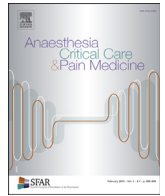




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Letter to the Editor

Shortage of sedatives and neuromuscular blockers during COVID-19 pandemic: The result of an overstocking procedure in French hospitals?



1. Introduction

The COVID-19 pandemic management in intensive care unit has dramatically increased the prescriptions of sedatives (propofol, midazolam) and neuromuscular blockers (NMB) at the international level, creating shortages in all countries. However, such shortages have been previously observed mainly for propofol in the beginning of 2020 [1,2].

This phenomenon has been reinforced by four parameters:

- increase of the number of intensive care unit (ICU) beds during the pandemic within our hospital [3,4];
- increase of acute respiratory distress syndrome (ARDS) patients in all ICUs from 10% to 90% [5,6];
- mean heavy weight of the COVID-19 patients hospitalised in ICU (mean of 91 kg for dosage expressed in mg/kg in our centre);
- increasing level of catabolism of NMB in hyperthermic patients.

In France, there is no national supplying office, nor drugs dispensing, but regional suppliers. During the more acute phase of the pandemic in March–April 2020, the competition for buying these drugs with other countries having national supplying chains for drugs engage French health authorities to create at the end of April 2020 a centralised chain in charge of supplying these sedatives and NMB drugs.

Justification for such national management was based on the hypothesis that the practice of overstocking in hospital pharmacy and intensive care units induced the risk of shortage.

2. Methods

To test this hypothesis of an overstocking process, the relation between supplying procedure and number of patients was followed during a six-week period, at the acute period of the pandemic crisis. This study was performed in the larger COVID-19 centre in Paris, focused on three targeted references in order to detect any misuse in the supplier processes, from receipt to dispensation of the sedatives and NMB.

A weekly database has explored each movement for the targeted drugs, corresponding to one DCI for all available formulation from March 16 to April 26, 2020. Its aim was to estimate the flow during this period. In parallel was registered the number of the COVID-19 patients hospitalised in ICU in order to identify the relation between supplying procedures and number of patients. All the ICUs have automated medicine cabinets allowing drug storage for a maximum period of 24 to 48 hours. Thus, the

inflow and outflow from the pharmacy during this six-week period was a surrogate of the prescription and administration of drugs in ICUs. Moreover, for atracurium, the mean dosage was estimated for each patient. This dose was calculated based on the outflow from the pharmacy and on the data provided by a study on a given day. This study showed that the mean weight was 91 kg and that 45% of patients received atracurium. This analysis has been split for non-ECMO and ECMO patients, as these patients did not required the same doses.

3. Results

The first result was that there was not a day that went by without sedatives or NMB.

There was a correlation between the increasing number of COVID-19 patients managed in ICUs and the outflow from pharmacy to ICU of sedative drugs and NMB during the ascending phase of the disease, which was also the acute phase of the shortage worldwide (Fig. 1).

Average calculated dose of atracurium per patient confirms that there was no additional storage in the pharmacy of the ICUs during the acute phase of the pandemic. Indeed, the mean dosage was 0.51 mg/kg/h for non-ECMO patients and 0.79 mg/kg/h for ECMO patients. For non-ECMO patients, the calculated theoretical dosage of atracurium was in accordance with French guidelines [5,6]. For propofol, the mean real dosage was 1.74 mg/kg/h for non-ECMO patients and 2.05 mg/kg/h for ECMO patients. It was respectively 0.21 mg/kg/h for non-ECMO patients and reached 0.34 mg/kg/h for ECMO patients treated with midazolam.

4. Discussion

These results highlighted the correlation between the flow of patients and the flow of the sedatives and NMB during the acute phase of the COVID-19 pandemic in a large teaching hospital. It denies the initial hypothesis that pharmacists and anaesthesiologists–intensivists in charge of this management tend to store drugs. The increase in the number of ARDS patients in ICUs, with deep sedation and NMB requirement is the only explanation of related drugs shortage. The resumption of elective surgery and anaesthetic activity will interfere with these allocations, as the needs will no longer be limited to the ICU. This must be taken into account before the end of the crisis.

Beyond these observations, the very high level of communication between anaesthesiologists–intensivists and pharmacists has contributed to the anticipation of the drug management and to the research of therapeutic alternatives for sedation of patients. Indeed, local guidelines were established for the sedation management during the pandemic crisis to face a hypothetical stockout.

