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Original Research Article

Effect of H_1 Blocker and Ganglion Blocker on Histamine Induced Response in Proximal and Distal Segment of Neonatal Rectum of ARM

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Abstract

Objectives: The present study was undertaken to assess the effect of H1 blocker and ganglion blocker on Histamine induced response of proximal & distal segments of high type of anorectal malformations (ARM) from neonates, for better understanding of functional status of rectum in ARM patient.

Methods: Present study was conducted on surgically excised segments of fresh specimens of fifteen cases of anorectal malformations, that have been collected from Department of Paediatrics Surgery, IMS, BHU. After that muscle strips were prepared for assessing in vitro contractile activity of the tissue. The chemical used were histamine and their antagonists as well as hexamethonium (ganglion blocker) in an organ bath filled with physiological solution. Force transducer and computerised data acquisition system were used to assess the activity.

Result: Histamine (0.1-100 µM) evoked contractions were significantly ($p < 0.05$) greater in proximal segments as compared to distal segments. Responses of histamine were significantly ($p < 0.05$) blocked by pre-application of H1 blocker pheniramine (90%) and hexamethonium (50%).

Conclusion: There is significant loss of spontaneous activity in anorectal malformation high type cases. Also, distal segment was affected more as compared to proximal segment as evidenced by Histamine application response. This study will help paediatric surgeons in managing ARM cases for better outcome.

Keywords: H_1 blocker, ganglion blocker, Histamine, neonatal & ARM.

Introduction

Anorectal malformation (ARM) is common congenital problem in neonates with the incidence of 1 in 2,500 to 1 in 5,000. [1&2] Boys are at higher risk than girls (1.3:1) (Stephens et al., 1988) [3]

Histological studies on ARM showed the immaturity of the enteric nervous system and absence or reduced number of Cajalcell [2] which might be cause of postoperative dysmotility responsible for

constipation, incontinence, soiling etc after surgical repair.

Management of the condition is chiefly surgical.[4] However very effective surgical procedures need to be found out to avoid any kind of complications related to altered bowel motility. Therefore, knowledge of application of different chemicals on contractile status of different segments of rectal tissue from ARM might provide important guidelines for preparation of appropriate surgical procedures.[5]

Materials & Methods

Sample collection

After receiving information about admission of any case of ARM in pediatric surgery, chief complains, relevant history (Name, Age, Sex, weight and address) was noted. Consent was taken from patient's guardian to use the excised part for experimental study. intestinal tissue specimen was collected in freshly prepared oxygenated Krebs-Ringer solution. After that processing were done in the laboratory of physiology department.

Muscle strips preparation

After removing the adventitious layer, 2 to 3 mm wide and 10 to 15 mm long, circular muscular strips were prepared from proximal and distal end of samples of ARM placed in tray containing ice cold (4°C-6°C) Krebs-Ringer solution continuously bubbled with 100% O2. Then mounted in in Krebs-Ringer filled organ bath.

Recording of contractile responses

Effect of Histamine and its blocker and effect of ganglion blocker on histamine treated sample recordings were recorded after stabilization. Bridge amplifier and displayed personal computer Power lab data acquisition system and software CHART-5 for windows (AD Instruments, Australia) were used and Isometric muscle contractions were recorded.

Chemicals used

Histamine (Hist), Hexamethonium (ganglion blocker) and Pheniramine maleate (Histamine antagonist) were used.

Analysis

Chart-5 software, paired t-test and two-way ANOVA were used for analysis, mean ± SEM calculated using pooled values. Amplitude of contractions was expressed as tension per unit mass (g/g wet tissue**.** P value < 0.05 was significant.

Observations and Results

With the help of 15 ARM cases, we prepared total of 40 rectal muscle strips and spontaneous as well as chemically evoked contractions were evaluated.

Contraction in ARM Cases

In six samples contractions were induced after application of different concentrations (0.1-100 µM) of Hist. The required conc. of Hist for such drug induced spontaneous contractions was higher in distal segment. Another four samples showed Hist evoked spontaneous contractions only in proximal segment.

