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Trends in sales of inhaled corticosteroids and asthma outcomes in Singapore

Asthma has become a major health problem in Asia, with a prevalence in many Asian countries approaching that of developed countries. The regular use of inhaled corticosteroids (ICS) has been shown in cohort and ecological studies to decrease hospital admission rates by up to 80%.

Asthma related mortality has also been shown to decline with ICS use, even at low doses. Asthma related morbidity has also been shown to decline with ICS use, even at low doses. Conversely, increased use of short acting β2-agonists (SABA) has been associated with increased hospital admission rates to decrease hospital admission rates by up to 80%.

The association between the use of ICS and SABA was not significant in the same model. The rate ratios of asthma mortality for those aged 5–64 years and hospital admission for all ages were 0.96 (p = 0.0461) and 0.98 (p = 0.0006) for every 10,000 units of ICS sold after adjusting for the sales of SABA (model 2 in table 1).

An ecological population based study was performed from 1994 to 2002 in patients aged 5–34 and 35–64 year age groups, and overall and age specific hospital admission rates were calculated for the 5–34 and 35–64 year periods. Figures on mortality and hospitalisations per 100,000 population (p < 0.001). In parallel, a corresponding increase was observed in mean annual drug sales for ICS from 100.7 units (×10⁵) in P1 to 204.3 units (×10⁵) in P2 (p = 0.0003). The mean sales of SABA also increased but the change in usage was not statistically significant (p = 0.0507).

Poison regression analysis confirmed the negative association between the use of ICS and both asthma mortality and hospital admission rates (p<0.05), with and without adjustment for the sales of SABA in all age groups (table 1). The association with the use of SABA was not significant in the same model. The rate ratios of asthma mortality for those aged 5–64 years and hospital admission for all ages were 0.96 (p = 0.0461) and 0.98 (p = 0.0006) for every 10,000 units of ICS sold after adjusting for the sales of SABA (model 2 in table 1).

Being an ecological study, we recognise that other factors such as improvements in patient education and medical facilities may also have contributed to the observed improvement in morbidity and mortality. Despite this, the data presented here support the current evidence that an overall increase in ICS use has a positive impact on asthma related morbidity and mortality in our population, and highlight the importance of ICS prophylaxis as the most cost effective form of asthma treatment available today.

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Table 1 Poisson regression analysis of asthma mortality and hospitalizations by age group, associated with the sales of ICS and SABA

<table>
<thead>
<tr>
<th>Health outcome</th>
<th>Model 1</th>
<th>Model 2 [Model 1–SABA]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICS</td>
<td>SABA</td>
</tr>
<tr>
<td></td>
<td>β₁</td>
<td>p value</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5–34 years</td>
<td>−0.0029</td>
<td>0.0179</td>
</tr>
<tr>
<td>35–64 years</td>
<td>−0.0023</td>
<td>0.0098</td>
</tr>
<tr>
<td>5–64 years</td>
<td>−0.0023</td>
<td>0.0196</td>
</tr>
<tr>
<td>Hospital admissions for asthma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–14 years</td>
<td>−0.0039</td>
<td>0.0003</td>
</tr>
<tr>
<td>15+ years</td>
<td>−0.0014</td>
<td>0.0030</td>
</tr>
<tr>
<td>All ages</td>
<td>−0.0024</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

* All models included an adjustment for extra-Poisson due to year to year variability.
† Model 1: Mortality: log (expected number of age-specific deaths due to asthma) = β₁ log (age specific population size) + β₂ steroids. Hospital admissions: log (expected number of age specific hospital admissions due to asthma) = β₁ log (age specific population size) + β₂ ICS. Thus, exp(β₁ × 10 000) is the rate ratio of asthma mortality/hospital admissions per 10 000 units of medication sold.
‡ exp(β₁ × 10 000) of ICS in model 2 is the adjusted rate ratio of asthma mortality/hospital admissions per 100 000 units of medication sold when SABA sales are held constant.

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Non-invasive monitoring of CO₂ levels in patients using NIV for AECOPD

Non-invasive ventilation (NIV) is the treatment of choice for persistent hypercapnic ventilatory failure during acute exacerbations of chronic obstructive pulmonary disease (AECOPD), despite optimal medical treatment. Assessment of the partial arterial pressure of carbon dioxide (PaCO₂) is the “gold standard” for the evaluation of the adequacy of alveolar ventilation in this setting. However, repeated intermittent invasive arterial puncture carries inherent risks, including pain. Transcutaneous measurement of carbon dioxide (TcPCO₂) theoretically appears more appropriate for monitoring PaCO₂. This measurement is based on the observation that CO₂ has a high tissue solubility and diffuses through the skin. While available data as to the precision of TcPCO₂ measurements have given conflicting results, no study has attempted to assess simultaneous recordings of TcPCO₂ and PaCO₂ in patients requiring NIV for AECOPD.

We prospectively studied the agreement between TcPCO₂ and PaCO₂ measurements in 22 consecutive patients with AECOPD admitted to the respiratory support unit (RSU) from the emergency department with persistent ventilatory failure (PaO₂ < 80 kPa) requiring NIV treatment. Paired arterial and blood gas samples taken from the radial artery and TcPCO₂ measurements were made on arrival in the RSU and 1 and 4 hours after commencing NIV. Patients were also given bronchodilators by nebuliser, corticosteroids, and antibiotics. Each subject gave their informed consent following a detailed presentation of the study objectives and protocol.

Thirteen women and nine men of mean (SD) age 72 (10) years and mean (SD) body weight 67 (13) kg were enrolled in the study. On arrival at the RSU, mean (SD) systolic blood pressure (BP) was 138 (33) mm Hg and diastolic BP was 70 (14) mm Hg. No patient received vasopressor or inotropic support. Arterial pH on arrival at the RSU was 7.27 (0.06). TcPCO₂ measurements were performed with a capnograph (Tosca Monitor; Linde Medical Sensors, Basel, Switzerland). The monitor measures TcPCO₂ using a Stow-Severinghaus electrode with a single ear sensor which works at 42°C to enhance blood flow in capillaries below the sensor. TcPCO₂ is measured by determining the pH of an electrolyte solution. The change in pH is proportional to the logarithm of the change in TcPCO₂. Reassembly of the sensor—which constitutes an electrolyte solution, a spacer, and a gas permeable Teflon membrane—has to be done every 14 days. The monitor displays when the sensor needs a new membrane. The system is equipped with an integrated unit for fully automatic calibration before measurements. In vitro response times are typically below 50 seconds.

Agreement between transcutaneous and arterial values for CO₂ was tested over a range of 5–22 kPa and calculated using Pearson’s coefficient of correlation. Both measurements were highly correlated on arrival in the RSU (r = 0.99, p < 0.0001) and 1 hour (r = 0.99, p < 0.0001) and 4 hours after commencing NIV (r = 0.98, p < 0.0001; fig 1). However, in two of our measurements—interestingly, at a lower PaCO₂—the agreement was less strong. We also calculated the bias and the limits of agreement between the parameters as described by Bland and Altman; 95% of the values were within the limits of agreement on arrival in the RSU and 1 and 4 hours after commencing NIV (fig 2). There were no adverse effects from or patient discomfort with the heating electrode.

These findings suggest that TcPCO₂ measurements are appropriate for clinical application in estimating the ventilatory response to NIV in patients with hypercapnic ventilatory failure due to AECOPD. However, a larger and more detailed study is needed to confirm these preliminary findings. TcPCO₂ measurements allow real time estimation of CO₂ levels over a prolonged period and therefore facilitate proactive rather than reactive ventilator manipulations. Moreover,
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