Effects of Neostigmine and Atropine on Motor Activity of Ileum, Colon, and Rectum of Anaesthetized Subjects

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British Medical Journal, 1970, **1**, 793–794

Summary: In unanaesthetized patients atropine and neostigmine in doses normally used by anaesthetists to reverse muscle relaxants produced a pronounced increase in bowel activity. This response occurred whether atropine was given before or simultaneously with neostigmine.

The response still occurred in 38% of patients anaesthetized without halothane, and possibly this increase in motility might endanger a recently constructed anastomosis. The ileum appeared particularly prone to neostigmine stimulation, and anastomoses involving ileum would seem especially at risk. When halothane was used during anaesthesia the response was completely inhibited during the period studied.

Introduction

The anastomotic leakage rate after ileorectal anastomosis in patients given neostigmine and atropine to reverse curarization was 36% (Bell and Lewis, 1968). The breakdown of the anastomosis was attributed to neostigmine-stimulated bowel activity which was not blocked by the atropine given at the same time. Hannington-Kiff (1969) suggested that if atropine was given before the neostigmine the prevention of the muscarinic effect might be more complete.

In the present study the effect of neostigmine and atropine on the motor activity of the ileum, colon, and rectum in anaesthetized and unanaesthetized subjects was investigated. The atropine was given both before and together with neostigmine to determine whether previous administration could prevent unwanted motor effects from the neostigmine.

Method

Intraluminal pressures within the ileum, colon, and rectum of conscious and anaesthetized human subjects have been recorded by means of small air-filled latex balloons (0·5 by 0·8 cm.) placed 5 cm. apart, connected by fine polyethylene tubing to transducers and a direct writing recorder (Hardcastle and Mann, 1968). The units were introduced into the intestine through a sigmoidoscope with as little distension of the lumen as possible. The ileum was studied in patients who had previously had a total colectomy with ileorectal anastomosis and in those with well-established cutaneous ileostomies. The colon was studied through mature healthy colostomies. After the units had been introduced the bowel was left undisturbed for 20 minutes before a study was begun.

The doses of intravenous atropine (0·6 to 1·2 mg.) and neostigmine (2 to 2·5 mg.) used in each study were recorded; they were always within the above ranges.

All the patients studied under general anaesthesia had either morphine or pethidine, with scopolamine or atropine as premedication. Induction with thiopentone sodium and muscle relaxation with curare was the usual method, but in some cases scoline was used instead of curare for the purposes of intubation. The anaesthesia was maintained with either nitrous oxide or halothane (1-2%) and oxygen.

The patients selected for study under anaesthesia were being anaesthetized for routine surgical procedures. The ileum was studied in patients having fulguration of rectal polyps following ileorectal anastomosis. The sigmoid colon and rectum were studied in patients having sigmoidoscopy before haemorrhoidectomy, or during inguinal herniorrhaphy. In every case informed consent was obtained for all these procedures.

Bowel activity was observed for a 10-minute control period before neostigmine injection, and for 30 minutes afterwards. If in any 10-minute period during the 30 minutes after neostigmine the bowel activity increased by over 200%, this was considered a positive response.

Results

Neostigmine alone

In eight patients the effect of neostigmine alone was studied—one on the ileum, five on the colon (Fig. 1), and two on the rectum. Seven were positive; the only negative result was from the colon of a patient under halothane anaesthesia (see Table).

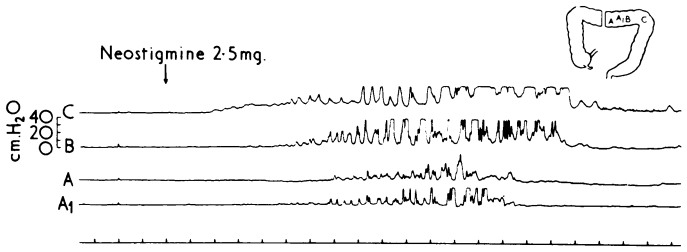

FIG. 1.—Effect of neostigmine 2·5 mg. intravenously on the colon. Not anaesthetized.