There was dose dependent increase in response to Hist in proximal and distal segments. Responses of different conc. of Hist on proximal segment were higher as compare to distal segment. The difference of responses of Hist was statistically significant (*P < 0.05, two-way ANOVA;)

Proximal and distal segment recordings of ARM before and after applying different concentrations (0.1, 1, 10 & 100 µM) of Hist. were made. Point of application of drug is indicated by an arrow. Tension (g) and time (min) calibrations were applied. Proximal segment shows presence of spontaneous contractions after application of Hist (Histamine). (C) On comparison of

dose-response curve of proximal and distal segments of ARM, data points represent Mean ± SEM values of Hist evoked contractions (g/g) with the different concentrations of Hist. Responses were significantly different (*P < 0.05, two-way ANOVA, n= 6)

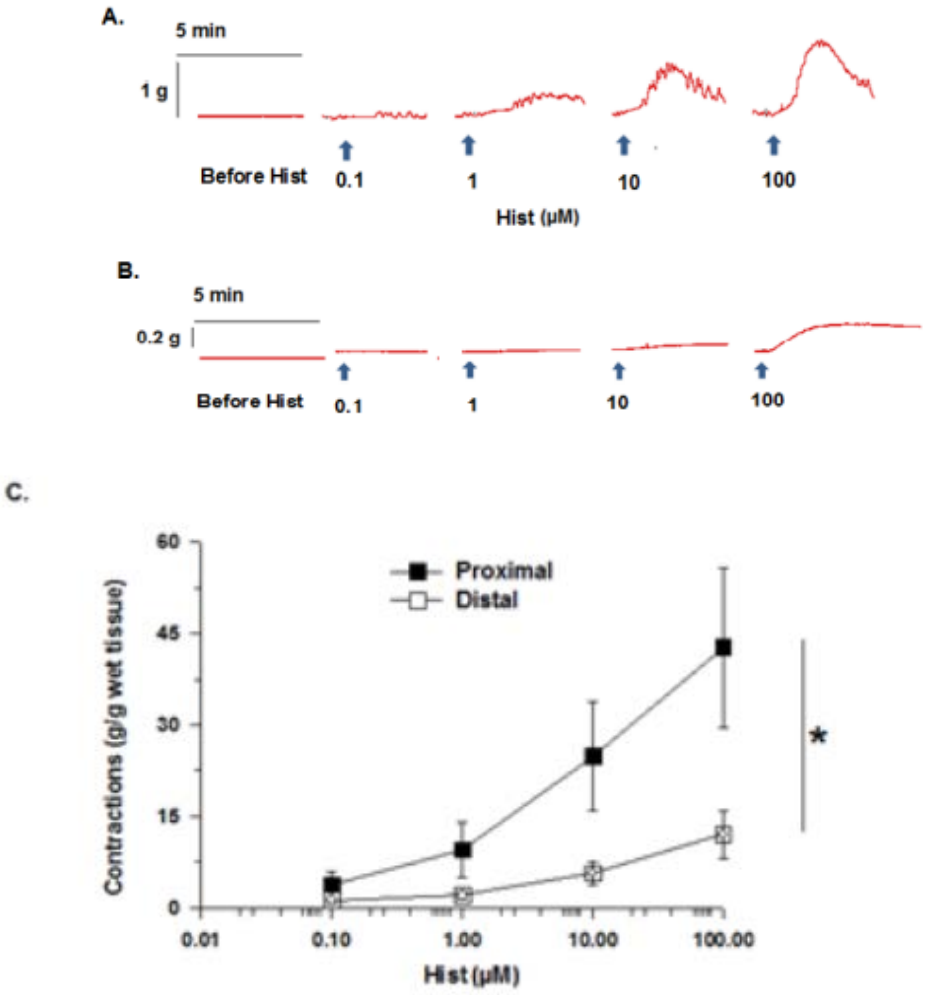

Figure 1:recordings of Proximal and distal segment ARM before and after applying different concentrations (0.1, 1, 10 & 100 µM) of Histamine

Responses of Hist (100 µM) were significantly (P < 0.05, paired t test, n=6) blocked after application of Phn (100 µM) in both proximal and distal segments. The blockade of responses in proximal and distal segments was 90 % and 85 % respectively after application of Phn (Fig 2)

Fig 2 Original recordings of effect of Phn (Pheniramine) on Hist (Histamine) induced contractions in (A) Proximal (B) distal segments of ARM. Arrows indicate the point of application of drug. Vertical & horizontal calibrations represent the tension (g) and time (min.) respectively. (C) Histogram showing Mean ± SEM values of % of the initial responses to Hist 100 µM before and after applications of Phn. Responses of Hist after Phn were

significantly decreased (*P < 0.05, paired t test, n=6)

