Angioedema in Australia: hospital admission rates and fatalities, 2000–2013

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Angioedema is the tissue swelling caused by increased vascular permeability elicited by histamine or bradykinin; it can be life-threatening when the upper airway is involved.[1] Most cases of isolated angioedema are idiopathic, but it may occur in patients treated with angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor antagonists (ARBs) or gliptins, or in individuals with hereditary angioedema (HAE), in which C1 esterase inhibitor is absent or non-functional, leading to elevated bradykinin levels.[2]

We examined the burden of isolated angioedema in Australia, specifically excluding angioedema related to IgE-mediated allergy or anaphylaxis. Our study was motivated by a number of isolated angioedema deaths identified during a previous investigation of fatal anaphylaxis in Australia.[3] We analysed Australian Institute of Health and Welfare data on hospital admissions for angioedema (International Classification of Diseases, revision 10, code T78.3) and Australian Bureau of Statistics (ABS) population data and fatality data to calculate age-specific admission rates (July 1999 – June 2013) and fatality rates (January 2006 – December 2013). Time trends were analysed by Poisson regression in SAS 9.3 (SAS Institute), with year as the continuous predictor and total population as the exposure variable. Information on angioedema-related fatalities was also obtained from coronial data reported to the National Coronial Information System (NCIS) between 2000 and 2013, including autopsy and police reports and coronial findings, information not available in raw ABS data. The NCIS Justice Human Ethics Committee approved the study (reference, CF/14/15532).

Consistent with overseas reports,[4,5] admissions to hospital for angioedema were relatively common (18 722 over 14 years), and the annual number increased across the study period (by 1.2% per year; 95% confidence interval [CI], 0.8–1.6% per year; $P < 0.001$) (Box). Eighty per cent of patients were aged 30 years or more; 55% were women. The ABS recorded 26 angioedema-related deaths over 8 years, all of patients over 50 years of age; 69% were women. Unlike the United States,[4,5] there was no significant change in the rate of angioedema-related deaths recorded by the ABS (median rate, 0.026 cases/100 000 population; annual change in rate, −4% [95% CI, −14.0% to 18.8%]; $P = 0.64$), although fatality rates in the two countries were similar.[4] Of four fatalities reported to the NCIS, the causation was idiopathic in two cases, unrecognised HAE in one, and ACEI-associated in one.

Differences between the US and Australia in angioedema-related fatality trends may reflect differences in the prevalence of risk factors, such as age, sex, hypertension, the use of ACEIs, and African–American ancestry.[4,5] Higher rates of admissions for angioedema without fatalities in Australia might also be explained as an artefact of our smaller number of deaths (type II error), or by the shorter period for which fatality data are available compared with admissions data, coding errors, earlier recognition of iatrogenic cases, more effective outpatient care, and potentially by differing prescription rates of ACEIs and ARBs in the two countries (angioedema is less frequently associated with ARBs).

HAE- and ACEI-related angioedema are associated with a high risk of recurrence, underscoring the importance of recognising potential causes early. Adrenaline, antihistamines, and steroids are effective for treating histamine-mediated angioedema associated with urticaria or anaphylaxis, but ineffective for bradykinin-related angioedema (associated with HAE, ACEIs, ARBs, gliptins).[2] In these patients, bradykinin antagonists (eg, icatibant) or purified C1 inhibitor concentrate (eg, Berinert) are effective,[6,7] and even off-label use may be cost-effective compared with the expense of intubation, intensive care admission, or prolonged hospitalisation.

Admissions to hospital for angioedema (ICD 10 code T78.3), Australia, July 1999 – June 2013

Age (years)	Admissions (per 100 000 population) 2000	2013	Annual rate of increase (95% confidence interval)	*P**
0–4	3.8	4.5	1.5% (−0.2 to 3.2%)	0.08
5–14	1.9	2.4	1.9% (0.1–3.7%)	0.040
15–29	2.7	3.8	1.7% (0.6–2.7%)	0.002
30–49	3.7	4.6	1.2% (0.4–2.0%)	0.003
≥ 50	12.9	13.9	0.3% (0.2–0.7%)	0.24
Total	5.8	7.2	1.2% (0.8–1.6%)	< 0.001

Source of admissions data: Australian Institute of Health and Welfare. Source of population data: Australian Bureau of Statistics. * Poisson regression. ◆

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Competing interests: Brynn Wainstein chairs the ASCIA Anaphylaxis Committee.

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