TABLE

		Unanaesthetized Patients Response Pos.	Unanaesthetized Patients Response Neg.	Anaesthetized Patients Without Halothane Response Pos.	Anaesthetized Patients Without Halothane Response Neg.	Anaesthetized Patients With Halothane Response Pos.	Anaesthetized Patients With Halothane Response Neg.
Neostigmine alone 2·5 mg. I./V.	Rectum	2					
	Colon	2		2			1
	Ileum					1	
	Total	4		2		1	1
Atropine 0·6—1·2 mg. I./V. followed by neostigmine 2—2·5 mg. I./V.	Rectum	1		1	3		2
	Colon	2			1		1
	Ileum	1		2			1
	Total	4		3	4		4
Atropine 0·6—1 mg. I./V. simultaneously with neostigmine 2—2·5 mg. I./V.	Rectum	4			2		1
	Colon	3		1	2		1
	Ileum	2		1			
	Total	9		2	4		2

Atropine and Neostigmine

Ileum.—Seven patients were studied (see Table). Three had atropine and neostigmine injection simultaneously, one being anaesthetized, but not with halothane; in all three there was a positive response (Fig. 2). Four had atropine injected 10 minutes before the neostigmine injection—three were an-

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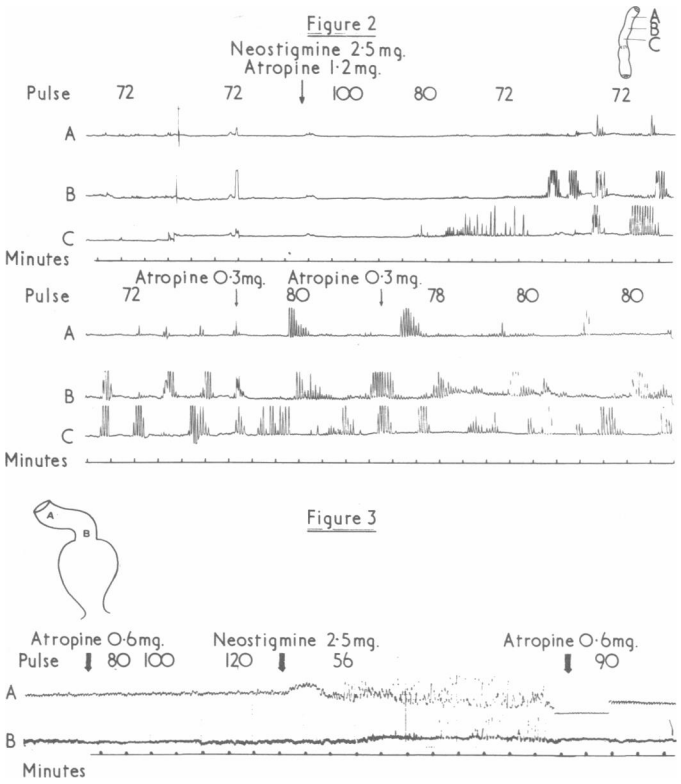

FIG. 2.—Effect of neostigmine 2·5 mg. intravenously simultaneously with atropine 1·2 mg. intravenously on the distal ileum of a patient with ileorectal anastomosis. Under general anaesthesia. Without halothane.
FIG. 3.—Effect of atropine 0·6 mg. intravenously followed by neostigmine 2·5 mg. intravenously on the distal ileum in a patient with ileorectal anastomosis. Under general anaesthesia. Without halothane.

aesthetized, one with halothane. The unanaesthetized patient and two of the three anaesthetized patients showed a positive response (Fig. 3). The only negative response was in the patient being anaesthetized with halothane.

Colon and Rectum.—Of 25 patients studied, 10 were not anaesthetized—in seven the atropine and neostigmine were injected simultaneously and in three the atropine was injected 10 minutes before the neostigmine—and in all 10 a positive response was noted (Figs. 4 and 5). Of the 15 studied under general anaesthesia seven had simultaneous injections of atropine and neostigmine, with one positive response, and

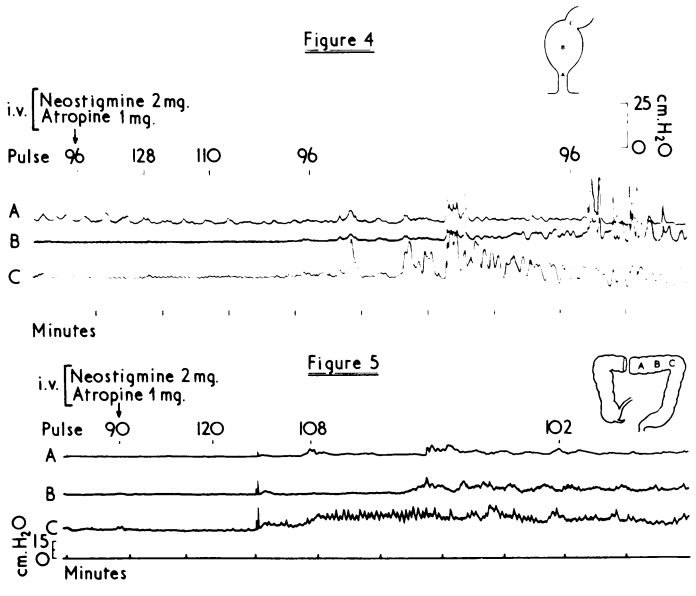

FIG. 4.—Effect of atropine 1 mg. intravenously simultaneously with neostigmine 2·5 intravenously on the rectum. Not anaesthetized. FIG. 5.—Effect of atropine 1 mg. intravenously simultaneously with neostigmine 2 mg. intravenously on the colon. Not anaesthetized.

