

This study has quantified the contribution of experts to a systematic review and has found them to be an essential source for identifying literature. We suggest that appropriate experts should be consulted when performing a systematic review in a developing field that does not have a clearly defined specialist literature.

Contributors: RJMCM participated in the analysis, wrote the first draft, and coordinated the redrafting and the editing of the paper. SW participated in the study design and coordinated the analysis. BCD participated in the study design, reviewed the initial search results and supervised the project. DAF participated in the study design and reviewed the initial search results. CJH participated in the study design and the analysis. RST participated in the design of the search strategy and in identifying and obtaining relevant citations from the searches. SJ participated in identifying and obtaining citations, designed the database used, entered the data and participated in the data analysis. FDRH participated in the study design and in obtaining national competitive funding to perform the work. All the authors contributed to redrafting and editing of the final paper. FDRH will act as guarantor.

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- 1 Chalmers I, Dickersin K, Chalmers TC. Getting to grips with Archie Cochrane's agenda. *BMJ* 1992;305:786-8.
- 2 Jadad AR, McQuay HJ. Searching the literature. Be systematic in your searching. *BMJ* 1993;307:66.
- 3 Hobbs FDR, Delaney BC, Fitzmaurice DA, Wilson S, Hyde CJ, Thorpe GH, et al. A review of near patient testing in primary care. *Health Technol Assessment* 1997;1(5).
- 4 Jaeschke R, Guyatt G, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? *JAMA*; 271:389-91.
- 5 Dickersin K, Scherer R, Lefebvre C. Identifying relevant studies for systematic reviews. In: Chalmers I, Altman DG, eds. *Systematic reviews*. London: BMJ Publishing, 1995.

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## Drug points

### Anaphylaxis induced by gabexate mesylate

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Gabexate mesylate (molecular weight 417) is a protease inhibitor<sup>1,2</sup> and has an effect against shock.<sup>3</sup> Ten cases of shock induced by gabexate mesylate have, however, been reported (Ono Pharmaceutical Company and Nichiiko Pharmaceutical Company, personal communication). We report an additional case and an analysis of the clinical features of the 11 cases.

A 59 year old woman (case 7 in table) developed pancreatitis in 1975. She visited our clinic because of epigastralgia in October 1996. Laboratory tests showed raised concentrations of amylase (123 IU/l in serum, 857 IU/l in urine; normal values <120 IU/l and <700 IU/l). She received an infusion of gabexate mesylate (100 mg), which resolved her symptoms. She re-experienced abdominal pain in February 1997, which was relieved with the same treatment. This time, however, she developed urticaria after the gabexate mesylate infusion. She developed another bout of epigastralgia one week after this episode. She again developed urticaria 10 minutes after the initiation of the infusion and subsequently experienced chest constriction. Injection of hydrocortisone caused no improvements. Finally, she became pale and drowsy. Her systolic blood pressure fell to 90 mm Hg and became normal 30 minutes after receiving additional injections of hydrocortisone and noradrenaline (norepinephrine). Results of a lymphocyte stimulation test against gabexate mesylate were negative. Her serum concentration of IgE was within the normal range.

Ten of the 11 patients were re-exposed to gabexate mesylate. Nine patients developed eruptions. In three patients urticaria preceded the signs of anaphylaxis. Shock developed within 30 minutes after the challenge in all patients, with the signs of anaphylaxis—that is, hypotension and erythema or urticaria induced by the hypersecretion of histamine (table). All patients recovered from the shock, although two patients required intubation and artificial ventilation.

Patients who are repeatedly treated with gabexate mesylate should be carefully monitored for at least 30 minutes after administration of the drug. Use of

### Clinical manifestations of shock induced by gabexate mesylate

Case	Age (years)	Sex	Blood pressure (mm Hg)	Eruption	Urticaria	Disturbance in consciousness	Time of onset (minutes)
1	26	F	60/0	++	NR	-	<5
2	46	F	UD	+	NR	+	<30
3	46	M	50/0	NR	NR	-	<5
4	48	M	UD	+	+	+	<5
5	54	M	60/0	++	NR	-	<5
6	57	M	60/0	+	+	-	5
7*	59	F	90/0	++	++	+	<30
8	60	M	55/26	++	NR	-	5
9	65	M	UD	++	NR	+	5
10	73	F	80/42	NR	NR	NR	5
11	76	F	44/0	+	+	+	30

NR = not reported; UD = not detectable. \*Current case.

corticosteroids and adrenaline (epinephrine) and respiratory care seems to be adequate for treating such patients.

- 1 Buchler M, Malfetter P, Uhl W, Scholmerich J, Stockmann F, Adler G, et al. Gabexate mesilate in human acute pancreatitis. *Gastroenterology* 1993;104:1165-70.
- 2 Cavallini G, Tittobello A, Frulloni L, Masci E, Mariani A, DiFrancesci V. Gabexate in Digestive Endoscopy—Italian Group. Gabexate for the prevention of pancreatic damage related to endoscopic retrograde cholangiopancreatography. *N Engl J Med* 1996;335:919-23.
- 3 Novelli GP, Casali R, Bonizzoli M, Giorgi L, Lemma M, Piscitelli P. Antioxidant action of gabexate mesilate (FOY) in an experimental model of endotoxin shock. *Minerva Anestesiol* 1995;61:509-13.

### Endpiece Orifices

First, there are orifices where we hear. For the area round the ear is hollow and hears nothing but noise and shouting. But whatever penetrates through the membrane to the brain is clearly heard there. This is the only perforation through the membrane which encloses the brain. At the nostrils there is no (such) opening but a soft area, like sponges. For this reason we hear over a greater distance than we smell.

Hippocrates, *Places in Man*, edited and translated by Elizabeth M Craik, 1998

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