



## CAJAL CELLS AND POST-SURGICAL DISMOTILITY IN HIRSCHSPRUNG DISEASE

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### Abstract

Hirschsprung disease (HD) is characterised by the absence of ganglion cells in plexus in the distal colon in its classical form; as a consequence intestinal motility dysfunction occurs, the clinical picture resembles structural obstruction. Interstitial Cajal cells (ICC) modulate the motor function of smooth muscle cells by the synaptic connection with the enteric nervous system. Numeric reduction of ICC in the ganglionic intestinal portion in patients with HD supports the hypothesis that reduction in Cajal cells number may cause symptoms of post-surgical intestinal dysmotility as constipation, abdominal distension and recurrent enteritis.

### Key words:

*Child, Hirschsprung disease, Interstitial Cajal Cells.*

### Introduction

Hirschsprung's disease (HD) is caused by abnormal migration of neural crest cells in the formation of the enteric nervous system. The diagnosis is suggested by contrast radiography, which shows the narrowing of the distal part of the aganglionic segment. Confirmation is obtained by biopsy from the distal intestinal wall. Treatment consists in the resection of aganglionic segment. Postoperative complications are bloating, constipation and recurrent enterocolitis. Interstitial Cells of Cajal are responsible for nerve ganglia and smooth muscle cells integration. In HD, the ICC may be reduced, although it is not known whether this reduction would be the cause of dysmotility or would result of ischemic injury of the affected segments. The aim of the study was to identify association between the number of ICC in ganglionic segment and clinical complications in the postoperative period.

### Results and Discussion

Medical records and histological samples of patients in post-surgical HD status and followed at Unicamp Clinics Hospital, operated from 2001 to 2014, were re-examined. Immunoistochemistry for Cajal cells were performed in order to count cells number and to compare to historical values found in healthy adults.

Postoperative clinical outcomes: constipation (50%), vomiting (37.5%), soiling (29.1%) recurrent abdominal pain (25%), abdominal distension (25%), surgical interventions (20, 8%), diarrhea (16.6%) and enterocolitis (4.1%). Five patients had no symptoms and one patient lost follow-up. ICC average count: 1.85 (Standard deviation: 1.87), and according to Hagger classification: sparse (N = 15), low (N = 3) and moderate (n = 6). Nineteen out of 24 patients showed postoperative symptoms, and 12 of them are in group 0-1, 3 in group 2 - 3 and 4 in group 4 - 8. Only 5 patients had good postoperative intestinal evolution: 3 are in group 0 - 1 and 2 are in group 4 - 8. There was no statistically significant difference in the distribution of patients with postoperative symptoms and asymptomatic ones between the groups ( $p = 0.506$ ).

The incidence of intestinal motility disorders after surgery varies between 20 and 60% in most studies. The latest reviews show that only about 50% of children will develop normal bowel function after surgery. Owing to the fact that

this survey has been conducted in a tertiary-care hospital of high complexity, it is possible to justify the high rate of long-term postoperative complications, low count of satisfactory evolution and high rate of surgical approaches due to bridges or expanded resection of new segments. In relation to disorders of intestinal motility, we have found a variation also present in the literature. Contrary to current reports, we have found a high rate of severe constipation, but with low count of associated soiling. In our survey we have found an incidence of enterocolitis lower than that reported in the literature, and one patient developed colonic rupture preoperatively and no case of death was recorded.

Several studies relate the histology of the remaining intestine after HD surgery with intestinal motor function disorders in postoperative. In the review conducted by Schulten *et al*, it was shown that abnormal histological patterns appear to increase the incidence of intestinal motility disorders while Newman *et al* did not observe any significant difference between the outcomes of patients with normally and abnormally innervated remaining colon.

### Conclusions

Although most of the cases present a low count of ICC, the count of these ganglion cells segment is not associated with the occurrence of postoperative symptoms. The findings of this survey are similar to other studies with similar methodology.

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