A randomized controlled clinical trial on the efficacy and safety of HyaRegen® gel in reducing adhesions after gynecological laparoscopic surgeries[1]

Background: Adhesion after gynecological surgery is still a challenge facing practitioners due to it's high prevalence and complications. Adhesions could happen in about 93% patients underwent abdominopelvic surgeries and 85% reformation of adhesion after adhesiolysis[2]. Adhesions may form in the surgical area and/or in locations away surgical intervention area. The ESGE guidelines for preventing adhesion include meticulous surgical skills to minimize tissue damage and using adhesion agents to reduce both *de novo* and reformed adhesions[3]. Different adhesion barriers are used with various level of success. However, to achieve broad coverage and comprehensive prevention is still an unmet issue. In present study, a new crosslinked hyaluronan gel (HyaRegen® Gel) was investigated for preventing adhesion formation through out the abdominopelvic cavity.

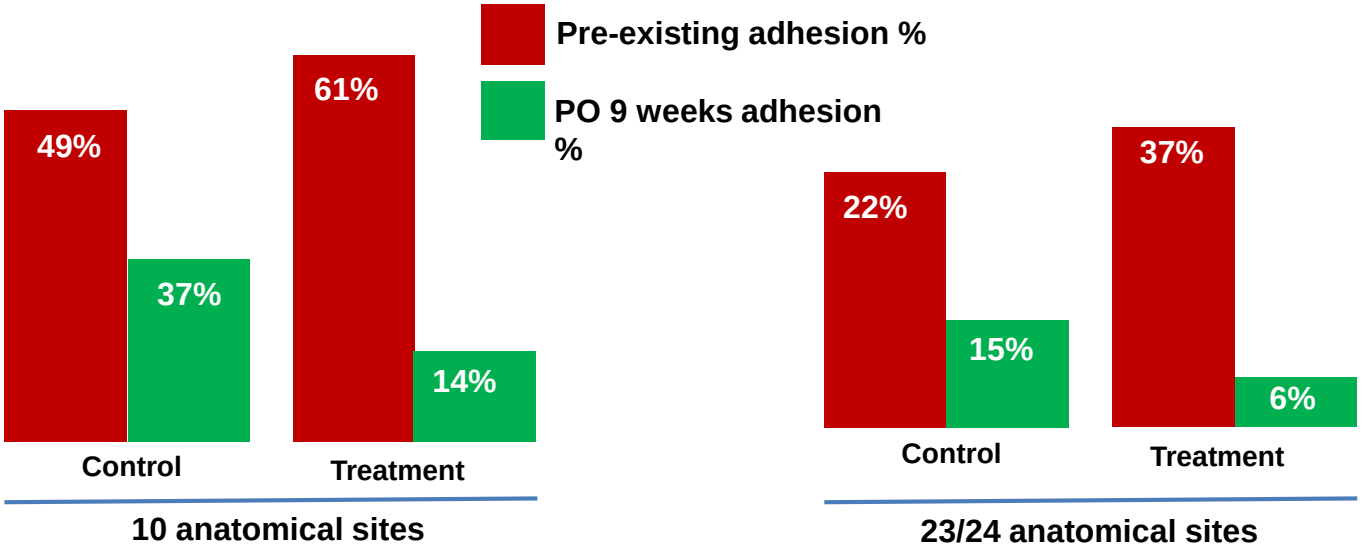
Objectives: To evaluate the safety and efficacy of HyaRegen® Gel in reducing adhesions in abdominopelvic cavity after gynecological surgeries via a second look laparoscopy.

Study Design: Randomized, third party blinded, multicenter clinical trial with 7 OB/GYN departments. In total, 216 patients scheduled to gynecological laparoscopic surgery for primary removal of adhesions, myomas, ovary cysts or endometric cysts were enrolled. For patients with pre-existing adhesions, their incidence, extent and severity were first scored following modified American Fertility Society (mAFS) scoring system (Table 1) at the 10 anatomical sites of ovaries/tubes and at the expanded 23 anatomical sites throughout abdominopelvic cavity by laparoscopy[4]. After completion of the primary procedures, patients were randomly assigned to the treatment group where HyaRegen® Gel were instilled into the peritoneal cavity or to the control group where equal amount of saline instead was used. HyaRegen® gel was able to coat organ and tissue surfaces that sustained surgical trauma and also their adjacent and suspected adhesiogenic surfaces remote from surgical area to achieve a broad coverage. The maximum volume of HyaRegen® gel used for one patient is upto 2.0ml per kg of bodyweight. Second-look laparoscopy was performed at 9 weeks after surgery. During the laparoscopies, video records were made. Adhesion scores were quantified by blinded videotape review. The primary endpoint was the incidence of moderate/severe adhesions at 10 sites (ovaries and tubes).

Severity	Extent			
	None	<1/3 (Grade 1, localized)	1/3-2/3 (Grade 2, moderate)	>2/3 (Grade 3, extensive)
Not present	0			
Mild (filmy) (1)		1	2	3
Severe (dense) (2)		4	8	16

Results: HyaRegen® gel significantly reduced adhesion incidences for 10 and 23/24* anatomical sites. Reduced adhesion was observed not only in the surgical area but also in remote locations, achieved broad adhesion prevention throughout abdominopelvic cavity. HyaRegen® gel is safe without any complications observed.

**At 2nd look arthroscopy the incision site was included reaching 24 locations.*

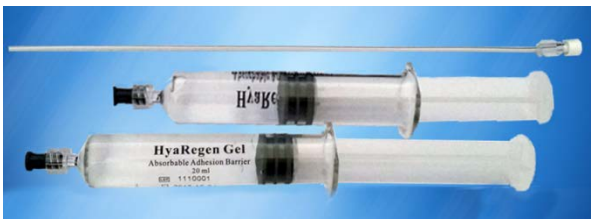


HyaRegen® Gel

HyaRegen® Gel (BioRegen Biomedical Co. Ltd.) is developed using a proprietary thiolated chemistry to crosslink the non-animal sourced HA molecules. The modification/crosslinking is controlled so that the crosslinked HA gel has adequate degradation profile and viscosity to match the critical period of tissue repair processes and inflammatory reactions.

➢ How is supplied

HyaRegen® gel is prefilled in a glass syringe containing 10 or 20cc gel. Individually packaged cannula is also provided to assist delivery of the gel.



References: **1.** Liu C., et al. Manuscript submitted for publication. **2.** Lower AM et al.: BJOG. 2000; 107:855. **3.** De Wilde RL et al.: Arch Gynecol Obstet. 2014; 290:581. **4.** The American Fertility Society. *Fertil Steril.* 1988;49:944.

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