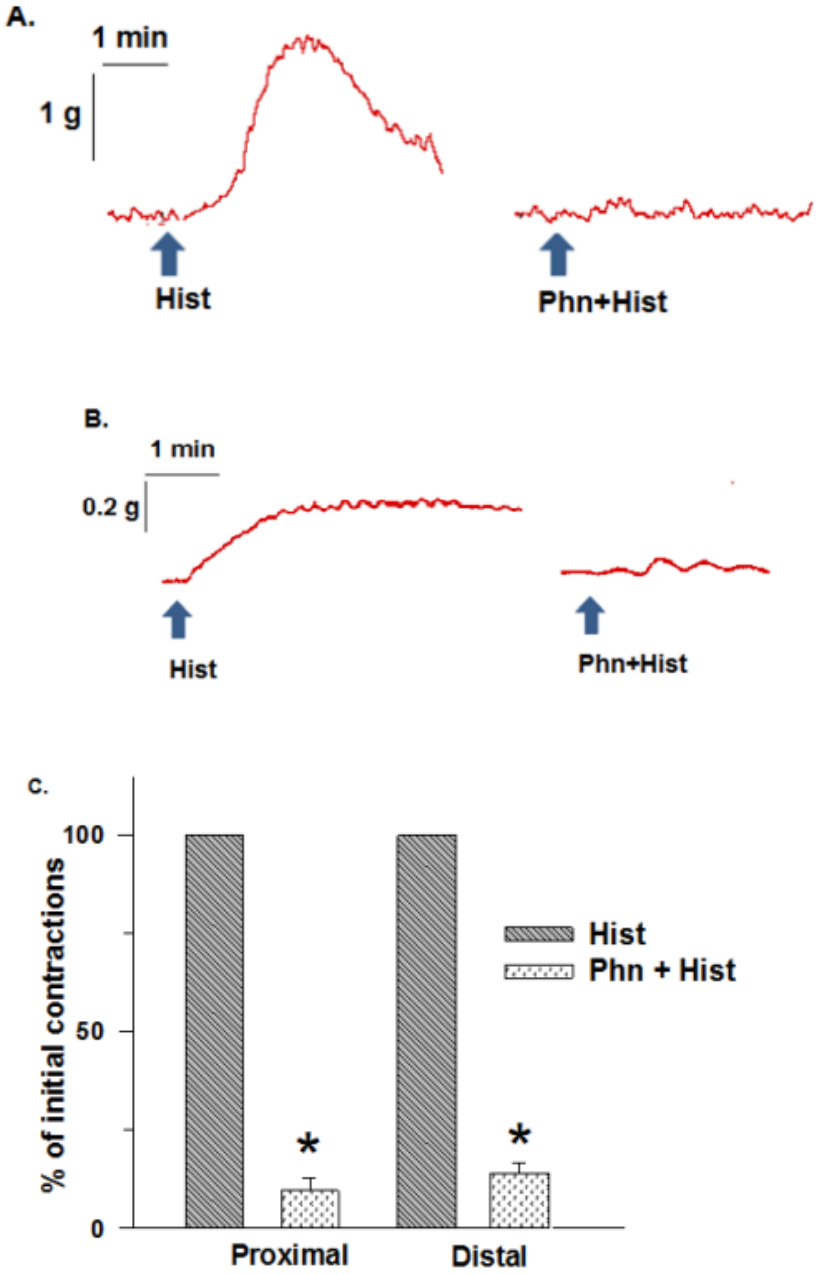

Figure 2: Effect of pheniramine maleate (H1 receptor blocker) on Histamine-induced contractions in proximal and distal segment of ARM

Hxm blocked nearly 55 % of Hist induced responses in proximal & distal segments and was statistically significantly (P < 0.05, paired t test, n=7)

Fig 3: Original recordings of effect of Hxm (Hexamethonium) on Hist induced contractions in (A) Proximal (B) distal segments of ARM. Arrows indicate the point of application of drug. Vertical

&horizontal calibrations represent the tension (g) and time (min.) respectively. (C) Histogram showing Mean ± SEM values of % of the initial response to Hist 100 µM before and after application of Hxm. Responses of Hist after Hxm were significantly decreased (*P < 0.05, paired t test, n=7))

