporaneous preparations based on clinical effectiveness: an application of SDD therapy in ICU

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### ABSTRACT

The preparation of clinical treatments extemporaneously is one of the activities that hospital pharmacists undertake; moreover, they are the only healthcare professionals who are competent to prepare 'specials' for particular patients. With this in mind, it was decided to calculate the economic value of extemporaneous preparations by studying antibiotic formulations that are used to treat oropharyngeal and gastrointestinal infections in the digestive tract.

From the literature, it appears that selective decontamination of the digestive tract (SDD) reduces the length of stay in an ICU by about 3.6 days on average. The clinical advantage of an SDD regimen corresponds to an economic saving of about Euros 2,401 and this value could represent the starting point for the single dose cost, which we found was about Euros 55.

### KEYWORDS

Antibiotic prophylaxis, economic value, extemporaneous products, selective decontamination

### INTRODUCTION

Preparing extemporaneous products is still one of the main activities that hospital pharmacists undertake. The formulation of personalised doses of magistral preparations and pharmaceuticals that cannot be purchased is an exclusive competence of such pharmacists. The Italian pharmacopoeia defines the conditions and operating paths for making such products so that they are safe and of high quality. However, it is necessary to establish a price that does not reflect the additional cost, e.g. raw materials, but is based on clinical efficacy, as happens for the cost definition of a medicinal specialty.

Taking this view, the aim of the study was to try to calculate the economic value of extemporaneous preparations by examining the formulation of an antibiotic mixture used for antimicrobial prophylaxis in ICU patients.

Nosocomial infections, mostly ventilator-associated pneumonia (VAP), occur frequently in ICU patients and contrib-

ute to high mortality [1]. These infections are caused by a limited number of potentially pathogenic microorganisms such as *S. pneumoniae*, *H. influenzae*, *S. aureus*, *Moraxella catarrhalis*, *E. coli* and *Candida albicans*, carried by healthy people, and by opportunistic aerobic Gram-negative ones, such as *Klebsiella*, *Proteus*, *Morganella*, *Enterobacter*, *Acinetobacter* spp. and *Pseudomonas*, bacteria that are present in individuals with an underlying pathology [2].

Selective decontamination of the digestive tract (SDD) is a strategy to prevent infection that was introduced into ICUs in 1984. The treatment consists of non-absorbable antibiotics that are administered to prevent or, if initially present, eradicate oropharyngeal and gastrointestinal microorganisms that are potentially pathogenic (Gram-negative bacteria, *S. aureus* and yeast) [3-5].

Different combinations have been applied in different studies, but the regimen most often used is colimycin, tobramycin and amphotericin B in association with a short course of a systemic antibiotic, usually cefotaxime, to prevent early infections, which can occur until the topical antibiotics have eradicated the potentially pathogenic bacteria [6].

Many authors have demonstrated a significant reduction in VAP and infections from potentially pathogenic microorganisms in SDD-treated patients compared with control subjects [7-19]; only two studies demonstrate a reduced mortality in SDD-treated patients in ICU [13, 15].

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## METHOD

A recent meta-analysis of randomised controlled trials (RCTs) of SDD was published in 2007 [20]. Silvestri et al. analysed 51 RCTs conducted between 1987 and 2005, and included 8,065 patients (4,097 received SDD, 3,986 were controls). Mortality analysis was conducted in 30 trials involving 4,527 patients (2,337 SDD, 2,190 controls).

The analyses have shown 451 deaths in the SDD group and 521 among controls, suggesting a significant 20% reduction in the odds of mortality (odds ratio 0.80; 95% confidence interval, 0.69–0.94;  $p = 0.0064$ ).

Sanchez-Garcia et al. investigated the SDD-treatment efficacy in the reduction of length of stay in ICUs. They observed that the median ICU stay was 11 days for patients treated with topical antibiotics and IV antibiotic therapy, and 16.5 days for controls (patients treated with topical placebo and IV antibiotic therapy) [14].

On the other hand, de Jonge et al. observed that median ICU length of stay was 6.8 days in the SDD group compared with 8.5 days in the control group ( $p < 0.0001$ ) [18].

In both studies, patients in the SDD-treatment group were given a suspension containing 80 mg of tobramycin, 100 mg of colimycin and 500 mg of amphotericin dispersed in sterile water. Patients were treated four times a day with the suspension administered through gastric tubes.

