SUMMARY

1. Pancreatic regeneration after partial pancreatectomy was used as a model system to study pancreatic β cell proliferation in rats.

2. \(^{3}H\)thymidine incorporation was used as an index for pancreatic DNA synthesis. DNA synthesis was peaked at 72 hours after partial pancreatectomy and reversed to control level by 7 days.

3. Acetylcholine esterase activity was measured in the brain regions. It increased in the brain regions during pancreatic regeneration.

4. NE content was analysed using HPLC. It decreased in the adrenals during active pancreatic islet regeneration. Plasma NE level decreased during pancreatic regeneration.

5. Muscarinic receptor functional status was analysed by Scatchard and displacement analysis using specific \(^{3}H\)ligands. Receptor analysis was confirmed by studying the mRNA status of the corresponding receptor using RT-PCR. During active pancreatic regeneration, total muscarinic receptors were down regulated. Muscarinic M3 receptors were up regulated while muscarinic M1 receptors were down regulated in the brain regions during pancreatic regeneration.

6. Muscarinic M1 and M3 receptors were up regulated in the pancreas at the time of pancreatic regeneration.

7. *In vitro* studies showed that acetylcholine agonist, carbachol, induced glucose stimulated insulin secretion in pancreatic islets. Muscarinic antagonist, atropine, inhibited glucose induced insulin secretion. Muscarinic M1 and M3 receptor antagonists, pirenzepine and 4-DAMP mustard, inhibited insulin secretion.
8. *In vitro* studies showed that acetylcholine dose dependently increased EGF induced DNA synthesis in rat pancreatic islets. The addition of atropine, a specific antagonist of muscarinic receptors, resulted in the inhibition of DNA synthesis. Muscarinic M1 and M3 receptor antagonists, pirenzepine and 4-DAMP mustard, inhibited carbachol induced DNA synthesis.

It is evident from our results that brain and pancreatic muscarinic M1 and M3 receptor functional balance plays a major role in regulating the pancreatic regeneration and insulin secretion. Central muscarinic M1 and M3 receptor subtypes functional difference regulates sympathetic and parasympathetic systems, which in turn control the islet cell proliferation and glucose homeostasis. Thus, our results suggest that acetylcholine, through muscarinic M1 and M3 receptors regulates the pancreatic islet DNA synthesis and insulin secretion.