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Challenges of Economic Analysis of Pharmaceuticals in the ICU Setting:Outcomes of Sedatives

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Despite considerable literature on the clinical use of sedatives in the intensive care unit (ICU) population, there is limited information on pharmacoeconomics of these agents and their effects on healthcare resources (Wittbrodt 2001). In fact, most studies are limited to an assessment of drug acquisition cost and not the total cost of care. Sedation is a typical therapeutic category in which, despite data on effectiveness, the unanswered question of “so what” remains. The goal of economic analysis of pharmaceuticals is to address these questions by showing the value of the therapy.

Key components of studies of ICU sedatives include drug acquisition costs, time to awakening after drug discontinuation, duration of mechanical ventilation, length of ICU stay and treatment of adverse drug events. The cost consequences of these variables can be ascribed. For example, we have shown that the cost of an ICU day averages $3,500 and the incremental cost of being mechanically ventilated in the ICU is $1,522 (Dasta 2005). Hence, a therapy that facilitates extubation will save money, even if the patient remains in the ICU. A recent program at the 2006 SCCM Congress was titled: “It’s more than just the drug costs.” The techniques used for cost analysis and the challenges in the critical care setting will be summarized here, (Cox 2006). It should be noted that these economic analyses do not make decisions; they provide quantitative data to assist in the decision- making process.

Cost minimization is the simplest technique, whereby costs of two equivalent therapies are compared and the “cheapest” is selected. One of the difficulties of this approach in critical care is documenting the equivalency of two drugs. Two sedatives may result in the same sedation scale score, but one requires more dosage adjustments and may require additional measurements of triglycerides, for example. So, the choice of the outcome of interest is crucial.

The next is cost-effectiveness analysis, which evaluates the joint economic and clinical outcomes of two therapies. It reports outcomes in units like ventilator-free days, cases of DVT prevented, and life-years saved. It is the most common and most appropriate approach in medicine today. The resulting incremental cost-effectiveness ratio between two therapies can be compared. One randomized study, for example, compared the clinical and economic outcomes of two sedatives, propofol vs. midazolam for ICU sedation (Anis 2002). More propofol patients achieved sedation target and had a shorter time to being ready for extubation. Despite higher propofol costs, the total cost of care was not different between the two groups. This surprising finding was explained by the insufficient number of beds available to accommodate these “discharge-ready” ICU patients. So, economic studies of ICU patients must consider complicating factors, such as throughput of patients in the hospital environment.

Another common technique is a cost utility analysis, which combines both the duration of effect and the quality of the patient’s life during this time. It converts effect to “healthy years.” There is not much known about sedatives’ effects on the quality of life during an ICU stay. On one hand, propofol in high doses can “snow” the patient during their critical illness and blunt their consciousness during their ICU stay. Dexmedetomidine, an alpha-2 agonist, in contrast, causes a “cooperative sedation,” whereby the patient is easily rousible and interacts with the nurse. Relevant outcomes haven't been quantitated by a formal cost utility study. Some data does exist on ICU patients with acute lung injury, relating the use of sedatives and neuromuscular blocking drugs to the development of posttraumatic stress disorder (Nelson 2000).

Another approach to economic analysis, particularly useful with new drugs, is a comparison of costs from a large database of patients. Since there is little information on the economics of dexmedetomidine, we compared hospital costs in post-operative bypass patients receiving this drug in addition to standard therapies from a retrospective database of 250 hospitals (Dasta 2006). We found that 356 patients receiving dexmedetomidine with midazolam plus propofol had lower total hospital charges ($18,000), despite higher pharmacy and anesthesia charges, compared to 9,996 patients receiving only midazolam plus propofol in the absence of dexmedetomidine. The difference in total charges was due mainly to a shorter ICU length of stay. While this study is limited by its retrospective methodology, it suggests the need for a prospective randomized study.

In summary, pharmacoeconomic analysis of clinical trials is needed to document the full value of therapies. This is particularly true in the ICU, since it combines intensive “care” and intensive “costs.”

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