

# Rebound following oxygen therapy in cluster headache

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## Abstract

**Background:** Rapid recurrence of a new cluster headache attack following oxygen treatment was named the ‘rebound effect’ by Kudrow (1981). It has never been studied properly. To study this effect, we defined it as a more rapid than usual (for the individual patient) recurrent cluster headache attack after complete relief following oxygen therapy, or an increase in the number of attacks per 24 hours while using oxygen therapy as acute attack treatment. We reviewed the literature and searched our cluster headache study databases.

**Case series:** In our eight patients with rebound cluster headache, the effect was experienced following 87.5% of oxygen treated attacks. Duration until the next cluster headache attack was on average 894 minutes shorter and frequency was on average 1.6 cluster headache attacks per day higher than without oxygen therapy.

**Conclusion:** Although the 1981 trial reported a prevalence of 25%, rebound cluster headache following oxygen therapy is rarely reported nowadays. This may be due to better techniques in oxygen application, the use of higher oxygen flow rates or underreporting. The few literature data and data on our eight patients did not provide clues about the mechanism of the rebound effect. Further study, applying the proposed definition, seems useful.

## Keywords

Cluster headache, oxygen therapy, oxygen response, rebound effect, recurrent headache

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## Introduction

Oxygen has been used to treat cluster headache (CH) attacks since 1952 (1). Not much is known about its mechanism of action and why it provides a successful or significant headache relief in 75–82% of the patients using a flow rate of 6–8 l/min (2). Therefore, we carried out a retrospective cross-sectional correlation study (2), in which we assessed the characteristics that differentiate between CH patients who respond to oxygen and those who do not. Currently, this subject is being investigated further in a prospective study.

One of the observations from these studies was that some patients reported a complete response to oxygen within 15 minutes, but noticed rapid recurrence of a new attack, giving the impression that oxygen only postpones the attack. Such attacks return sooner than attacks not treated at all. The phenomenon was described in Kudrow’s 1981 oxygen trial and called ‘rebound headache’ (3). Given that the rebound effect of oxygen therapy in CH patients has never been studied adequately, we studied the phenomenon by doing a

literature search and describing the patients we observed. We therefore defined the rebound effect as a more rapid than usual (for the individual patient) recurrent CH attack after complete relief following oxygen therapy, or an increase in the number of attacks per 24 hours while using oxygen therapy as acute attack treatment.

## Case series

We describe four of 115 (3.5%) patients from our retrospective study (2), three of 43 (7.0%) patients from

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our current prospective study and one outpatient, all of whom reported a complete relief of a CH attack following oxygen therapy, followed by a more rapid recurrence of CH attacks or an increase in the attack frequency. All patients used oxygen only as acute CH attack treatment. One hundred percent oxygen was applied using a non-rebreathing facial mask. Rebound CH was reported spontaneously in the retrospective study. In our current prospective study, we specifically asked about a change in attack frequency after start of oxygen therapy. Patients 4 and 8 (Tables 1 and 2) spontaneously reported a more rapid recurrent CH attack, although attack frequency and time between the initial and rebound CH attack were not reported. The outpatient said that 'In my opinion, oxygen seems to postpone about 50% of the CH attacks, finally leading to a shorter period between the attacks which increase in both duration and severity'. Patient and headache characteristics and effectiveness of oxygen therapy are summarized in Tables 1 and 2. Patients could clearly make a distinction between a CH attack and interictal headache. On average, rebound CH was experienced in 87.5% of oxygen treated CH attacks (range 50–100%); the mean duration until the next CH attack was 39 minutes (range 0–120) when using oxygen instead of 933 minutes (range 165–1440) without using oxygen; the mean frequency was 4.1 CH attacks/day (range 2–8) when using oxygen instead of 2.5 CH attacks/day (range 0.5–7) without using oxygen.

## Discussion

A PubMed search did not provide additional information about the rebound effect, except that most of those referring to the phenomenon quoted Kudrow (3). Searching the books *The Headaches* (4) and *Cluster headache syndrome* (5) did not result in additional references.

Kudrow (3) was the first to report the rebound effect in 1981. Twenty-five percent of the patients, who initially responded well to 100% oxygen administered through a facial mask at a flow rate of seven l/min for 15 minutes, reported rebound CH (3). Mathew experienced that a number of patients responding to oxygen reported having recurrent headache within a short time, for which repeated oxygen administration was required (6). Torelli and Manzoni described the rebound effect as a 'reappearance of pain after 1–2 hours of oxygen inhalation' (7). It is not clear for what reason they chose this time limit.

Using our definition, we found seven patients in our combined study group of 158 patients (4.4%) who reported the rebound phenomenon, which is much

less than the 25% reported by Kudrow (3). Possibly, the phenomenon occurs more rarely because of better techniques in applying oxygen or because of the tendency to increase the oxygen flow rate. Another explanation may be that patients are rarely interviewed about the phenomenon, as might have been the case in our retrospective study.

