Revisit the drug-interaction between carbapenem and valproic acid: Refining process on Computerized Physician Order Entry (CPOE) system integration & challenge

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Background
The seizure-inducing potential of carbapenems has been noticed since the first introduction of imipenem/cilastatin. This interaction has several properties, including rapid decline in valproic acid (VPA) and slow recovery from the nadir. Risk of seizure attack might be observed during this "drug-free" period. Several studies were conducted to confirm the combination. To reduce the incidence of combination use, we constructed the interrupted alert information within CPOE under periodical monitoring.

Methods
Integration of evidence-based knowledge and our research results in CGMH was conducted for the construction of alert information within CPOE. Our research result is compatible with the highest level of evidence (meta-analysis) during 3-database searching. The refining process is composed of two phases (2 PDCA cycles).

A. Construction Phase: We establish the alert based on the integration of knowledge tools previously mentioned. SAS e-monitoring platform and control chart were also applied for automatically retrieving combination use cases. Effective reduction on combination use has been observed initially, but elevated cases were noted again through the monitoring process.

B. Improvement Phase: Further investigation on the non-adherence for the existing alert was conducted due to out-of-control condition has been noted on control chart. We further modify the alert content to fulfill the anticipation after discussion with health professionals. Outcome on the modification of prescription was also documented.

Results
Our research results share the similar result from meta-analysis, which manifested elevated risk on carbapenem and valproate combination use. Furthermore, subgroup analysis shows that dialysis and history of seizure status did not modify the result from meta-analysis.

A. Construction Phase: We extracted the incidence of combination use among in-patients. Incidence of pre-intervention phase is 50%, and the incidence decreased to 21.2% during post-intervention phase (p=0.04). Effective implementation has been observed.

B. Improvement Phase: We collect combination use data through SAS e-monitoring platform. Out-of-control trends has been observed from control charts since 2016 Q2. Causes of non-adherence are composed of lack of insight on the sequelae after combination use among health professionals, lack of concise and corresponding recommendation when facing the interaction, and discrepancy among different doctors. Incidence of TDM application increased (5.7%→40%), and increased rate of anti-epileptic drug modification was observed as well (14.3%→60%).

Conclusions
Evidence-based alert system construction can be beneficial on quality improvement of clinical care. Close monitoring and automatic data collection and analysis are essential as the timing for the further evaluation.

Figure 1. Control chart of evolution process (2013/12-2017/03)

Figure 2. Construction Phase: Carbapenem + valproate interaction alert implementation