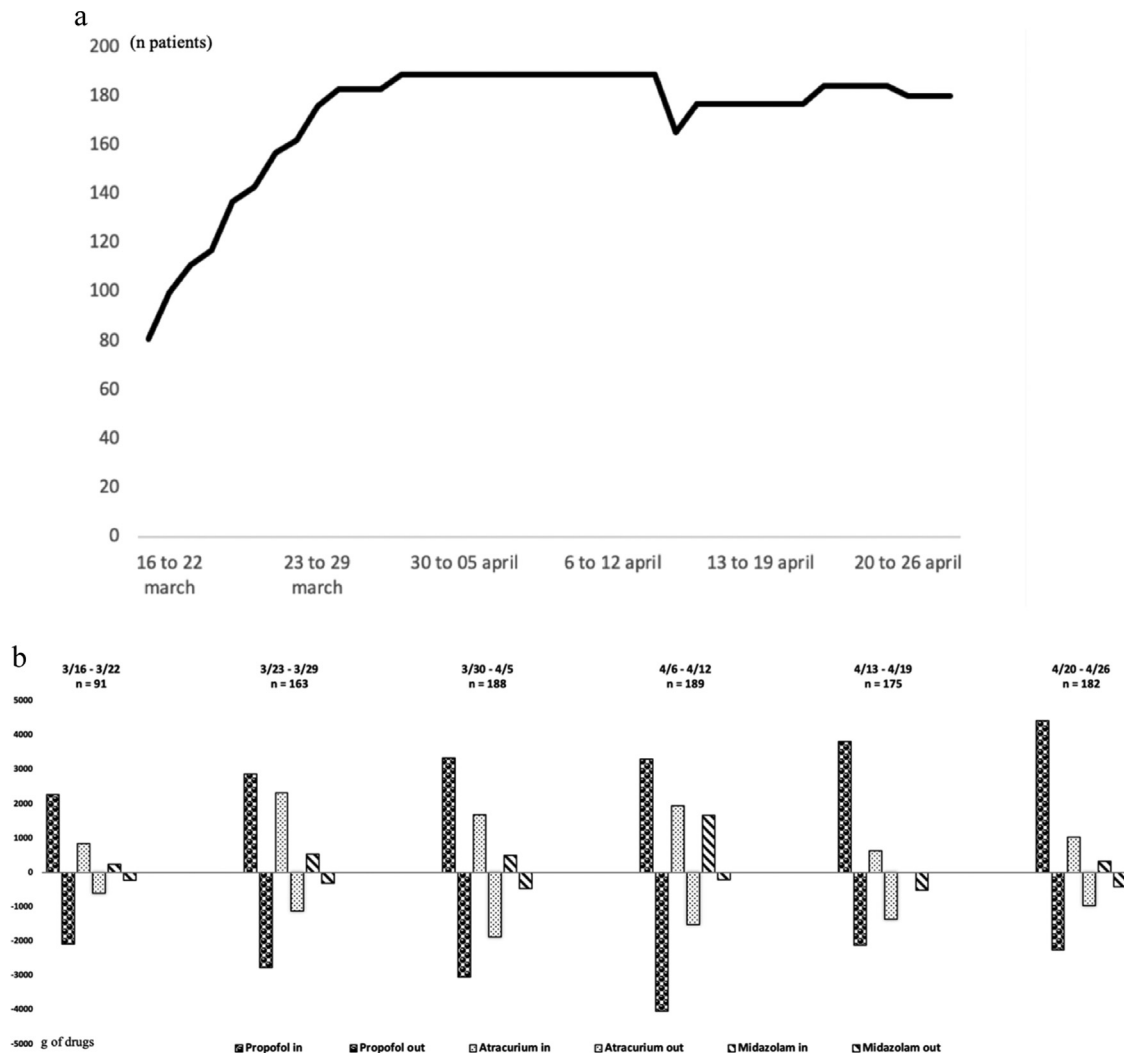


Fig. 1. a: evolution of the number of patients in intensive care units in Pitié-Salpêtrière hospital during COVID-19 pandemic crisis; b: intensive care drugs inflow in the pharmacy (at the top of the axis) and outflow to the ICU (at the bottom of the axis) during the COVID-19 pandemic. For the readability of the figure, the proportions have been doubled for atracurium and midazolam.

All these processes allowed teams to accept the daily constraints associated with the day-to-day management of the drug stock adapted to the right number of patients.

Disclosure of interest

The authors declare that they have no competing interest.

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Available online 30 June 2020