Recurrence of CH attacks has been reported in long-term (8) as well as short-term (9) treatment with subcutaneous sumatriptan. In the latter, sumatriptan provided 'relief' (in one patient) or 'complete relief' (in five patients) within 5 minutes following subcutaneous administration, but the CH attack frequency increased to 150–1100% of its original frequency. The increased attack frequency occurred already after 48 hours in one patient and after the second dose in another. The attack frequency also showed a linear relationship with the number of sumatriptan injections per 24 hours. Owing to the high number of CH attacks, sumatriptan quickly became overused. Rossi et al. state that the increased CH attack frequency suggests a drug-induced event, probably because of the short-lasting effect of subcutaneous sumatriptan (9). The rebound effect of oxygen therapy was also experienced immediately by three of our patients, and therefore seems to occur as early as in sumatriptan use. Six of our eight patients had used triptans at some point, and none of them experienced rebound CH following their use. It is not known whether patients experiencing rebound following use of subcutaneous sumatriptan are more prone to rebound following oxygen therapy.

Taken together, these preliminary data on the rebound effect following sumatriptan and oxygen use in CH patients suggest an effect of specific substances with a short half-life. Because of the immediate development of rebound CH after the first use of oxygen therapy in three patients, rebound CH is not (only) the result of medication overuse or tachyphylaxis, which would be more likely after intake over longer periods.

As mentioned earlier, we hypothesize that oxygen flow rates may play a part in the effectiveness of oxygen therapy, as four out of the six patients with known oxygen flow rates who experienced rebound CH used an oxygen flow rate of 7.0 l/min or less. The effectiveness of use of high oxygen flow rates (12–15 l/min) was recently reported by Rozen (10) and Cohen et al. (11). Cohen et al.'s trial did not report a rebound effect; the investigators (11) asked the patients to report the time between achievement of a pain free state and the next attack, but only few data points were obtained, for which reason they did not study it further (personal communication by P. Goadsby, 25 August 2010). Further research on this subject is obviously necessary.

**Table 1.** Patient characteristics

Patient	Retrospective study			Prospective study			Outpatient	
	1	2	3	4	5	6		7
Gender, age (yrs)	M, 39	F, 47	M, 48	M, 24	F, 26	M, 32	M, 23	M, 61
Age at onset of CH (yrs)	34	30	42	18	25	25	22	52
Type of CH	E	E	C	C	C	E	E	E
Duration of cluster period*	15 weeks	3 weeks	Not known	Not known	1.5 yrs	4 weeks	8 weeks	13 weeks
Interictal headache	+	+	+	+	-	+	+	-
Past medication (before O <sub>2</sub> therapy)	Triptans	Verapamil, triptans (simultaneous use with O <sub>2</sub> is not clear)	Triptans, acetaminophen (simultaneous use with O <sub>2</sub> is not clear)	Verapamil, NSAIDs (simultaneous use with O <sub>2</sub> is not clear)	-	-	Metoprolol, sodiumvalproate, naproxen, amitriptyline, triptans	Triptans
Current medication (during O <sub>2</sub> therapy)	Verapamil	Verapamil, triptans (simultaneous use with O <sub>2</sub> is not clear)	Verapamil	Verapamil, NSAIDs (simultaneous use with O <sub>2</sub> is not clear)	Verapamil	Verapamil, triptans, NSAIDs	Verapamil	Verapamil
History of other headache disorders	-	TTH	+ <sup>†</sup>	-	MO	-	+ <sup>‡</sup>	-

CH: cluster headache, E: episodic, C: chronic, yrs: years, M: male, F: female, O<sub>2</sub>: oxygen, TTH: tension type headache, MO: migraine without aura.

\*Duration of cluster period' is the mean duration of past cluster periods of patients 1 and 2 and current duration of the cluster period in patients 5, 6, 7 and 8.

<sup>†</sup>Type of headache disorder unknown.

<sup>‡</sup>Chronic headache; no medication overuse headache.