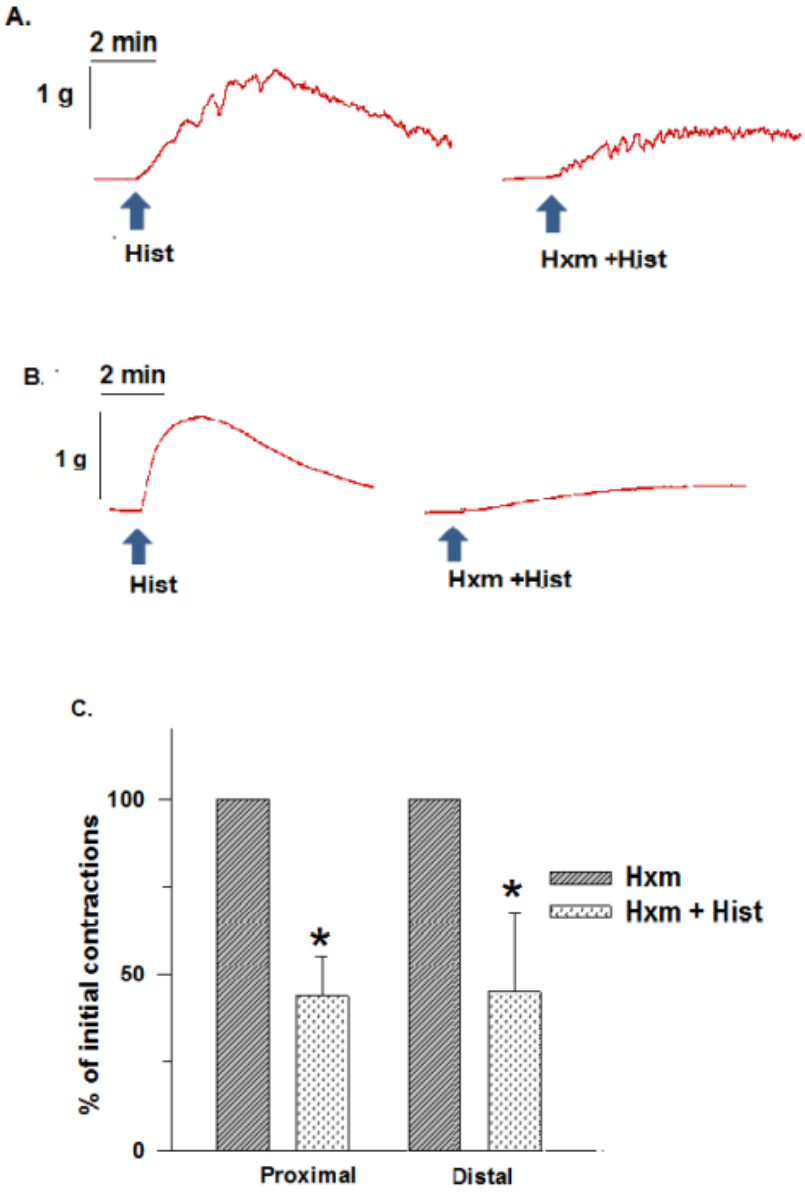

Figure 3: Hexamethonium (ganglion blocker) pre-treatment blocked histamine induced contractions

Discussion

Thecontractility of rectal smooth muscle was evaluated by recording of application of histamine and its blocker and effect of histamine in ganglion blocker pre-treated muscle tissue. Five silent samples demonstrated spontaneous contractions

after application of Hist.[6] This indicated that the ICC may get activated by an agonist like Hist suggesting a effect of on ICC. Dose of Hist required to stimulate ICC were higher in distal segment as compared that of proximal segment. On examination of Hist induced contractile strength of proximal and distal segment, it was noted that there was dose dependent increase in the response.[7] This agonistic effect is known to be mediated by H1 receptors Hist. In this study also it was observed that Phn (H1 blocker) could largely block the response. Rectal tissue of high type of ARM demonstrated higher contractility in proximal segment for Hist.[8]

In order to understand the role of the ganglionic tissue in enteric nervous system of ARM, experiments were designed to record the Hist induced activity following application of Hxm (ganglion blocker). Further, it was also observed that the Hist induced responses after pre - application of Hxm were blocked nearly by 55%. This indicated that the responses of Hist are mediated partly by its direct action on the muscle and partly through ganglion.[9]

Thus, the present investigation demonstrated that in high type of ARM, the rectal tissue is excitable by Histamine. However, the tissue appeared to be functionally abnormal on account of severe impairment of contractility in the distal segment.[10] These observations may have implications in surgical management of ARM problem in neonate, pertaining to the most controversial issue of preserving or excising the distal most part of the rectal tissue of high type of ARM

Conclusion

There is significant loss of spontaneous activity in anorectal malformation high type cases. Also, distal segment was affected more as compared to proximal segment as evidenced by Histamine application response. This study will help paediatric surgeons in managing ARM cases for better outcome.

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