## RESULTS AND DISCUSSION

From an analysis of the literature, there is variability in the cost of a single SDD preparation, which fluctuates between Euros 4 [14] and Euros 7 [21] per patient per day.

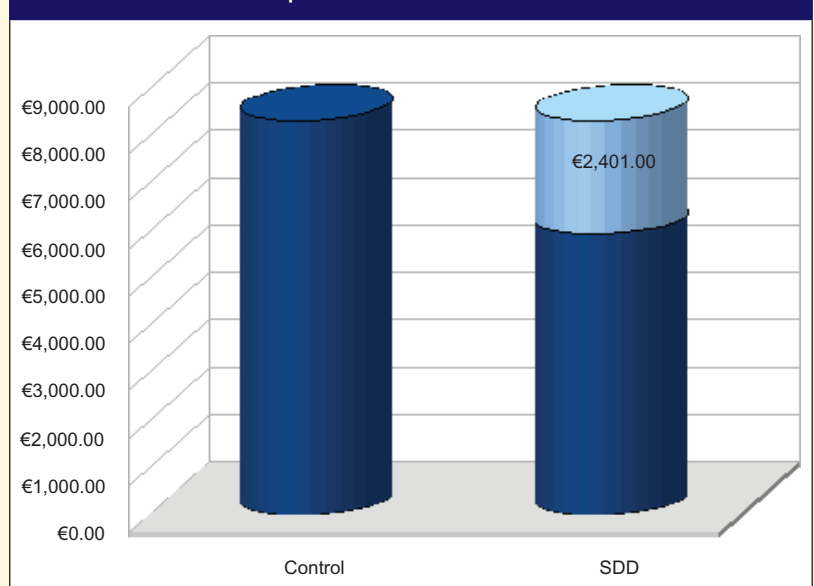
To calculate the cost of SDD, three different methods can be used:

1. Cost of raw materials plus the pharmacist's fee, giving a total of about Euros 8 per dose
2. Cost of raw materials plus the hourly rate of a pharmacist and nurses, giving a total of about Euros 5 per dose
3. Evaluation of clinical advantage: looking at two studies [14, 18], the SDD treatment seems to reduce the hospital stay to about 3.6 days on average (see Table 1).

Table 1: Evaluation of treatment costs

	de Jonge et al.	Sanchez-Garcia	Average
ICU stay (days)			
SDD	6.8 (3.7–12.8)	11 (7–21.5)	8.9
Control	8.5 (4.8–15.7)	16.5 (10–30)	12.5
P value	0.0064	<0.0001	
Gained days	1.7	5.5	3.6
ICU cost per day	€667		
Economic saving	€2,401 (€667 x 3.6)		
Number of syringes for SDD therapy/patient	44 (4 syringes x 11 days)		
Cost of single SDD syringe	€55		

Figure 1: Comparison of cost of hospital stay of SDD-treated patients versus control patients



If one day in the ICU costs about Euros 667, the SDD regimen saves Euros 2,401 (See Figure 1). Patients are treated for a median of 11 days, with four SDD syringes per day; therefore 44 syringes per patient are necessary in an SDD regimen. Consequently, the single SDD syringe value is Euros 55; this price is derived by taking into account the clinical advantage.

## CONCLUSION

A recent meta-analysis has demonstrated that antibiotic administration of an SDD, in addition to IV antibiotic prophylaxis, demonstrates a higher survival rate, reduction in stay in ICU and a reduction in pulmonary infection during the stay in ICU.

Application of pharmaceuticals results in simple preparations with no stability or compatibility problems. Using extemporaneous preparations is a therapeutic path that can improve clinical outcome.

The SDD treatment was administered for a median of 11 days and gave a reduction in ICU stay of 3.6 days compared with only giving IV antibiotic prophylaxis. This clinical advantage corresponds to an economic saving

(Euros 2,401); this represents a base value of Euros 55 for each dose.

In conclusion, the pharmaceutical cost should not be considered merely as the sum of the price of raw materials and the hourly rate of a pharmacist and nurses, but it should be defined by the clinical benefits. Consequently, the attribution of a pharmaceutical price should be calculated similarly to that for drug costs determined by a health authority.

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