

Methacholine induced headache

Carmen Carratala, Joaquim G Gea,
M Carmen Aguar, Santiago Grau,
Joan M Espadaler-Medina,
Joan M Broquetas

Abstract

A lung function technician developed episodes of headache, probably related to the use of methacholine. The headache disappeared with breathing 100% oxygen. Cholinergic agents are known to induce headaches but the mechanism remains unclear. Vascular factors could be implicated.

(*Thorax* 1995;50:319)

Keywords: methacholine, headache.

Headache is a common symptom that occasionally gives rise to disability. Cluster headache attacks are a specific clinical form of headache.¹ Although its pathogenesis still remains controversial, different toxic and metabolic agents such as monosodium glutamate, nitrates, and histamine can induce it.²

We report the case history of a technician working in a lung function laboratory who presented with repeated episodes of headache mimicking cluster headaches and related to the use of methacholine in bronchoprovocation trials.

Case report

A 41 year old woman, non-smoker with no previous illness, had been working in the lung function laboratory for the previous 10 years. She had occasionally suffered from severe hemicranial headaches with temporofrontal predominance which normally lasted 2–3 hours. Ocular oedema, ptosis, photophobia, phonophobia, and flushing were also present. The headache did not improve with treatment which included paracetamol, non-steroidal anti-inflammatory drugs, and codeine. Above all, the symptoms appeared to be related to the use of methacholine used in bronchoprovocation tests. The technician obtained the prepared solutions from the pharmacy and these were nebulised by the patient. Although she did not initially use gloves, this precaution was later taken to prevent the possibility of a skin-mediated mechanism. The whole procedure was performed indoors, in a room equipped with a mechanism for continuous air renewal. The physical examination when a headache was present was normal, except for the above-mentioned symptoms and signs. As a cluster-like headache was suspected, treatment with

100% oxygen was administered for 15 minutes during one of the episodes. The technician breathed through a mouthpiece and a two-way valve with the inspiratory arm connected to a 50 litre Douglas bag (WE Collins, Braintree, Massachusetts, USA) containing 100% oxygen. The bag was washed out twice before the technician began to breath from it. The headache progressively disappeared and had cleared when oxygen breathing was stopped.

Discussion

Methacholine is the β -methyl homologue of acetylcholine, the main neurotransmitter of the cholinergic system. Acetylcholine is a parasympathomimetic agent characterised by minor nicotinic action and a predominance of muscarinic effects.³ Side effects resulting from the activation of muscarinic receptors in different organs and tissues (heart, blood vessels, digestive and urinary tracts, respiratory system, eyes, central nervous system, and exocrine glands) can occur after drug administration.^{4,5} Methacholine (a substance with similar effects) is used in bronchoprovocation tests and is administered by inhalation. Fortunately, side effects are rare using this method.⁶

In our case report the close and repeated association between the onset of symptoms and the use of methacholine made an adverse drug reaction probable. The likelihood of a drug causing an adverse event is usually based on clinical judgement, but a more objective assessment is possible using Naranjo's weighted score which is one of the most valid and widely used methods for this purpose.⁷ This method assigns a score (0–13 points) for 10 different items and classifies the probability of an adverse drug reaction into "definite" (≥ 9 points), "probable" (5–8), "possible" (1–4), and "doubtful" (≤ 0). Using this system the Naranjo score was between 8 and 11, making the cluster-like headache a "definite to highly probable" adverse drug reaction.

The pathogenesis of these headaches is not known. Cholinergics can induce headache⁶ but the mechanism remains unclear. The headache attacks in the present report were very similar to those in a cluster of histaminic headache,¹ however, suggesting a vascular mechanism.

The authors acknowledge Joseph A Salazar for his help with editing.

- Horton BT. Histaminic cephalgia. *Lancet* 1952;72:92–108.
- Headache and other craniofacial pains. In: Adams R, Victor R, eds. New York: McGraw-Hill, *Principles of neurology*. 1985:129–48.
- Taylor P, Brown JH. Acetylcholine. In: Siegel G, Agranoff B, Albers RW, Molinoff P, eds. *Basic neurochemistry*. New York: Raven Press, 1989:203–31.
- Dutz W. Drugs affecting autonomic functions or the extrapyramidal system. In: Dukes MNG ed. *Meyler's side effects of drugs*. 12th edn. New York: Elsevier, 1992:325.
- The turnover of acetylcholine. In: Pycocock CJ, Taberner PV, eds. *Central neurotransmitter turnover*. London: Croom Helm, 1981.
- Sewester CS. Methacholine. In: Sewester CS, ed. *Drug facts and comparisons*. St Louis: JB Lippincott, 1990: 2407–8.
- Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;30:239–45.

Department of
Pneumology
C Carratala
J G Gea
M C Aguar
J M Broquetas

Department of
Pharmacy
S Grau

Department of
Neurology
J M Espadaler-Medina

Hospital del Mar,
Unitat de Recerca de
Pneumologia, IMIM
Universitat Autònoma
de Barcelona, 08003
Barcelona, Spain

Reprint requests to:
Dr J G Gea.

Received 4 January 1994
Returned to authors
24 March 1994
Revised version received
12 April 1994
Accepted for publication
7 June 1994