eight had atropine 10 minutes before neostigmine injection, with one positive response. None of the patients in either group having halothane anaesthesia showed a positive response.

Discussion

Neostigmine has a muscarinic action on smooth muscle and increases bowel activity, and may in the conscious patient result in intestinal colic (Doughty and Wylie, 1952; Bárány and Jacobson, 1964). This effect has been investigated by other workers (Chaudhary and Truelove, 1961; Deller and Wangel, 1965; Misiewicz *et al.*, 1966). They have shown a definite increase in small-bowel and large-bowel activity, which is less pronounced in the right colon. In the sigmoid colon the frequency and amplitude of the activity increases by 300 to 400%. It has been suggested that this increase in activity might result in disruption of a recently constructed bowel anastomosis and that atropine does not entirely reduce this risk (Bell and Lewis, 1968).

Previous experimental work on the action of atropine alone on bowel activity has shown a variable incidence of inhibition (Adler *et al.*, 1942). When it does occur it is of short duration, lasting 10 to 15 minutes (Posey *et al.*, 1948; Kern *et al.*, 1952).

In all the unanaesthetized patients studied we found that considerable bowel activity was induced by neostigmine, whether atropine was given before or with the drug. It appears that the muscarinic action of neostigmine is not effectively blocked by atropine. The increased activity usually began between 10 and 15 minutes after the neostigmine administration, at the same time as the pulse rate began to fall. Not only would the atropine effect be wearing off at this time, but there is evidence that neostigmine exerts its greatest effect about 20 minutes after being given.

Of the 19 patients in the anaesthetized group, halothane was not used in 13, and five of these (38%) showed a positive response. In the other six 1-2% halothane was used during anaesthesia, and none had a positive response. All subjects in the unanaesthetized group showed a positive response. These results confirmed that general anaesthetics reduce bowel activity (Uleri and Ruggerini, 1968). particularly if halothane was used.

The 36% incidence of anastomotic breakdown reported by Bell and Lewis (1968) was noted in patients who did not receive halothane during anaesthesia. In our study a similar incidence of increased bowel activity (38%) was noted in patients under general anaesthesia without halothane, and it is possible that this increased motility might endanger a recently constructed anastomosis, particularly as the neostigmine is given at the end of the operation when the overall level of anaesthesia is light. The use of halothane may greatly reduce this risk.

Ileorectal anastomoses appear to be particularly at risk when neostigmine is used to reverse muscle relaxation. The ileum of three out of four patients showed a positive response to neostigmine and atropine under general anaesthesia; this contrasted strongly with the effect on the colon and rectum, on which we obtained only two positive responses in 15 tests on anaesthetized subjects.

REFERENCES

Adler, H. F., Atkinson, A. J., and Ivy, A. C. (1942). *Archives of Internal Medicine*, **69**, 974.
Bárány, F., and Jacobson, B. (1964). *Gut*, **5**, 90.
Bell, C. M. A., and Lewis, C. B. (1968). *British Medical Journal*, **3**, 587.
Chaudhary, N. A., and Truelove, S. C. (1961). *Gastroenterology*, **40**, 1.
Deller, D. J., and Wangel, A. G. (1965). *Gastroenterology*, **48**, 45.
Doughty, A. G., and Wylie, W. D. (1952). *British Journal of Anaesthesia*, **24**, 66.
Hannington-Kiff, J. G. (1969). *British Medical Journal*, **1**, 418.
Hardcastle, J. D., and Mann, C. V. (1968). *Gut*, **9**, 512.
Kern, F., Jun., Almy. T. P., and Stolk, N. J. (1952) *American Journal of Medicine*, **11**, 67.
Misiewicz, J. J., Connell, A. M., and Pontes, F. A. (1966). *Gut*, **7**, 468.
Posey, E. L., jun., Bargen, J A., Dearing, W. H., and Code, C. F. (1958). *Gastroenterology*, **11**, 344.
Uleri, G., and Ruggerini, R. (1968). *Annales de l'Anesthésiologie Française*, **9**, 135.