**Table 2.** CH characteristics (including baseline parameters and with oxygen therapy)

	Retrospective study			Prospective study				Outpatient
	1	2	3	4	5	6	7	
Average number of CH attacks/day without O <sub>2</sub> therapy	7	1	1	2	4	1	0.5-1	3
Average number of CH attacks/day with O <sub>2</sub> therapy	8 <sup>‡</sup>	2	6	*	4 <sup>‡</sup>	3-4 <sup>‡</sup>	2-3	3
Average duration of CH attacks without O <sub>2</sub> therapy (minutes)	45	450 <sup>‡</sup>	83	60	23	120	120	180
Average duration until complete relief of CH after start O <sub>2</sub> therapy (minutes)	7.0	10.0	20.0	1.5	5.0	15.0	12.0	10.0
Average duration until new CH attack after initial attack for which O <sub>2</sub> was used (hours)	2.75	24	Not known	*	3	24	24	*
Average duration until new CH attack after initial attack for which O <sub>2</sub> was used (hours)	0.50	Immediately	Not known	*	0.38	0.75	2.0	0.25
Use of O <sub>2</sub> therapy	5 yrs	3 yrs	Not known	Not known	4 weeks	8 weeks	10 weeks	7 yrs
Frequency of O <sub>2</sub> therapy (times/day), (days/week)	3-4/day, 7 days/week <sup>‡</sup>	2/day, 7 days/week <sup>‡</sup>	Not known	Not known	2/day, 5 days/week <sup>‡</sup>	2/day, 7 days/week <sup>‡</sup>	3/day, 7 days/week	3/day, 7 days/week
O <sub>2</sub> flow rate (l/min)	6.0	Not known	7.0	Not known	7.0	7.0	12.0	12.0
Time between first use of O <sub>2</sub> therapy and developing rebound CH attacks	Immediately	2.5 yrs	9 weeks	10-15 times O <sub>2</sub> therapy	Immediately	1 week	9 weeks	Immediately
Percentage of rebound attacks	100% <sup>¶</sup>	100% <sup>¶</sup>	100% <sup>¶</sup>	100% <sup>¶</sup>	50% <sup>¶</sup>	100% <sup>¶</sup>	100% <sup>¶</sup>	50% <sup>¶</sup>

CH: cluster headache, O<sub>2</sub>: oxygen, yrs: years.

<sup>‡</sup>Patients 4 and 8 spontaneously reported a rapid recurrent CH attack after using oxygen therapy for the initial CH attack. Attack frequency and time between initial and rebound CH attack were not reported.

<sup>¶</sup>Patients did not necessarily have to fulfil the criteria of a maximum attack duration of 3 hours, as Van Vliet et al. state that this upper limit of a cluster headache attack may be too strict (12).

<sup>‡</sup>The total number of CH attacks in a day on which a patient used oxygen. The frequency of oxygen therapy can be less, because oxygen is not used during every CH attack. Patient 6 used triptans to treat some of the CH attacks.

<sup>¶</sup>All patients experienced rebound cluster headache during each cluster.

## Conclusion

Rebound CH following oxygen therapy has rarely been reported in the literature since it was mentioned to occur in 25% of the patients in Kudrow's 1981 trial (3). The phenomenon may have occurred more rarely since, because of better techniques in applying oxygen or because of the tendency to increase the oxygen flow rate. Another explanation may be underreporting. To identify patients with rebound CH following oxygen therapy, we defined this rebound effect as a more rapid than usual (for the individual patient) recurrent CH attack after complete relief following oxygen therapy, or an increase in the number of attacks per 24 hours while using oxygen therapy as acute attack treatment. We believe rebound CH following oxygen therapy deserves more attention and should be asked about when treating CH patients with oxygen. Given that little is still known about the origin and the development of the rebound effect, more prospective research on this subject is obviously necessary, in particular on a possible relationship between oxygen flow rates and rebound CH.

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## Conflicting interests

The authors declare that there is no conflict of interest.

## References

- Horton BT. Histaminic cephalgia. *Lancet* 1952; 72: 92–98.
- Backx APM, Haane DYP, De Ceuster L and Koehler PJ. Cluster headache and oxygen: is it possible to predict which patients will be relieved? A retrospective cross-sectional correlation study. *J Neurol* 2010; 257: 1533–1542.
- Kudrow L. Response of cluster headache attacks to oxygen inhalation. *Headache* 1981; 21: 1–4.
- Sandrini G and Ward TN. Acute treatment of cluster headaches. In: Olesen J, Goadsby PJ, Ramadan NM, Tfelt-Hansen P, Welch KMA (eds) *The Headaches*, 3rd edn. Philadelphia: Lippincott Williams & Wilkins, 2006, p.804.
- Sjaastad O. Episodic cluster headache. In: Sjaastad O (ed.) *Cluster Headache Syndrome*. London: WB Saunders, 1992, p.126–127.
- Mathew NT. Advances in cluster headache. *Neurol Clin* 1990; 8: 867–890.
- Torelli P and Manzoni GC. Cluster headache: symptomatic treatment. *Neurol Sci* 2004; 25(Suppl 3): 119–122.
- Paemeleire K, Bahra A, Evers S, Matharu MS and Goadsby PJ. Medication-overuse headache in patients with cluster headache. *Neurology* 2006; 67: 109–113.
- Rossi P, Di Lorenzo G, Formisano R and Buzzi MG. Subcutaneous sumatriptan induces changes in frequency pattern in cluster headache patients. *Headache* 2004; 44: 713–718.
- Rozen TD. High oxygen flow rates for cluster headache. *Neurology* 2004; 63: 593.
- Cohen AS, Burns B and Goadsby PJ. High-flow oxygen for treatment of cluster headache: a randomized trial. *JAMA* 2009; 302: 2451–2457.
- Van Vliet JA, Eekers PJ, Haan J, Ferrari MD and Dutch RUSSH Study Group. Evaluating the IHS criteria for cluster headache – a comparison between patients meeting all criteria and patients failing one criterion. *Cephalalgia* 2006; 26: 241–245.